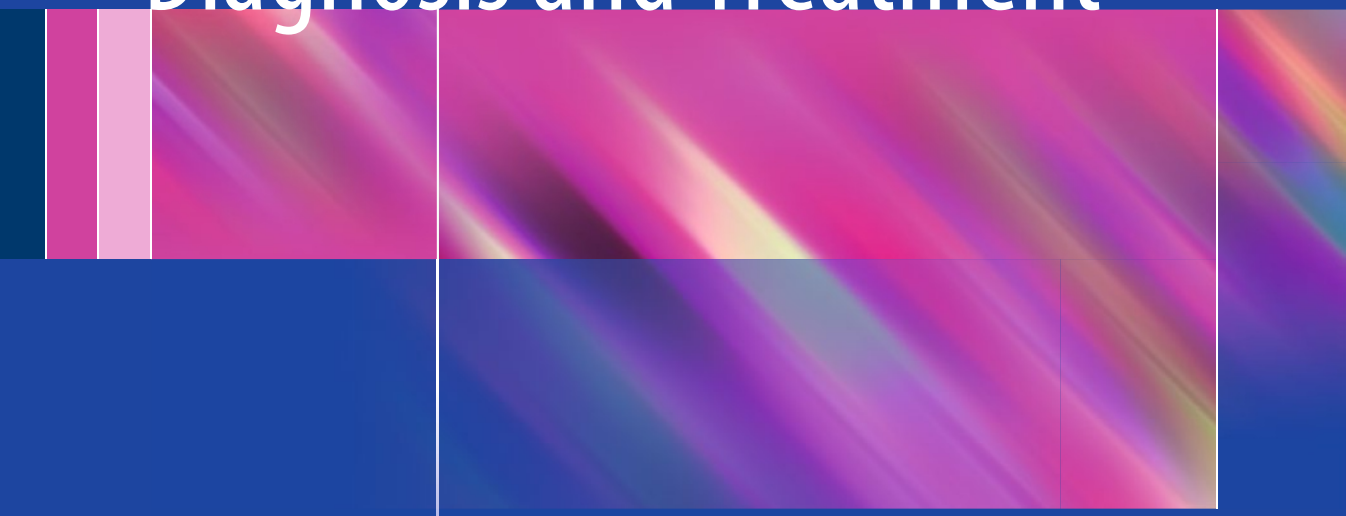
Mehmet Turgut
Editor

Hydatidosis of the Central Nervous System: Diagnosis and Treatment



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Foreword

It gives me great honor to write a prelude to this important work undertaken by Assistant Professor Mehmet Turgut, in collaboration with several other well-known specialists in hydatid disease from all over the world.

This parasitosis is a devastating but curable worldwide calamity, with a cosmopolitan predominance. Unfortunately, it is mainly found in the less resourced regions of the world, namely, the Mediterranean, African, and South American countries.

Throughout my entire more than 40-year-long career as a pediatric radiologist and biophysicist, I have had numerous opportunities to be involved in the diagnosis, prevention, vaccination, and treatment programs against this dreaded illness.

My personal interest in hydatid disease dates back to my medical school days. I was born in Thala, a small village in the center of Tunisia, an intensive sheep-farming but heavily hydatidosis-infested endemic region. I vividly remember a young lad, Houcine, employed on my father's farm, as shepherd, who presented with hemoptysis. I brought him to the small hospital in Thala where I did a chest conventional fluoroscopy, with a very old machine. I discovered that he had a large impressive opacity involving his entire right lung which turned out, at surgery, to be a pulmonary hydatid cyst (Hospital Ariana, Tunis).

Thanks to surgical and medical treatment, it is now 60 years after that incident but that lad, now an elderly man in his 80s, is still alive and enjoying perfect health.

That experience awakened a lifelong curiosity within me to do something about this devastating malady – a medical student dream.

On returning from Paris, as a recently graduated radiologist, biophysicist, and later on echographist, using my recently acquired skills in those fields, I straight away embarked on the hydatid disease fight.

I started diagnosing and mapping out the epidemiology of this illness and endeavored to find a remedy for it. I had the chance of collaborating with the greatest names of those days in radiology, parasitology, and gastroenterology fields in Tunisia, France, and Italy. Jointly we innovated a new strategy for treating hydatidosis. This involved the use of ultrasound to diagnose and guide a new mode of therapy which later came to be known as puncture-aspiration-injection-reaspiration (PAIR). This novel mode of staging was adopted by the World Health Organization and extended to other parasitic diseases, such as *Schistosoma haematobium* and *S. mansoni*.

Ultrasound imaging modality and PAIR are rarely used in cerebral hydatidosis (orbit), but they should contribute effectively to the eradication of this calamity and ought to be included in the strategy for the diagnosis and the treatment of cerebral hydatidosis.

It gives me great pleasure to appraise this great multidisciplinary undertaking by Dr. Turgut and his colleagues: radiologists, neurologists, neurosurgeons, pathologists, veterinarians, surgeons, orthopedists, ophthalmologists, psychologists, parasitologists, internists, and biologists. This book no doubt adds to and complements the existing armament in the fight against hydatidosis, more especially the disease's elusive cerebral location.

I am confident that this publication will be a great success and a landmark in the war against hydatidosis, eventually contributing to the ailment's total annihilation. Together, through a global effort, we can fight this and many other tropical parasitic diseases.

I am sure that this book will not only be academically and professionally inspiring but also an enjoyable piece of reading.

Congratulations Assistant Professor Turgut for this noble task.

Tunis, Tunisia Hassen A. Gharbi, MD

Professor of Radiology and Medical Biophysics
Honorary member of the International Association of Hydatidology
President elect of the World Federation for Ultrasound in Medicine and Biology, 2011–2013
Honorary President of the Tunisian Society of Radiology,
Honorary Fellow of the American College of Radiology,
Honorary Member of the Society for Pediatric Radiology

Preface

This book is designed to deliver succinct, up-to-date reference information to practicing physicians about imaging findings, differential diagnosis, pathology, clinical findings, and relevant surgical information of hydatidosis of central nervous system. Because of the fact that the problem is rare, no multidisciplinary information has been gathered from an exclusive source, although a significant amount of data is available on the care of patients with hydatidosis. The book is divided naturally into three major parts: the first section includes topics addressing epidemiological aspect of hydatidosis, the second section contains nonsurgical topics that affect decision-making in the patients, and the third section covers the topics on specific neurosurgical disorders. The relevant information given here is often very difficult for neurosurgeons to access elsewhere. The chapters in the book are written by authors who are world-renowned specialists in their respective fields of interest. The framework of each chapter has been designed according to their specific clinical and diagnostic considerations, but an identical format has been followed for all. It is believed that the information which is so crucial for the clinical neurosurgery practice is presented in this way. The detailed surgical information given in this book is intended to illustrate the basic techniques of the neurosurgical procedures and to give guidance which is expected to be useful for the execution of every operative approach. In fact, it should also give technical guidance to operations which are not specifically discussed. Apparently, all authors contributed to this book with their personal experience they have gained in their own institutions and with unusual images they have offered to illustrate each topic. At the end of each chapter, selected references are included for further review. I hope that the sections in which specific neurosurgical disorders are emphasized on an individual basis will prove helpful in surgical planning and in surgical management of patients for the individual neurosurgeon.

My particular thanks go to Dr. Inga von Behrens from Springer DE (Heidelberg, Germany) for his invaluable advice and support in the planning of the present book.

I would like to thank Professor Fuad Sami Haddad for his critical review and insightful supervision.

I owe thanks to my dear sons, Yaşar Barış and Ali Çağlar, for their devotion and constant support.

May I not forget Ms. Elise M. Paxson from Springer (New Jersey, USA) for her kindly assistance in the preparation of the figures for reproduction.

Aydın, Turkey Mehmet Turgut, MD, PhD

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Historical Aspects of Hydatidosis of the Central Nervous System

1

Nikolaos Syrmos, Vaitsa Giannouli,
Evangelia Chatzinasiou, and Foteini Chatzinasiou

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Introduction

Echinococcosis could be characterized as a zoonotic infestation caused by cestode species of the genus *Echinococcus*. These parasites have life cycles that involve two mammalian hosts. The procedure is as follows: the adult cestode inhabits the small intestine of a carnivore (defined as definitive host) and produces eggs containing infective oncospheres. Cestode segments (proglottids) containing eggs or free eggs are released from the intestinal tract of the carnivore into the environment. After oral uptake of eggs by an intermediate host animal, a larval stage, the metacestode, develops in internal organs (Eckert and Deplazes 2004).

The complete life cycle of *Echinococcus* includes several carnivores, but humans are infected incidentally and usually in childhood by ingestion of the ova from contaminated hands or food. In case an embryo of *Echinococcus granulosus* lodges in the brain, a solitary cyst develops. Hydatid cysts are slow-growing lesions that do not invade the brain; they produce symptoms when the increasing size of the cysts exerts local pressure. Usually the late appearance of focal neurologic deficits follows a long history of epileptic attacks and general symptoms compatible with increased intracranial pressure (Abbassioun and Amirjamshidi 2001). The neuropsychological profile of each patient is mainly due to the differences in the affected brain structures and the possible relevant cognitive deficits (Luria and Karasseva 1968).

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Geographic Range

Hydatidosis is mainly detected in areas such as the Middle East (Lebanon, Syria, Palestine, Kuwait, Egypt and Libya), Australia, New Zealand, Latin America (Argentina, Uruguay and Paraguay), Central Europe, South Africa and the Mediterranean countries (Spain, France, Italy, Greece and Turkey). The geographic range of hydatidosis is discussed in detail in Chaps. 2, 3 and 4.

Hydatid Disease in Humans

The three forms of echinococcosis occurring in humans—cystic echinococcosis caused by *E. granulosus*, alveolar echinococcosis caused *by E. multilocularis* and polycystic echinococcosis caused by *E. oligarthrus*—have special importance due to their wide geographic distribution and their medical and economic impact. The cystic echinococcosis and alveolar echinococcosis are statistically the most widespread, but polycystic echinococcosis is less frequent and is found only in Central and South America (Eckert and Deplazes 2004). The forms of hydatidosis are discussed in detail in Chaps. 2, 3, 4 and 24.

Historical Periods

The presence of hydatid cysts in both humans and animals was well known in ancient times (Prousalidis 2007; Syrmos 2007). In fact, the term "hydatid" is historically derived from Greek "ydatos" which means water (Abdennebi 2009).

"Hydatids" or watery vesicles seem to have been widely present since ancient times, discovered in the entrails of ritually slaughtered animals as well as those butchered for food. One hint that ruptured cysts located in human livers were invariably fatal appears in aphorisms attributed to Hippocrates (Foster 1965). According to Aristotelian ideas, these lumps were spontaneously generated in the afflicted organs themselves (Patterson 1993).

Egyptian Medicine

The ancient Egyptians suffered numerous epidemics and often tomb art described epidemics and parasitic infestations such as hydatidosis (Ruffer 1921a, b; Bryan 1930; Castiglioni 1936; Sullivan 1995).

We have a space occupying cranial lesion, maybe a tapeworm, cyst in mummy 22940 of the Manchester Museum Mummy Collection (Ruffer 1921a, b; Sullivan 1995).

Also we have the presence of "hydatid disease" in the lung cavity of the Mummy of Asru (Ruffer 1921a, b; Bryan 1930; Sullivan 1995).

The Ebers papyrus is an Egyptian medical papyrus dating to circa 1550 BC. Although the papyrus was written in about 1500 BC, it is believed to have been copied from earlier texts, perhaps dating as far back as 3400 BC (Ruffer 1921a, b; Bryan 1930; Castiglioni 1936; Sullivan 1995).

Ebers papyrus together with the Kahun Gynaecological papyrus (circa 1800 BC), the Edwin Smith papyrus (circa 1600 BC), the Hearst papyrus (circa 1600 BC), the Brugsch papyrus (circa 1300 BC) and the London Medical papyrus (circa 1300 BC) is among the oldest preserved medical documents (Ruffer 1921a, b; Bryan 1930; Castiglioni 1936; Sullivan 1995; Cox 2003).

In Ebers papyrus, we have the first written records of what are almost certainly parasitic infections such as hydatidosis that came from a period of Egyptian medicine from 3000 to 400 BC. We have the record that hydatid disease is caused by the larval stage of the dog tapeworm (Ruffer 1921a, b; Bryan 1930; Castiglioni 1936; Sullivan 1995; Cox 2003).

Greek Period

In ancient Greece, according to Galen, hydatidosis was described in the works of Hippocrates and Aretaeus (Castiglioni 1936; Prousalidis 2007; Syrmos et al. 2010).

Hippocrates of Kos (|ππoκράτης) (460 BC–370 BC) (Fig. 1.1) was an ancient Greek

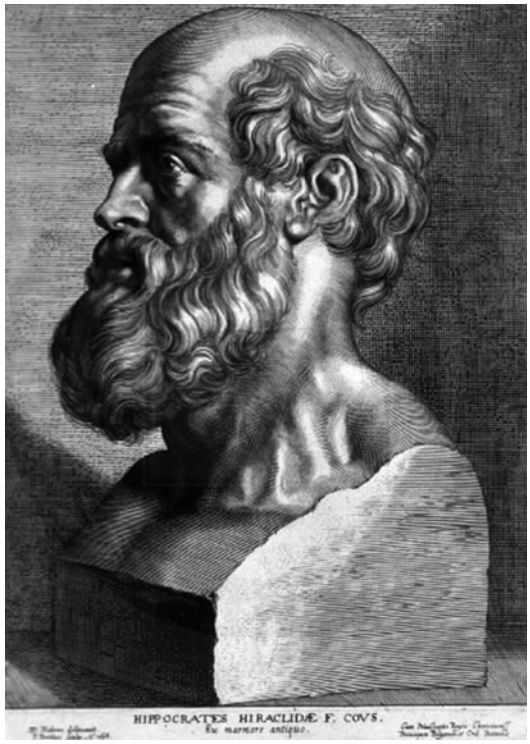

Fig. 1.1 Hippocrates of Kos (460 BC–370 BC)

physician of the Age of Pericles (The Golden Age, *Χρυσούς* Αιών) and is the most outstanding figure in the history of medicine worldwide (Castiglioni 1936; Syrmos 2007, 2009, 2011; Syrmos et al. 2010).

He is referred to as the father of modern medicine in recognition of his lasting contributions to the field as the founder of the Hippocratic School of Medicine. This intellectual school revolutionized medicine in ancient Greece, establishing it as a discipline distinct from other fields that it had traditionally been associated with (theurgy- θεουργία and philosophy- φιλοσοφία), thus establishing medicine as a profession (Castiglioni 1936; Syrmos 2007, 2009, 2011; Syrmos et al. 2010).

According to Galen, Hippocrates used the term "liver filled with water" for hydatid disease in a man (Pissiotis et al. 1972). In this earliest mention of hydatidosis, he suggested that "it breaks in the epiploon, when liver is distended with water; therefore the abdomen is full of water and the sick dies" (Pissiotis et al. 1972; Prousalidis 2007; Abdennebi 2009; Syrmos et al. 2010).

Hippocrates knew that rupture of the cyst meant the death of the patient, the disease represents the tumoral-vesicular growth of the *E. granulosus* larva into space occupying cysts, filled with an extremely allergenic fluid and the primordia of the worm, protoscoleces (Prousalidis 2007; Arseni et al. 1981; Lazar 2010; Syrmos et al. 2010).

Aretaeus of Cappadocia (Αρεταῖος) was also one of the most celebrated of the ancient Greek physicians (Haas 1991; Weber 1996; Syrmos et al. 2010). In the first century (AD), he wrote in Ionic Greek a general treatise on diseases such as hydatidosis, which is extant, and is certainly one of the most valuable relics of antiquity. Aretaeus had knowledge of hydatidosis and his consequences (Castiglioni 1936; Kudlien 1970; Weber 1996; Prousalidis 2007; Syrmos 2007, 2009, 2011; Syrmos et al. 2010).

Jewish Period

Hydatidosis was described in the Talmud (דומ ְל·ת_) (Fig. 1.2), a central text of mainstream Judaism (Castiglioni 1936; Fielding 1966; Saidi 1976).

Talmud takes the form of a record of rabbinic discussions pertaining to Jewish medicine, ethics, law and culture. It has two components: the Mishnah (Hebrew: הנשמ), the first written compendium of Judaism's Oral Law, and the Gemara, an elucidation of the Mishnah and related Tannaitic writings that often ventures onto other subjects and expounds broadly on the Hebrew Bible (Castiglioni 1936; Fielding 1966; Saidi 1976).

In the Talmud, we have a primitive description about hydatidosis as bladder of water and his consequences (Castiglioni 1936; Fielding 1966; Saidi 1976).

Roman Period

Galen of Pergamon (Aelius Galenus or Claudius Galenus, Γαληνός, *Galēnos*) (Fig. 1.3) was an

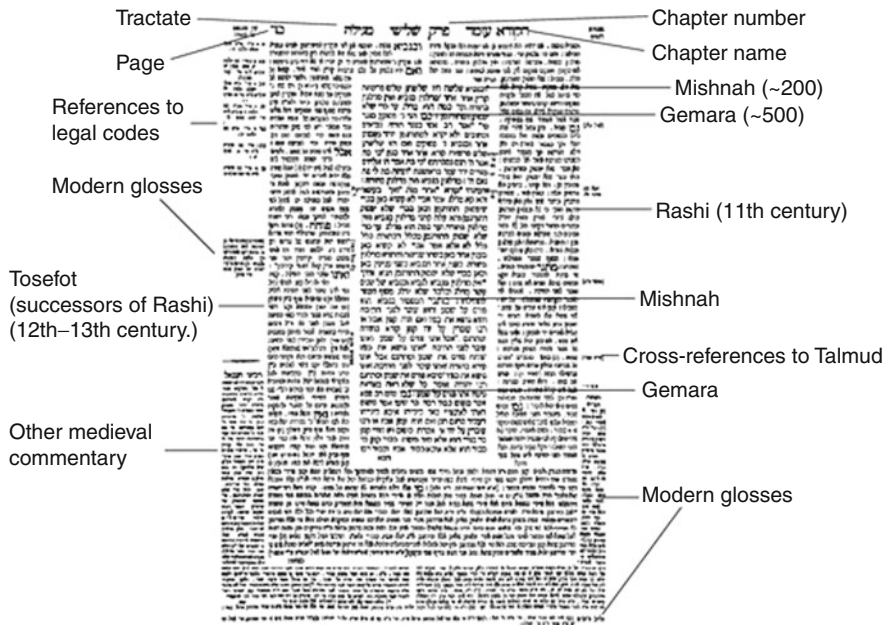

Fig. 1.2 Talmud

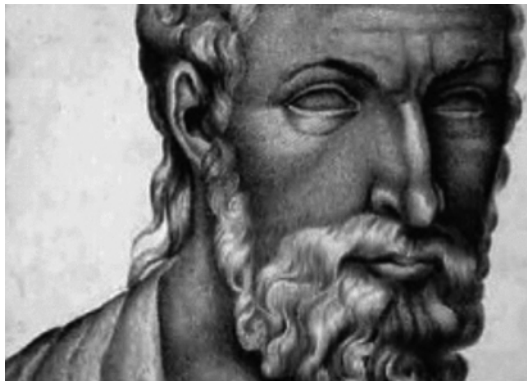

Fig. 1.3 Galen of Pergamon (129–199)

important Roman physician (of Greek ethnicity). In the second century (AD), Galen contributed greatly to the understanding of numerous scientific disciplines, including anatomy, physiology, pathology, pharmacology and neurology. He also describes hydatidosis in his works and he reported about Hippocrates and Aretaeus knowledge of the disease (Castiglioni 1936; Syrmos 2007, 2009, 2011; Syrmos et al. 2010).

According to Galen, Hippocrates used the term "liver filled with water" for hydatid disease in a man (Pissiotis et al. 1972).

Arabic Period

In the Arabic Period, the descriptions of infections such as hydatidosis became more accurate with the works of Jurjani, Rhazes and Avicenna (Ruffer 1921a, b; Bryan 1930; Castiglioni 1936; Sullivan 1995; Cox 2003; Proussalidis 2007; Syrmos et al. 2010).

Jurjani

Abu Sahl 'Isa ibn Yahya al-Masihi al-Jurjani (الجرجاني المسيحي يحيى بن عيسى ابوسهل) was a Persian Christian physician, from Gorgan, east of the Caspian Sea, in Iran. He was the teacher of Avicenna. He wrote an encyclopaedic treatise on medicine of one hundred chapters (*al-mā'a fi-l-sanā'a al-tabi'iyyah*; الطبيعية الصناعة في الماء), which is one of the earliest Arabic works of its kind and may have been in some respects the model for Avicenna's Qanun. In his work, he reported on human involvement by hydatidosis (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

Rhazes

Rhazes (الرازي بن زكريا محمد *Mohammad bin Zakariā- al Rāzi*) (860–932AD) was a Persian polymath, a prominent figure in Islamic Golden

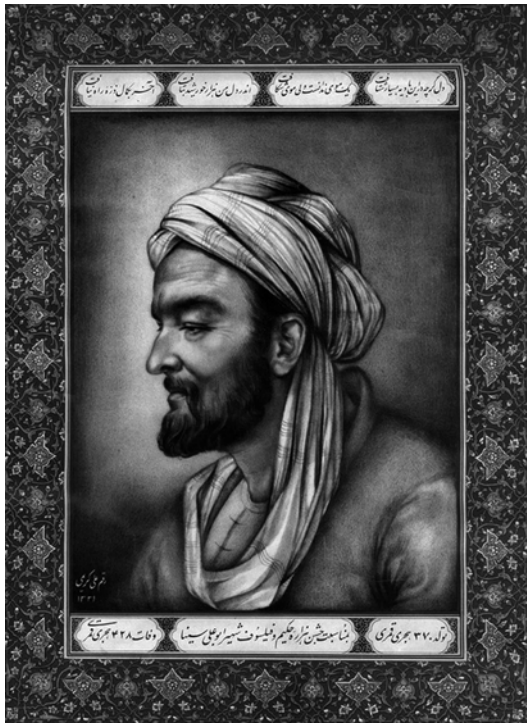

Fig. 1.4 Avicenna (980–1037) (From Aciduman et al. (2009); with permission)

Age. Edward Granville Browne considers him as "probably the greatest and most original of all the physicians and one of the most prolific as an author". He described hydatosis and its consequences (Castiglioni 1936; Fielding 1966; Goichon et al. 1999; Syrmos et al. 2010).

Avicenna

Avicenna (Ibn Sīnā, ابن سينا) (980–1037) (Fig. 1.4) was the most prominent philosopher in the Islamic tradition who wrote many works concentrated on medicine. He is regarded as the most famous and influential polymath of the Islamic Golden Age. Into his works (The Book of Healing and The Canon of Medicine), he made an attempt to describe hydatidosis. Ibn Sīnā's Canon of Medicine provides a complete system of medicine according to the principles of Galen and Hippocrates (Castiglioni 1936; Fielding 1966; Goichon et al. 1999; Cox 2003; Abdennebi 2009; Syrmos et al. 2010).

He reported on human involvement by hydatidosis and he wrote important medical works that contain a great deal of information about diseases clearly caused by parasites (Cox 2003; Abdennebi 2009).

The Seventeenth Century

By the seventeenth century, authors once more pointed out pathological similarities between the watery sacs in humans and those in domesticated animals, especially sheep and cattle (Patterson 1993).

The contribution of the animal factor of the hydatid disease was not suspected until the research in the seventeenth century by Redi, Tyson and Morgani (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

Redi

The first step towards figuring out the cause of echinococcosis occurred during the seventeenth century thanks to the studies of Francesco Redi (Fig. 1.5) (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

Francesco Redi (1626–1697) was an Italian physician, naturalist and poet. He is best known for his series of experiments, published in 1668 as Esperienze Intorno alla Generazione degl'Insetti (Experiments on the Generation of Insects), which is regarded as one of the first steps in refuting "spontaneous generation"—a theory also known as Aristotelian abiogenesis. As a physician, he became court physician to Ferdinando II de' Medici, Grand Duke of Tuscany, and, his successor, Cosimo III (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

He made a number of observations and experiments in rabbits regarding the presence of parasitic worms in cysts. With his studies, Redi demonstrated the animal origin of the disease, and his results were later confirmed by Edward Tyson and Philip Hartmann Redi (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

Tyson

Edward Tyson was a British scientist and physician, commonly regarded as the founder of modern comparative anatomy, which compares

Fig. 1.5 Francesco Redi (1626–1697)

the anatomy between species. Edward Tyson and Philip Hartmann in Germany promoted the idea that hydatid cysts contained embryonic forms of insects or worms. Some of Tyson's dissections were carried out on "rotten sheep" (Castiglioni 1936; Risse 2005).

In 1680, he established that porpoises are mammals. In 1698, he dissected a chimpanzee and the result was the book, Orang-Outang, sive Homo Sylvestris: or, the Anatomy of a Pygmie Compared with that of a Monkey, an Ape, and a Man. In this book, he came to the conclusion that the chimpanzee has more in common with man than with monkeys, particularly with respect to the brain. This work was republished in 1894, with an introduction by Bertram C. A. Windle that includes a short biography of Tyson (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

Edward Tyson in 1687 suggested the parasitic nature of hydatid disease (Kattan 1997).

Morgagni

Giovanni Battista Morgagni (1682–1771) was an Italian anatomist, celebrated as the father of modern anatomical pathology. He reported a post-mortem patient with a large hydatid cyst in the retroperitoneal tissue near the left kidney, containing many daughter cysts (Castiglioni 1936; Androutsos 2006). The spinal canal had been invaded through the intervertebral foramina, which was dilated (Castiglioni 1936; Androutsos 2006).

The Eighteenth Century

In the *eighteenth* century, the larva of *Echinococcus* and the similarity of the hydatid cysts in humans and other animals were described (Castiglioni 1936).

Bidloo

Govert Bidloo (1649–1713) was a Dutch Golden Age physician, anatomist, poet and playwright. He was the personal physician of William III of Orange-Nassau, Dutch stadholder and king of England (Castiglioni 1936). In 1708, Bidloo was the first to report osseous hydatidosis in a case involving the humerus (Işlekel et al. 1998a, b; Schnepper and Johnson 2004).

Peter Simon Pallas

Peter Simon Pallas was a famous German and Russian naturalist, scientist and traveller who became chief of Mineral cabinet (Fig. 1.6) (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

In 1760, Pallas noticed the similarities between hydatid diseases in humans and other mammals. In 1766, he was the first scientist to mention the similarity of the hydatid cysts in humans and other animals (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

John Hunter

John Hunter (1728–1793) was a Scottish surgeon regarded as one of the surgeons advocating of careful observation and scientific method in medicine. In 1773, he described the morphological picture the hydatid cyst (Abdennebi 2009).

Fig. 1.6 Peter Simon Pallas (1741–1811)

Goeze

Johann August Ephraim Goeze was a German zoologist from Aschersleben. He did much work with aquatic invertebrates, particularly insects and worms. In 1773, he was the first to describe tardigrades which are commonly known as water-bears or moss piglets (Castiglioni 1936; Fielding 1966; Goichon et al. 1999).

In 1782, Goeze was the first to describe microscopically the scolices of the larva of *Echinococcus* (Castiglioni 1936; Fielding 1966; Goichon et al. 1999; Abdennebi 2009).

Edward Jenner

Edward Jenner (1749–1823) was an English naturalist and country physician. Famous for his cowpox vaccine, he recorded his dissections of numerous farm animals. Known to many as "the father of immunology", Edward Jenner made a lot of research and post-mortem studies in animals with hydatidosis and he gave his pioneer contribution to the first steps for the understanding of the disease (Castiglioni 1936; Prousalidis 2007).

Modern Era

In 1786 *E. granulosus* was introduced when it was discovered by Batsch (Eckert et al. 2001).

The French physician Cullerier, senior surgeon to the civil Parisian Venereal Hospital, was the first to describe a case of hydatid cyst of the bone in 1806 (Dew 1928; Dowling and Orlando 1929; Arana Iniguez 1978; Abdennebi 2009).

François Chaussier was a French anatomist. He reported a case of spinal hydatid disease in 1807. Initially he studied medicine in Besançon, and later returned to Dijon, where he worked as a hospital physician and performed pioneer research in forensic medicine. Later he became professor at the École Polytechnique and chief obstetrician at the Paris Maternité. In 1822, he was elected as a member of the Academy of Sciences. He performed early studies of neuralgia and introduced a procedure for revival of "near-dead" newborns. He also performed a descriptive survey of all muscles in the human body and developed a new system of designation for muscles (Dew 1928; Dowling and Orlando 1929; Arana Iniguez 1978; Benkhadra et al. 2008; Abdennebi 2009).

The term "echinococcus" was coined by Karl Asmund Rudolphi in 1808 (Craig and Faust 1970).

Rudolphi was a Swedish-born naturalist, who is credited with being the "father of helminthology". He worked widely across the fields of botany, zoology, anatomy and physiology. He investigated the anatomy of nerves, carried out studies of plant growth and was an early champion of the view that the cell is the basic structural unit of plants (Castiglioni 1936; Fielding 1966; Goichon et al. 1999) (Fig. 1.7).

In 1819, the first patient treated surgically for spinal hydatidosis was reported by Reydellet (Pamir et al. 2002; Abdennebi 2009). The patient was a 22-year-old lady who had a hydatid cyst in the lumbar spine, and the young lady died 12 months later from the occurrence of profuse suppuration in the sac (Maguire 1819; Castiglioni 1936; Ba'assiri and Haddad 1984; Pamir et al. 2002; Schnepper and Johnson 2004; Abdennebi 2009).

Fig. 1.7 Karl Asmund Rudolphi (1771–1832)

In 1827, Montansey described the brain of an idiot-epileptic woman containing a large number of cerebellar and cerebral hydatid cysts (Castiglioni 1936; Ba'assiri and Haddad 1984; Pamir et al. 2002; Schnepper and Johnson 2004; Abdennebi 2009).

In 1855, Rudolph Carl Virchow firstly suggested the helminthic nature of alveolar hydatid disease caused by *E. multilocularis*. Rudolph Carl Virchow (1821–1902) was a German doctor, anthropologist, pathologist, prehistorian, biologist and politician, known for his advancement of public health. Referred to as "the father of modern pathology", he is considered one of the founders of social medicine (Castiglioni 1936; Abdennebi 2009).

In 1863, two researchers stepped into the spotlight. Leuckart discovered *E. multilocularis* and Diesing *E. oligarthus* (Eckert et al. 2001).

In 1888, Naunyn, Krabbe, Finsen and Thomas proved that the definitive host of the disease is the dog (and its relatives, wolves, jackals, hyenas, dingo dogs), and starting with the year 1901 (with Felix Devè's thesis Secondary Echinococcosis), hydatidology was born as a "science" (Arseni et al. 1981).

Felix Devè continued his work and published an astonishing 325 papers which turned the city of Rouen (France) into the Mecca of hydatid disease researchers for 50 years (Arseni et al. 1981).

Surgeons and pioneer neurosurgeons led the way in clarifying the pathology and advising the correct treatment for cranial hydatid cyst (Webster and Cameron 1967; Anderson et al. 1975; De Villiers and Joubert 1975; Kune et al. 1983; MacPherson et al. 1984; Walters 1984; Syrmos et al. 2010).

Maunsell (1845–1895) was an Irish surgeon. He was initially educated in Ireland, where he worked hard both in experimental and also in natural science. In 1867, he became chief surgeon in Australia and there assisted William Gillbee with the application of the antiseptic principles advocated by Joseph Lister in Glasgow. Later he practiced surgery in New Zealand, until 1891 (Dew 1955).

Henry Widenham Maunsell in 1889 operated successfully on a case of probable subtentorial hydatid cyst in an 18-year-old boy in New Zealand (Dew 1955).

In 1890, the Australians Graham and Clubb were the first to report the successful removal of an undoubted hydatid cyst of the brain (Arana Iniguez 1978; Abdennebi 2009). Barnett in 1896 (from New Zealand) and Luis Morquio in 1901 (from Uruguay) reported, among others, their success in the medical treatment of hydatid cyst of the brain in children (Webster and Cameron 1967; Anderson et al. 1975; De Villiers and

Joubert 1975; Kune et al. 1983; MacPherson et al. 1984; Walters 1984).

Luis Morquio (1867–1935) was first qualified in medicine in Uruguay. Later he studied in Paris at the Pasteur Institute. He specialized in paediatrics. In 1894, he returned to Uruguay, where he became the director of a newly established paediatric clinic and professor of paediatrics in Montevideo. He studied the presence of intracranial hydatid cyst in children (Haas 2002).

The Australian professor of surgery, Sir Harold Robert Dew (1891–1962), in 1928 published the first classic book on hydatid disease (Dew 1928).

Harold Robert Dew was first educated at the Melbourne Continuation School and at Scotch College. In 1909, he entered Ormond College, University of Melbourne. After a year as resident medical officer at (Royal) Melbourne Hospital, he sailed for England where he was commissioned temporary lieutenant in the Royal Army Medical Corps. Later he served in France and in 1918 was officer commanding the cholera laboratory at the 3rd Egyptian Stationary Hospital, Kantara; there he also performed general and clinical pathology and surgery. He assembled a fine collection of pathological specimens of endemic Egyptian diseases, particularly those that illustrated dysentery and bilharziasis. The French government awarded him the médaille d'honneur des épidémies in August 1917. Later, Dew went to London for postgraduate study and hospital experience and in 1920 was admitted to the Royal College of Surgeons, England, as a fellow. After his European experience, he returned in Melbourne, and he became resident tutor in surgery and anatomy at Ormond College. As an honorary associate at the Walter and Eliza Hall Institute, he collaborated with Neil Fairley on such topics as dysentery, malaria and schistosomiasis and—in what was to become his outstanding work—hydatid disease and testicular tumours (Carmody 2012).

During the last century, Dowling and Arana-Iniguez described a perfect surgical procedure for hydatidosis of the brain, providing intact removal of the cyst, named as "hydatid birth", by irrigation with isotonic saline solution between cyst wall and the brain, called hydraulic method (Abdennebi 2009).

The Dowling-Orlando technique has been the main surgical choice for the intact removal of intracranial hydatid cysts. Dowling described his technique in 1929, well before the introduction of the microscope in neurosurgery. Using the operating microscope has not been reported in the removal of a large hydatid cyst (Balak et al. 2006).

Arana-Iniguez from Uruguay was Professor of Neurology Institute of Medical School; he had studied abroad, first next to Bailey and later at the Brain Research Institute at the University of California with Segundo JP, French J, Naquet R and Hernández-Peón R, and linked the growth of diverse basic disciplines with clinical disciplines and techniques over space and time (Azambuja 1977).

The last true discovery concerning the *Echinococcus* species occurred in 1972 when Rausch and Bernstein discovered *E. vogeli* (Eckert et al. 2001).

Conclusion

The presence of hydatid cysts in both humans and animals was well known in ancient times and was described in the works of Hippocrates in the fourth century AD and Aretaeus and Galen in the first and second centuries AD, respectively. However, it was not until the seventeenth century that the parasitic natures of these cysts were recognized by Francisco Redi. In 1766 German Pierre Simon Pallas formulated the hypothesis that hydatid cysts were the larval stages of tapeworms, and later in 1853 Carl von Siebold demonstrated that cysts from sheep lead to adult tapeworms in dogs. It was not until a decade later that Bernhard Naunyn recognized that the adult tapeworms directly develop from hydatid cysts. Full understanding of the clinical features of this disease came in the late 1800s, which progressed to the development of immunological diagnostic tests by the early 1900s. Surgical techniques to remove cysts were first attempted in the 1600s, which have proven to be an effective treatment which evolved with medical technology.

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Hydatidosis of the Central Nervous System in Mediterranean Countries and the Middle East

2

Mohammed Benzagmout and Meryem Himmiche

Contents

Introduction

Hydatidosis, also known as echinococcosis or hydatid disease, is a parasitic infection caused by the larval stages of taeniid cestodes of the genus *Echinococcus*. Six species have been identified, but four are of public health concern: *Echinococcus granulosus* (which causes cystic echinococcosis), *E. multilocularis* (which causes alveolar echinococcosis), and *E. vogeli* and *E. oligarthrus* (which cause polycystic echinococcosis) (Moro and Schantz 2009).

Both cystic echinococcosis (CE) caused by *E. granulosus* and alveolar echinococcosis (AE) caused by *E. multilocularis* have been reported in several countries of the Mediterranean region and Middle East. *E. granulosus* is the most common species present in the Mediterranean region, while *E. multilocularis* has been reported only sporadically in limited areas of France, Italy, Serbia and Montenegro, Tunisia, and Turkey (Dakkak 2010).

Hydatidosis has a wide geographical distribution affecting many countries of all continents. Indeed, hydatid disease affects about two to three million people living in endemic areas around the world, particularly in South America, the Mediterranean littoral, Middle East, Central Asia, Australia, New Zealand, and South Africa (Carrea et al. 1975; Altinörs et al. 1995; Khanfar 2004). This disorder is widespread in all mentioned countries, especially in rural communities, and continues to be a major public health problem in the entire Mediterranean zone and all

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the Middle East countries (Anderson et al. 1997; Turgut 1997; Al Zain et al. 2002; Charrada-Ben-Farhat et al. 2006; Limaiem et al. 2010).

The liver and lung are the most frequently infected organs. The brain is involved in 2–3 % of all body localizations, whereas the spine in less than 1 %. Hence, central nervous system (CNS) involvement is fortunately rare compared to somatic localizations. However, it causes severe and permanent disabilities affecting functional and vital prognosis and gives rise to high economic losses.

Despite its morbidity and mortality and its perceived importance by the World Health Organization (WHO), prevention, early diagnosis, and treatment of hydatid disease still remain a serious health problem in developing countries of the world including South America, Australasia, the Mediterranean region, and the Middle East. In this review, we will focus on the epidemiological data of hydatidosis in the Mediterranean littoral and Middle East countries. Finally, we will stress the socioeconomic impact and control measures which should be applied to eradicate this parasitic infection.

Epidemiology

Countries of the north bank of the Mediterranean have more favorable socioeconomic conditions than those of the south bank and thus different prevalence of the disease. In fact, hydatidosis is endemic across the Mediterranean basin especially in the south bank and in all the west Asian countries of the Middle East (Anderson et al. 1997; Dar and Alkarmi 1997). The annual incidence of hydatidosis in these countries varies between 1 and 27 cases per 100,000 inhabitants with most being in the 5–10 cases per 100,000 ranges. It is estimated that close to half a million people across this endemic area are living with CE (Craig et al. 2007).

This geographical region is characterized by major shared affinities of a hot and dry climate; an arid, desert, or semiarid land mass; and linguistic and sociocultural ethnocentricity. It is well known that the rural population of the Mediterranean region and the Middle East has always depended on animals as sources of food, transport, labor, and companionship. Besides the rapid socioeconomic growth, agricultural and animal husbandry practices have great impact on the maintenance of the endemicity of CE in these regions (Dar and Alkarmi 1997).

In this chapter, we summarize the epidemiological status of hydatidosis in each country of the Mediterranean basin and the Middle East. The prevalence of hydatidosis in Mediterranean and Middle East countries could be divided in three different levels of endemicity: high, medium, and low. The geographical map shows the distribution of the disease in each country according to the strength of the endemicity (Fig. 2.1). However, various data are still missing considering the lack of complete epidemiological information about some countries allowing a better mapping of the disease.

Hydatidosis in Countries of the North Bank of the Mediterranean

Spain

Hydatidosis is still an endemic disease in Spain. The prevalence reached considerable rates up until a few years ago. Although specific control programs initiated in the 1980s have led to marked reductions in CE infection rates, the disease remains an important human and animal health problem in the northeastern, central, and western parts of Spain (Carmena et al. 2008). In the municipality of Madrid, hydatidosis affected 2.88 % of sheep (Rodrigo et al. 1997). In La Roja region, the overall prevalence reached 20.3 % of adult sheep and up to 23 % of sheep and cows (Jiménez et al. 2002).

The Spanish official statistics showed a decrease in the human incidence of CE from 2.52 (in 1982) to 1.01 cases per 100,000 inhabitants (in 1996) (Rojo-Vazquez et al. 2011). In the northeastern, central, and western parts of the country, human incidence rates are in the range of 1.1–3.4 cases per 100,000 inhabitants. However, in Salamanca, the incidence rate reached 10.8 per 100,000 inhabitants in the same period, twice

Fig. 2.1 The geographical map demonstrating the distribution of the disease according to the strength of endemicity in Mediterranean and Middle East countries

as many as previously reported, suggesting a potential reemergence of the disease (Pardo et al. 2005).

France

The prevalence of hydatidosis from 1994 to 1996 in the Midi-Pyrénées showed a marked decrease in livestock (2.5 %), while local human cases of hydatidosis were less than 0.28 per 100,000 inhabitants (Bichet and Dorchies 1998). From 1966 to 1970, the average annual incidence of human CE was 10 and 4.5 per 100,000 inhabitants in Corsica and in some eastern regions, respectively (Seimenis and Battelli 2003). In addition, AE has been reported in central France, while the Auvergne region represents the most southwestern extension of this disease (Magnaval et al. 2004). Recently, the European Centre for Disease Prevention and Control reported 17 human cases of AE in 2005.

Cerebral occurrence of *E. multilocularis* disease is rare, accounting for only 1 % of cases. In a survey of 387 patients with AE, Piarroux et al. (2011) have showed that isolated extrahepatic locations of AE account for 4 % of the French cases with spinal and brain involvement in five cases and three cases, respectively (Piarroux et al. 2011).

Italy

Most cases of hydatidosis are recorded in the south of Italy and islands (Fabiani et al. 1980). In fact, the incidence of CE is considered high in Sardinia and Sicily, moderate in the central and southern regions, and low in the remaining areas of Italy (Garippa 2006). With over 1,000 cases requiring surgery each year, Italy is considered as a medium- to high-risk country for human hydatidosis (Dionigi et al. 2007).

The latest surveys on animal epidemiology have shown persistent high regional prevalence in sheep: 76 % in 1995–2000 and 68–75 % during the more recent 2004–2009 survey, ranging from 58 to 83 % in the different provinces, with 10–28 % of sheep harboring fertile cysts (Conchedda et al. 2010).

Human incidence rates in Sardinia was as high as 14.32 per 100,000 inhabitants in the 1940–1950s (Giromini and Granati 1954). Twenty years later, different surveys showed

that the human incidence decreased from 14.6 per 100,000 inhabitants in 1969–1973 to 9.8 per 100,000 inhabitants in 1990–1995. During the period 2001–2005, CE still represents a serious health problem in Sardinia. Currently, the mean annual incidence is 6.62 per 100,000 inhabitants (Conchedda et al. 2010).

Former Yugoslavia-Affiliated Countries

CE is known to be endemic in these countries (Seimenis and Battelli 2003; Dakkak 2010). In Bosnia and Herzegovina, the disease is endemic particularly in the region of Herzegovina (Obradović et al. 2006). In Albania, 169 cases of unilocular echinococcosis were recorded in the country in 2010. Approximately 50 % of cases were aged between 16 and 40 years old (Berger 2010). Nevertheless, the AE incidence in Slovenia in 2001–2005 has been estimated at 0.45 per 100,000 inhabitants, with a mean annual incidence of 0.09 cases per 100,000 inhabitants (Logar et al. 2007).

Greece

CE remains a serious problem in Greece for both the public health and the livestock economy. The disease was widely prevalent long before the 1970s. The prevalence of infection in farm animals was as high as 82 % in cattle, 80 % in sheep, 24 % in goats, and 5 % in pigs. The surgical human cases reached 12.9 per 100,000 inhabitants in 1984 (Sotiraki et al. 2003). According to the National Statistical Service of Greece and the Greek Ministry of Health, the incidence of human CE in the period of 1977–1981 was estimated to be 10.9 per 100,000 inhabitants (Sotiraki et al. 2003).

Between 1969 and 1975, Karpathios et al. (1985) carried out a retrospective study to estimate the surgical incidence of hydatidosis among Greeks over 18 years old by collecting records from various communities and private hospitals (Karpathios et al. 1985). According to their findings, 4,202 adult patients were diagnosed with hydatidosis (600 per year) giving an annual incidence of 9.77 per 100,000 inhabitants while 3,397 (80.8 %) underwent surgery (485 patients per year or 7.9 surgical cases per 100,000 inhabitants). Recent data from reported cases indicate a further reduction in incidence. More precisely, the number of human cases reported was 46 (0.45 per 100,000 inhabitants) in 1999 and 0.3 per 100,000 inhabitants in 2008 (Sotiraki and Chaligiannis 2010).

Hydatidosis in Countries of the South Bank of Mediterranean

Morocco

CE is hyperendemic in Morocco, where it is one of the most important zoonoses, and represents a potentially serious public health and economic problem. Epidemiological studies have shown high prevalence rate both in humans and domestic animals, in most agropastoral regions. The first Moroccan series was reported in 1924 by Duckster including 24 cases from Cocard Hospital of Fez (Moroccan Ministry of Health 2007). The repartition of the disease is variable. The Atlas Mountains area is mostly infested compared to the Saharan regions. Indeed, 1.1 % of Berber people in the mid-Atlas mountain region are infested (Macpherson et al. 2004).

In Morocco, the disease is predominant in cow- and sheep-farming regions especially the region of Chaouia-Ouardigha, Meknes-Tafilalet, and Doukkala-Abda (Moroccan Ministry of Health 2007). Recently, Azlaf and Dakak (2006) conducted an epidemiological study aimed to update the prevalence of CE in different animal species living in the most important areas of the country. The global CE infection prevalence rates obtained were 10.58 % in sheep, 1.88 % in goats, 22.98 % in cattle, 12.03 % in camels, and 17.80 % in equines. The infection rates were high in middle Atlas in cattle (48.72 %) and in Northwest in cattle and sheep (37.61 % and 31.65 %, respectively).

In humans, the incidence of CE infection varies between 3.6 and 15.8/100,000 inhabitants (Anderson et al. 1997). Recently, 1,403 surgical human cases were recorded in the country in 2006, representing an annual rate of 4.55 cases per 100,000 inhabitants. Surgeries had to be repeated in 7–10 % and a mortality rate of 2–3 %

was observed (Moroccan Ministry of Health 2007). In addition, a human ultrasound screening performed in the middle Atlas Mountains showed much higher prevalence (1 %) than the surgery cases (Kachani et al. 2003).

Concerning CNS hydatidosis, most of the reports consisted of single case reports or small series (Ouboukhlik et al. 1994; Tizniti et al. 2000; El Quessar et al. 2001; Basraoui et al. 2010). These reports state that CNS hydatidosis is rare and constitutes 2 % of all locations (Tizniti et al. 2000). It mostly involves children and young adults (Basraoui et al. 2010; El Abbassi-Skalli et al. 2000) with a mean age of 30 years and male predominance (Ouboukhlik et al. 1994; El Abbassi-Skalli et al. 2000).

Algeria

CE is hyperendemic in Algeria essentially in the northeast of the country and constitutes an important public health problem. Several studies were performed at the beginning of the last century. A retrospective epidemiological study was made in 1979 by Larbaoui and Alloula and showed a clear predominance of cystic hydatidosis in rural areas (74 %). 75.3 % of the affected patients were younger than 40 years old (Larbaoui and Alloula 1979). Each year, more than 700 surgical cases are recorded by the Ministry of Health. Based on hospital records, the reported annual incidence was 3.6–4.6 per 100,000 inhabitants (Shambesh 1997).

Brain hydatidosis is a disease of childhood. This data was confirmed in a series of 99 patients operated for intracranial hydatidosis between 2000 and 2007 in four departments of neurosurgery in Algeria (two in Algiers, one in Annaba, and one in Constantine). 59.5 % of patients were 15 years old or younger (Abdennebi 2009).

Tunisia

CE is hyperendemic in Tunisia and represents a major public health problem due to its high prevalence, morbidity, and economic losses. It is a predominantly rural disease (80.3 % of patients). The annual human incidence of surgical cases of CE is approximately 15 cases per 100,000 inhabitants (Anon 1993). In central Tunisia, 3,986 cases of surgical echinococcosis were identified during 1982–1985, corresponding to an annual rate of 19.3 cases per 100,000 inhabitants (Bchir et al. 1989). Additionally, two autochthonous cases of *E. multilocularis* infection have been reported in humans from a mountainous region of northern Tunisia (Eckert et al. 2001).

Recently, Bellil et al. (2009) have analyzed the epidemiological features of 265 Tunisian cases of extrapulmonary hydatid cysts collected from 1990 to 2007 in the La Rabta Hospital, Bab Saâdoun, Tunis. They found that hydatidosis involved the CNS in 22.6 % of cases (Bellil et al. 2009). From the same hospital, Limaiem et al. (2010) reviewed retrospectively a series of 39 cases of primary CNS hydatid cysts operated between 1998 and 2007. They found that the disease involved mainly children (33.3 %). The mean age of all patients was 26.5 years old and the male/female ratio was equal. In this series, intracranial hydatid cysts represent 69.2 % (27 cases) and spinal hydatid cysts 30.8 % of cases (12 cases).

Libya

Echinococcosis is highly endemic in Libya. The incidence of surgically confirmed CE in eastern Libya was estimated to be at least 4.2 cases per 100,000 inhabitants, with a clear female predominance (Tashani et al. 2002). In addition, the ultrasound and serology investigations revealed that 1.6 % of population living in the northern Libya had the disease (Shambesh et al. 1999).

Hydatidosis in Western Middle East Countries

Turkey

Turkey is the typical example where echinococcosis is a common parasitic disease causing a serious public health and economic problem (Altinörs et al. 2000). Both CE and AE have been reported. CE is widespread throughout Turkey, whereas AE predominantly occurs in the eastern Anatolian region of the country (Altintas 2003).

According to the Ministry of Health records, 21,303 patients were operated for CE between

1987 and 1994; this corresponds to approximately 2,663 patients per year (Altintas 2003). The estimated surgical case rate ranged from 0.87 to 6.6 per 100,000 inhabitants in Turkey between 1987 and 1994 (Altintas 2003).

A retrospective study based on hospital, regional, and ministerial documents has shown that, from 2001 to 2005, a total of 14,789 CE surgical cases were recorded including 13.13 % that were diagnosed in the Marmara region, 16.94 % in the Aegean region, 16.09 % in the Mediterranean region, 38.57 % in the middle Anatolian region, 5.70 % in the Black Sea region, 6.80 % in the eastern Anatolian region, and 2.75 % in the southeastern Anatolian region (Yazar et al. 2008).

Brain hydatidosis represents 2 % of all space-occupying lesions in Turkish population (Engin et al. 2000). In 2001, Turgut reviewed a series of 276 Turkish cases of intracranial hydatidosis published since 1960. He noticed that most patients with intracranial hydatidosis were males (61 %), from rural areas (Turgut 2001). Cysts were generally located in the cerebral hemispheres and 18 % of patients had other organ infestation (Turgut 2001). He concluded that dimensions, localizations, and numbers of the cysts are the most important prognostic factors (Turgut 2001). The operative mortality rate in this series was 9 % (Turgut 2001). Similarly, Turgut (1997) have reviewed 28 reports of spinal hydatid disease from Turkey published between 1944 and 1996 (Turgut 1997). Turgut (2001) found a clear male predominance (73 %) and that 75 % of patients were aged between 30 and 50 years old. Cysts affecting the spine were commonly observed in the thoracic region and most patients had intraspinal extradural hydatid cysts associated with vertebral involvement (Turgut 2001). He concluded that spinal hydatid disease is still a life-threatening condition in Turkey despite all advances achieved in diagnostic procedures, surgical techniques, and antimicrobial therapeutics (Turgut 2001).

Cyprus

CE was widespread in Cyprus before the 1970s. It was a serious public health problem, with an annual surgical incidence rate of 12.9 per 100,000 inhabitants. In 1971, the first CE eradication campaign was implemented. After 1974, the control program was suspended in the north, while it continued in the southern part of Cyprus until 1985. At that time, the parasite was considered eradicated from both livestock and dogs, and the campaign was officially terminated. However, intermittent outbreaks discovered during slaughterhouse inspections led to reintroduction of the control program in 1993 (Economides and Christofi 2000). Currently, it is considered that echinococcosis transmission has been successfully interrupted in Cyprus as well as Iceland, New Zealand, and Tasmania (Eckert 2001).

Syria and Lebanon

CE is endemic in Syria, mainly in southern and northeastern provinces. Northern Syria, the main area of the country for livestock production, sheep rising, and nomadic tribal life, seems to be the most affected area. In Syria and Lebanon, the prevalence of *E. granulosus* infection in dogs appears to vary between 9 and 15 % (Seimenis and Battelli 2003), while in livestock, CE prevalence rates are estimated to be between 5 and 17 %, with the highest level in ruminants and donkeys (Seimenis and Battelli 2003).

In Lebanon, Abou-Daoud and Schwabe (1964) reported an incidence of 3.8 cases per 100,000 populations based on surgical records. The annual rate was estimated at 1.38 per 100,000 (1970–1985) (Berger 2010). However, there is no available published data on the current prevalence of human CE in these countries.

Palestine and Israel

Hydatidosis is endemic in Palestine. Abdel-Hafez and Kamhawi (1997) reported that the annual surgical prevalence of CE recorded from the Al-Maqased Hospital in Jerusalem was 1.76 per 100,000 inhabitants in 1995. Abu-Hassan et al. (2002) investigated the surgical incidence of the Palestinian West Bank hospitals between January 1990 and December 1997 (Abu-Hasan et al. 2002); he showed that the annual mean incidence was 3.1 per 100,000 inhabitants, with the highest rates of 4.9, 5.0, and 5.1 per 100,000

inhabitants found in Hebron, Jericho, and Bethlehem, respectively.

Epidemiological studies have reported a high prevalence of CE in both humans and animals in northern Israel (Shimshony 1997). In 2002, Youngster et al. conducted an epidemiological study in northern Israel and found a cumulative infection rate of 1.5 per 100,000 inhabitants, which is comparable to reports of worldwide endemic areas.

Jordan

Human CE is one of the most important endemic infectious diseases in Jordan. The annual rate of human infection was estimated to 2.9 per 100,000 in 1995 (Berger 2010). In serological study, serum samples from 2,388 subjects living in rural-agricultural, semi-Bedouin and Bedouin communities of Jordan showed 7.7 % positivity (Qaqish et al. 2003). Between January 1994 and September 2003, 65 patients from northern Jordan were treated for hydatid cyst in the Department of Surgery, Jordan University hospitals of Irbid. Forty-six percent of patients were below 40 years old and 57 % were females (Yaghan et al. 2004).

CNS hydatidosis is much more common in children than adults. The infant intracranial hydatid disease represents 50–75 % of total infection; the parietal lobe was mostly involved (Khanfar 2004). These data was in accordance with Al-Akayleh who prospectively analyzed five cases of intracranial hydatid cysts managed at the King Hussein Medical Centre, Amman, between 1993 and 2002. Al-Akayleh (2003) found that intracranial hydatidosis represented an incidence of 0.04 % of all space-occupying lesions operated during the studied period. All patients came from rural area and the average age of presentation was 9.4 years old (Al-Akayleh 2003).

Egypt

A survey for hydatidosis among slaughtered animals at two abattoirs in Ismailia and Cairo showed an infection rate of 4.8 % in sheep, 1.2 % in goats, 0.95 % in cattle, 0.46 % in buffalo, and 18.9 % in camels (Sadjjadi 2006). Although human CE is currently of low endemicity, this zoonotic disease may represent a public health concern in Egypt. A retrospective hospital study conducted by Kandeel et al. (2004) showed an annual surgical incidence varying between 1.34 and 2.60 per 100,000 inhabitants (Kandeel et al. 2004).

Hydatidosis in Eastern Middle East Countries

Iran

CE is highly prevalent in Iran, especially in sheep-grazing areas of East Azerbaijan and Kurdistan (Miabi et al. 2005). Cases of human hydatidosis are regularly reported from medical centers in different parts of the nation. Indeed, CE is responsible for approximately 1 % of admission to surgical wards and the rate of human infection is 0.6–1.2 (Rokni 2009). CNS involvement is seen in 2–3 % of patients and affects mainly young adults (Miabi et al. 2005). In addition, Iran is known as endemic areas of *E. multilocularis*. During a period of 3.5 years, 37 human cases of AE were diagnosed in various hospitals, most of them in the Ardabil province (Zariffard and Massoud 1998).

Iraq

Epidemiological studies on CE in Arbil province, northern Iraq, between 1990 and 1998 showed a human prevalence of 2/100,000 inhabitants (Saeed et al. 2000). In 2002, Al Zain et al. published a series of 34 patients with multiple intracranial hydatidosis collected from a retrospective study of intracranial hydatidosis cases managed at the Neurosurgical Hospital, Baghdad, and the Department of Neurosurgery, College of Medicine, Baghdad University, between 1976 and 1999. The age of patients varied between 3 and 55 years, with 26 patients under 20 years old (76.5 %) (Al Zain et al. 2002). There was a female predominance and the duration of symptoms was between 1 month and 3 years (Al Zain et al. 2002).

Hydatidosis in Arabic Persian Gulf Countries

CE is endemic in Kuwait, Yemen, Oman, Saudi Arabia, and some region of the United Arab Emirates (Sadjjadi 2006; Idris et al. 1999).

In Kuwait, the first report of human echinococcosis was published in 1962 (El Gazzar 1962). It concerned 51 cases of proved hydatidosis (including only five native Kuwaitis) admitted to the State hospitals from 1956 to 1960 inclusive. This represents an average of ten admissions per year and an incidence of 3.8 per 100,000 inhabitants. In 1990, an estimated incidence rate of 3.6 per 100,000 inhabitants has been reported (Shweiki et al. 1990; Dar and Alkarmi 1997). About 2 % of cases of hydatid disease have cerebral involvement (Rudwan and Khaffaji 1988).

In Saudi Arabia, echinococcosis is most common in southwestern province, followed by central province. Sixty-three percent of patients are women involved in sheep raising (Laajam and Nouh 1991). Besides, Malaika et al. (1981) reported that hydatidosis surgical cases represent 5 % of all major surgical operations performed in Saudi Arabia hospitals.

Socioeconomic Impact

Hydatidosis is highly prevalent in Mediterranean and Middle East countries; it continues to be a public health concern with negative impact on patients' health status on one hand and on financial resources of the nation (due to prolonged hospitalization periods and sick leaves and expensive treatment) on the other hand (Eckert et al. 2000). Benner et al. (2010) attempted to calculate the overall economic losses due to human and animal CE in Spain in 2005. They estimated the annual loss to approximately 149 million Euros (133 million Euros due to human ill health and 16 million Euros to animal health losses).

Economic evaluations have been undertaken also in Tunisia (Majorowski et al. 2005) and in Jordan (Torgerson et al. 2001). Results indicated that echinococcosis represents a substantial economic effect in relation to the respective countries' gross domestic product, probably up to 0.5 % of the total economic activity for these countries. Indeed in Turkey, the annual production losses due to CE in livestock have been estimated at 89 million dollars (Sariozkan and Yalcin 2009). These show a need to increase monitoring and control of CE in countries where the disease is widely distributed and still represents a considerable public health problem.

Control Program

During the last 20 years, considerable progress in the control of the disease has been recorded in countries of the northern Mediterranean littoral such as Spain, France, Italy, Greece, and Cyprus as a result of various implemented control measures. However, it should be reminded that the social, cultural, and economic conditions in these countries are more favorable for eradicating the hydatid disease.

In fact, the intersectorial collaboration and coordination between all competent authorities including the veterinary, medical, public health, and other governmental and nongovernmental organizations are the key to a successful control of echinococcosis (Seimenis 2003). However, prevention remains the best strategy of control and has been successful in many experienced countries, such as New Zealand, Australia, and China.

Unfortunately, effective control of hydatidosis has not yet been achieved in many countries of Mediterranean as well as Middle East regions despite extensive health education campaigns. Therefore, further efficient control programs are mandatory in order to reduce the incidence of this devastating parasitic disease (Limaiem et al. 2010).

Conclusion

Mediterranean and Middle East countries remain the predilection sites of hydatidosis. However, it is impossible to establish a precise hydatidosis epidemiological profile of each Mediterranean and Middle East countries. The current available data are very heterogeneous depending on each country and do not allow drawing equivalent epidemiological profiles based on the same epidemiological factors.

In addition, the human mass migration interferes considerably in determining the exact incidence of hydatidosis in concerned

countries. Indeed, societies of Mediterranean and Middle East countries became more and more open to human and animal exchange. This makes individual country program less efficient and only collaborative programs between all involved countries including those "exporting" the disease might help to better eradicate the hydatid disease.

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Hydatidosis of the Central Nervous System in South America

3

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Introduction

The most frequent species of *Echinococcus* in humans based on morphological criteria are *E. granulosus* and *E. multilocularis*; however, from the 1960s onward, two species from Central and South America, *E. vogeli* and *E. oligarthrus*, have been found (Gutiérrez 2000). The life cycle of these worms is similar to that of *E. granulosus*. Echinococcosis in animals is important because of the economic losses that the infection causes in livestock. Hydatidosis is endemic in several Latin American countries, such as Argentina, Bolivia, Brazil, Chile, Peru, and Uruguay. In the South American continent, *E. granulosus* is the most widespread parasite in dogs and sheep. There are no standard guidelines for case reporting, and methods differ by country. The main site of human infection is the liver. While secondary lesions mainly occur in the lungs, they can also affect the central nervous system (CNS) (Nourbakhsh et al. 2010). *E. granulosus* causes liver cysts in over half of the cases, with lung involvement in 10–40 % of the cases, while brain, periorbital tissue, kidney, and pericardium are affected in 5 % of cases. In contrast, *E. multilocularis* is almost invariably found in the liver but may also reach the lungs or the brain in 5–10 % of cases (Kammerer 1993). Table 3.1 shows the frequency of human cyst localization in Argentina (Guarnera 2009).

E. granulosus infection of the CNS has been estimated at below 2 % (Schantz 1972) and may be primary, often presenting as solitary

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Table 3.1 Frequency of location sites of human hydatid cysts in Argentina

Localization	Percentage (%)
Liver	68
Lung	23
Kidney	2
Brain	2
Bone	2
Striated muscle	1
Spleen	1
Multiple sites	1

Modified from Guarnera (2009)

parenchymal cysts, while intraventricular and meningeal locations are most exceptional (Arana Iñiguez et al. 1951). Secondary involvement is due to cyst rupture or hydatid fluid dissemination from a distant organ. CNS echinococcosis is more frequent in children up to 15 years of age with an estimated prevalence rate of 50–75 % (Dew 1955; Slim et al. 1971). A series of cerebral hydatid cysts in children describing diagnostic difficulties, surgical treatment, and possible complications have been reported (Krajewski and Stelmasiak 1991; Ersahin et al. 1993; Ozek 1994; Peter et al. 1994; Turgut 2002). Signs and symptoms include increased intracranial pressure, headache, vomiting, papilledema, and hemiparesis as well as occasional seizures, while meningeal or cranial nerve involvement is most unusual (Arana Iñiguez 1978; Kammerer 1993).

Epidemiology

Hydatidosis in South America

Hydatid disease is endemic in cattle- and sheep-raising regions of the world such as Central Europe, the Mediterranean countries (Tunisia, Spain), the Middle East (Turkey, Lebanon, Emirates), South America (Argentina, Peru, Uruguay, Brazil, Chile, and Bolivia), Australia, New Zealand, India, and South Africa (Carrea et al. 1975). South America is one of the regions of the world most affected by cystic echinococcosis.

Three of the four species of *Echinococcus*, *E. granulosus*, *E. vogeli*, and *E. oligarthrus*, have been described in South America (Fig. 3.1). However, *E. granulosus* presents transmission cycles in domestic animals, being sheep the principal intermediate hosts in this region. The reason for this fact is the great concentration of sheep in this part of the continent and the close relationship between this intermediate host and the definitive host, the dog. There are now approximately 65 million sheep in South America, out of which 63 million (97 %) are found in Argentina, Brazil, Chile, Peru, and Uruguay. These data turn nearly 9 % of the South American territory into a sheep-raising area (Organización Panamericana de la Salud [OPS] 2004). However, in certain regions, various animal species such as pigs, goats, and camelids have gained importance as intermediate hosts. In South America, a few described human cases of alveolar echinococcosis were due to *E. patagonicus* and *E. oligarthrus* (Taratuto and Venturiello 1997). The prevalence rate of infection in the asymptomatic human population obtained from ultrasonographic (US) screenings was 1.6 % in Tacuarembó, Uruguay; 1.6 % in Florida, Uruguay; 3.6 % in Durazno, Uruguay; and 5.1 % in Vichaycocha, Peru. In Argentina, the prevalence rate was 5.5 % in Rio Negro province and 14.2 % in Loncopue, Neuquen province (OPS 2004). Successful control programs based on systematic dog deparasitation with praziquantel have been developed in Uruguay, Chile, and Argentina.

In general, hydatid disease of the CNS is rare, with a reported incidence of 0.9–2.1 % of all cases of hydatidosis (Tamer et al. 2004). A differential diagnosis with other diseases such as abscesses, neoplasias, and other parasitoses such as coenurosis and congenital cysts should be determined (Mahadevan et al. 2011).

Hydatidosis in Argentina

In Argentina, *E. granulosus* is the most prevalent zoonotic helminth. It has been estimated that approximately 30 % of the Argentine territory harbors the domestic life cycle of *E. granulosus*. The provinces where sheep, goat, and cattle rear-

Fig. 3.1 Distribution of *Echinococcus granulosus*, *E. vogeli*, and *E. oligarthrus* in South America (Modified from OPS (Organización Panamericana de la Salud) 2004; with permission)

ing is quite common are the ones with the highest prevalence rates of infection. In particular, Neuquén is one of the provinces with the highest incidence (OPS 2004).

Although *E. granulosus* is widespread all over Argentina and hydatid disease is considered endemic in this country, the infection has a non-homogeneous geographic distribution (Fig. 3.2). The contribution of each kind of livestock (cattle, pig, sheep, etc.) to disease transmission depends on the region: for example, while sheep are the principal intermediate hosts in the Patagonian and Mesopotamic region, cattle are the prevalent hosts in the Pampas and northern regions of the country (Denegri et al. 2002). Particularly in the southeastern region of Buenos Aires province, echinococcosis is considered an important human and veterinary health problem, cattle being the main livestock involved in the transmission of this disease (Andresiuk et al. 2009). In a case-control study in Argentina, one of the risk factors for cystic echinococcosis was human exposure to a great number of dogs during the first years of life (Larrieu et al. 2002). In a survey of asymptomatic patients, Coltorti et al. (1988) found that 47 of 5,839 patients (80 %) were seropositive for *E. granulosus* antigens. These authors used antibodies against *E. granulosus* arc 5 antigens by the double diffusion arc 5 test (Coltorti et al. 1988).

Fig. 3.2 Major endemic foci of echinococcosis in Argentina (Modified from OPS (Organización Panamericana de la Salud) 2004; with permission)

Argentine medicine has greatly contributed to the comprehension of hydatid cysts of the CNS. In Buenos Aires in 1889, Dr. Alejandro Castro performed a surgical operation for a cerebral hydatid cyst and introduced the new principles of surgical asepsis that had been previously developed in Europe. In 1895, Dr. Alejandro Posadas was the first surgeon to successfully treat hydatid cysts of the CNS in Argentina. In 1929, Dr. Ernesto Dowling performed his so-called "cyst delivery" method. The hydatid cyst is surgically removed intact. This technique (Dowling-Orlando technique) is mandatory in order to avoid further dissemination of the scolices (Obrador Alcalde 1964). In Buenos Aires, during the 1933–1974 period covering almost 42 years, 29 brain hydatid cysts and one of the spinal cord out of 35 pediatric cases of hydatidosis of the CNS were operated. No surgical mortality was reported in these cases (Carrea et al. 1975). The 20 patients who had their cysts removed unruptured with the Dowling technique (Dowling and Orlando 1939) remained alive, and only two patients suffered blindness as a sequela (Carrea et al. 1975). In Buenos Aires, in 1980, three patients (two adults and one child) were admitted to hospital with various neurological signs and symptoms. Although there was no evidence of cysts in the liver or lungs, hydatid disease was only suspected in the child, since he came from an endemic rural area in Buenos Aires

province. A high degree of accuracy in identifying multiple supratentorial cysts by computed tomography (CT) scanning was obtained in all the cases, and the patients were followed by CT scans after surgery (Insausti et al. 1980). In Buenos Aires in 1998, Ure and Maegli reported a case of an adult patient born in Santiago del Estero province, who was admitted to a psychiatric hospital after surgery performed in Buenos Aires 1 year before (Ure and Maegli 1998). He suffered from alcoholism, diabetes mellitus, and Chagas trypanosomiasis. He had lived on a farm for several years and then moved to Buenos Aires. He presented with excruciating headache, vomiting, papilledema, left hemiparesis, somatic sensitivity in the left leg, slow mental activity, and urinary incontinence. A CT scan revealed a large right frontal cystic mass surrounded by a circular calcification. The mass turned out to be a hydatid cyst, which was opened and treated with formaldehyde. No extracerebral localizations were observed. Five years later, new CT scans revealed the bilateral and diffuse extension of the hydatid process with several small new cystic lesions unable to be treated by surgical reoperation. The patient died 2 months later (Ure and Maegli 1998).

In 2004, a case of a temporal hydatid cyst in a child was reported. The diagnosis was considered preoperatively on the basis of magnetic resonance imaging and magnetic resonance spectroscopy (MRS) findings. The MRS pattern appeared to be different from that seen in other cystic lesions of the CNS. Lactate, alanine, acetate, and a large pyruvate peak were observed. The cyst was surgically removed (Tamer et al. 2004).

Some orbital infections have been diagnosed in Turkey and Morocco (Turgut et al. 1992, 2004; Benazzou et al. 2009). A hydatid infection of the orbit recently diagnosed in Buenos Aires in a patient from Neuquén was characterized as an unusual localization of a hydatid cyst (Menghi and Gatta 2011).

Hydatidosis in Brazil

In Brazil, *Echinococcus* is widespread in an area of approximately 100,000 km^2, which is close to the Uruguayan and Argentinean borders. Several studies have shown that 14–50 % of farm dogs were infected with *E. granulosus* (de la Rue 1997). Particularly in the state of Rio Grande do Sul in southern Brazil as well as in other countries in South America, the habit of feeding sheep raw offal to dogs perpetuates the parasite's life cycle. The etiological agent found in dogs and other wild animals is predominantly *E. granulosus*.

In 1983, the first serological survey for echinococcosis was performed in seven municipal states near the border with Uruguay. A prevalence of 8.06/1,000 population was observed (OPS 2004). In 1999, another serological survey was conducted in 5 % of the total human population in rural areas of 18 municipal states of Brazil. The highest prevalence was observed in Municipio de Barra do Quaraí (89.44 %) and the lowest in Piratini (8.82 %) (Souza et al. 1999). To our knowledge, there have been no reported cases of hydatidosis of the CNS in the Brazilian literature.

Hydatidosis in Chile

In Chile, several serological surveys have been conducted throughout the country to document the prevalence of human echinococcosis from 1988 to 1997 (Nourbakhsh et al. 2010). The prevalence of human cases in apparently healthy people may reach up to 754.6/100,000 population in some regions of the country (Apt et al. 2000). Another serological survey reviewed 60,790 individuals and found that 82 had positive serological findings, resulting in a total incidence of 136/100,000 population. The calculated incidence rates for urban and rural regions were 87/100,000 and 241/100,000, respectively (Schenone et al. 1999). Pursuant to National Resolution N° 712/2000, echinococcosis is a disease of mandatory notification (OPS 2004) in Chile. Human echinococcosis is a prevalent disease in Chile with an incidence rate of 2–2.5/100,000 population. Considering the existing subdiagnoses, the incidence of this disease has been reported to be 10/100,000 (OPS 2004).

In Chile, dogs are the main definitive hosts for *E. granulosus*. Between 1977 and 1979, 71 % of dogs from the XII region were found to be infected with *Echinococcus* In 1984, after the control program, this prevalence decreased to 1.5 % (OPS 2004).

Between 1997 and 2000, of 15 patients studied at Dr. L. Calvo Mackenna Hospital in Santiago de Chile, only 2 had cerebral hydatid cysts, whereas the rest had other cyst localizations (Hauck et al. 2003). More recently, in March 2012, four cases of cysts located in the brain were reported. Three of the patients were admitted with intracranial hypertension, whereas the fourth one presented with left hemiparesis. Imaging studies of all intracerebral cysts showed features compatible with hydatidosis in all cases. All lesions were completely removed surgically, and the pathological study of the excised piece confirmed the diagnosis of hydatidosis (Tapia et al. 2012).

Hydatidosis in Peru

In Peru, echinococcosis is a major health problem in the central Peruvian Andes where sheep raising is widespread. In a Peruvian study, the prevalence of human hydatidosis has been reported to be 1.9 % by the enzyme-linked immunoelectrotransfer blot and double diffusion assays in endemic areas (Moro et al. 1994).

Studies in Peru have shown high prevalence of cystic echinococcosis in humans, particularly in the central and southern highlands (Gavidia et al. 2008). During 1997–1999, prevalence in the central Andes was 5.7–9.3 % according to US, radiography, or both studies and up to 18.2 % according to immunoblot testing (Moro et al. 1997, 1999). Portable US has facilitated the study and a more accurate reporting of cystic echinococcosis prevalence in endemic regions (Macpherson et al. 2003; Moro et al. 2005). Among the available serological tests, the immunoblot assay that uses bovine hydatid cyst fluid has been successfully applied in cystic echinococcosis in endemic areas of Peru (Moro et al. 1997, 2005).

Local control measures should focus primarily on decreasing dog and sheep infection. Cystic echinococcosis is a major public health problem in Peru, having a prevalence of 6–9 % in many areas of the country and numerous reported human cases every year. The Peruvian central highlands comprise approximately 70 % of the endemic areas for cystic echinococcosis in Peru (Santivañez et al. 2008).

By 1993, just one case of a 7-month evolution cerebral hydatid cyst was reported at Hospital Nacional Cayetano Heredia in a 12-year-old girl residing in Paracaos (Sierra de Lima). The patient presented with cephalalgia, progressive loss of strength in the right hemibody, and vomiting. She was diagnosed with cerebral and hepatic echinococcosis by CT and abdominal echography, respectively, and treated with albendazole. On the 7th day, the cyst was excised from the brain with no complications using the Dowling-Orlando technique. The cyst measured 9×6×7 cm. After 4 months, a hepatic cyst of similar size was removed. The patient is currently on anticonvulsant treatment and has remained asymptomatic, with no evidence of sequelae (Guillen et al. 1994).

Hydatidosis in Uruguay

Seroprevalence studies in rural communities using an enzyme-linked immunoassay test with crude sheep hydatid cyst fluid antigen to detect antibodies (total immunoglobulin) revealed an overall human seropositive rate of 1.2 % (Bonifacino et al. 1991). In 1990, in certain rural areas, 10.7 % of dogs were infected with *E. granulosus*. After the canine control program, the percentage of infected dogs had lowered from 10.7 to 0.74 %. Nevertheless, prevalence was 44.7 % in sheep and 64.8 % in cattle. By 2003, serological tests (enzyme-linked immunosorbent assay [ELISA]) had been performed on 41,004 school children with 20 positive cases (OPS 2004). The average annual morbidity for hydatid disease in Uruguay in 1969–1971, expressed as the incidence of all hospital cases (20.7/100,000 population) or only of new cases (17.7/100,000

population), is the highest yet reported for any country. Many Uruguayan health authorities now consider hydatid disease to be the most important rural health problem of specific etiology (Purriel et al. 1973). To our knowledge, there has been no reported case of hydatidosis of the CNS in the Uruguayan literature.

Hydatidosis in Bolivia

From January 1984 to February 1999, a total of 40 cases of hydatid cyst in 31 children were studied. Their medical histories were thoroughly checked, emphasizing all clinical aspects, cyst location, type of treatment, evolution, and readmission. Of the 31 children studied, 9 were admitted twice for the same reason, some of them with the cyst located in the same place as when they were first admitted and others in a different location. Most came from urban low-middle class neighborhoods in La Paz and El Alto. The most frequent cyst location was the lungs (25 cases), followed by the liver (10 cases); there were 8 cases with cysts in both organs; the rest had different and often unusual locations such as the peritoneum (3 cases). In the other six cases, the cysts were localized in the brain, parotid gland, spleen, posterior mediastinum, vertebral area, and retrovesical region. The only case of cerebral hydatidosis presented with meningeal signs and viable scolices in cerebral spinal fluid. Surgery was performed in all cases. From 1996 onward, albendazole was systematically administered before and after surgery following the confirmation of the diagnosis. This study reports an increasing frequency of this disease and confirms its high mortality rate as well as its high cost due to mandatory surgery, related infections, long hospital stays, and complications due to the disease. In 80 % of all cases, it was confirmed that patients lived in close proximity to dogs. The cysts excised from the children had an average size of 7 cm; the smallest ones were removed from the parotid gland and the vertebral area and measured 3 cm. The largest ones were lodged in the peritoneal cavity, lungs, and brain and measured 15 cm (Tamayo Meneses et al. 2004).

Control Program

In the Argentine province of Rio Negro, a control program including dog treatment with praziquantel (5 mg/kg of bodyweight) every 2 months for about 20 years (1979/1980 to 1999) reduced the prevalence of cysts in sheep from 61 to 18 % and of intestinal stages in rural dogs from an estimated 40 % to 2–3 % (Larrieu et al. 2001).

Conclusion

Based on our experience and the literature data upon hydatidosis of the CNS in South America, the following conclusions may be drawn from this chapter:

1. Argentina, Chile, Uruguay, Peru, Bolivia, and Brazil show the highest rates of incidence of human hydatidosis in South America. Nevertheless, the incidence of hydatid cysts of the CNS is very low.
2. The main reason for these high rates is, among others, the unawareness of risky behaviors, such as the regular habit of feeding raw sheep offal to dogs.
3. Since hydatidosis is most prevalent in cattle-raising areas, it is also an important veterinary problem leading to economic consequences.
4. The high morbidity in certain regions, the potential lethality if the disease is not adequately treated, the high incidence in young people, and the high costs involved in hospitalization and surgery highlight the epidemiologic importance of hydatidosis in South America.

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Hydatidosis of the Central Nervous System in Central and Eastern Europe

4

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Contents

Introduction

Hydatidosis (also known as echinococcosis or hydatid disease) is one of Europe's neglected infections of poverty (Hotez and Gurwith 2011). Cystic echinococcosis (CE), which has *Echinococcus granulosus* as the pathogenic agent, is endemic to Southwestern and Eastern parts of Europe (Sotiraki and Chaligiannis 2010). Although alveolar echinococcosis (AE), produced by *E. multilocularis*, was considered to be rare in Central Europe, recent studies have shown its emerging nature and demonstrated that the endemic areas for this parasite are broader than previously thought (Kern 2010). The yearly disease incidence (cases per 100,000 inhabitants) in

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Europe's endemic areas has increased from a mean value of 0.1 (1993–2000) to 0.26 (2001–2005) (Moro and Schantz 2009; Sotiraki and Chaligiannis 2010). Farming was noted as an important risk factor for infected people. It has also been suggested that AE may be underdiagnosed in Europe because it is inadequately considered in the differential diagnosis. Regarding the location of lesions developed in AE, 34 % of the European patients had liver lesions with simultaneous involvement of other organs (Kern 2010).

This chapter aims to review and, at the same time, bring to light new epidemiological, clinical, and surgical information regarding hydatidosis of the central nervous system (CNS) in many countries in Eastern and Central Europe where data was available (Fig. 4.1). At the same time, it intends to shed light on particularly interesting cases reported in the literature. A special emphasis will be given to the casuistic from Romania, one of the countries with the highest prevalence of hydatidosis worldwide. Evidence regarding the status of the disorder in the former Soviet Union and Russia, considered Eurasian states, is also discussed in this chapter.

Epidemiological and Clinical Features Regarding Hydatidosis of the Central Nervous System in Central and Eastern European Countries

Hydatidosis in Romania

Epidemiology

In 1995, Romania was in the forefront of the European countries and among the first countries worldwide as regards the incidence of hydatid disease (Neghina et al. 2010, 2011a). Moreover, the severity of hydatidosis in Romania is emphasized by the fact that at least one person from 45.5 % of Romanian localities underwent surgery for this condition (Iacobiciu et al. 2005; Neghina et al. 2010, 2011b). Following the analysis of the available global data, Stefanoiu concluded in 2000 that the number of human cases of hydatidosis in Romania surpassed the number of cases from Lithuania, Belarus, Poland, Slovakia, Ukraine, Bulgaria, Czech Republic, and Latvia combined (Iacobiciu et al. 2005; Neghina et al. 2010). Nevertheless, hydatidosis is not a notifiable disease in Romania, and no cases were mentioned in the annals of the World Health Organization (WHO) during the period from 1996 to 2000 (Iacobiciu et al. 2005; Neghina et al. 2010). Studies performed in the entire country have shown that the incidence of the disease decreased from 5.6 cases per 100,000 inhabitants during the period 1953 to 1963 to 2.6 cases per 100,000 inhabitants from 1987 to 1991 (Neghina et al. 2010, 2011b; Calma et al. 2011). The most recent studies undertaken in four counties of western Romania indicated an average incidence between 2.4 and 4.4 cases per 100,000 inhabitants (Calma et al. 2011, 2012; Moldovan et al. 2012).

Hydatidosis of the Brain and Cranium

In 1900, Thoma Ionescu, considered the godfather of Romanian surgery, presented at the International Congress of Medicine and Surgery held in Paris a case of cerebral hydatidosis that he successfully operated on through temporal craniotomy, and at the same time, he emphasized the possible surgical risks. Two years later, he published in a reputable national journal new and useful data on the topic of cerebral hydatidosis with particular emphasis on the case he had previously managed (Arseni et al. 1988). In 1905, Antoniu reported for the first time in Romania a rare case of cranial hydatidosis. At that time, only seven such cases were registered in the medical literature worldwide. His paper, entitled "Hydatid Cyst of the Cranial Bones," represented a valuable starting point toward the knowledge of this pathology in Romania. The patient, hospitalized in Turnu Severin (southwestern Romania), presented with a single tumor that caused cerebral compression with epileptic crisis. Unfortunately, the patient died before the onset of any exterior signs suggesting cranial involvement (Arseni et al. 1988).

During the period of 1935–1968, there were 46 cases of cerebral hydatidosis reported in Romania (Arseni and Samitca 1957; Arseni et al. 1981)

Fig. 4.1 Map of Europe. The status of central nervous system hydatidosis is discussed in the Eastern and Central European countries (sprayed on map) where data were available

(Table 4.1). Information that is more detailed was available for the cases managed during 1935–1955 in a Neurosurgery Clinic in Bucharest. Of 2,226 cases with intracranial space-occupying disorders, 36 patients (1.6 %) were found with cranial and intracranial hydatidosis (Arseni and Samitca 1957). The most significant epidemiological and clinical characteristics of this study group are summarized in Table 4.2.

Until 1980, the number of cases with cerebral involvement rose to 83 in the Neurosurgery Clinic in Bucharest. Of these patients, 55.4 % were males and more than 43 % were children. The youngest patient was 1.5 years old, and the oldest one was 65 years old (Arseni et al. 1981). A further study in the same clinic presented the characteristics of 27 pediatric cases who underwent surgery during the period from 1980 to 1992 (Ciurea et al. 1995). An additional 52 cases diagnosed during the same period were not discussed due to different reasons. The studied cases represented 2.8 % of the children with expansive nontraumatic lesions hospitalized in this clinic. The mean age of the study group was 8.2 years, and the youngest patient was 3.3 years old. A 67 % male prevalence was registered, and most of the patients (41 %) belonged to the age group 6–10 years. The most prevalent symptoms were headache and vomiting (96 %), followed by papillary edema (89 %) and hemiparesis (70.3 %). In the majority of patients (40.7 %), two cerebral lobes were affected. Recurrences occurred in 40.7 % of patients (in all the cases where total removal of the cysts could not be achieved). Another study undertaken at the same clinic included 76 patients who underwent surgery for

Table 4.1 Cases of cerebral hydatidosis in Romania during the period 1935–1968

Year(s)	Authors	Hospital, city	No. of cases	Specific comments	References
1935–1955	Arseni and Samitica	Neurosurgery Clinic, Bucharest	36	Presented in Table 4.2	Arseni et al. (1981), Arseni and Samitca (1957)
1954[a]	Marcovici and Steriade	Unspecified	1	Giant cerebral cyst, recidivated, with abscess	Arseni et al. (1981)
1957[a]	Russu	Unspecified	2	Study in children. The prevalence of cerebral hydatid cysts was 5.4 % of all locations One of the cysts (very voluminous) developed in a child who previously underwent surgery for a hepatic hydatid cyst	Arseni et al. (1981)
1960[a]	Waitsuk, Andrasofski, and Mera	Neurosurgery Clinic, Targu Mures	6	One of the cysts was situated in the right premotor cortex and had calcified walls	Arseni et al. (1981)
1968[a]	Theodorescu and Mitroi	Neurosurgery Clinic, Constanta	1	The cyst, about the size of a small fist, was located in the left parieto-occipital cortex At hospital admission, the patient was comatose with respiratory failure. Patient's condition worsened as a consequence of a lumbar puncture performed 1 month later The patient died	Arseni et al. (1981)
Total cases			46		

[a]Year when the cases were reported

cerebral hydatidosis during the period from 1981 to 2003 (Ciurea et al. 2006a). The main epidemiological and clinical characteristics of the study group were the following: 95.7 % of patients were children; the median age was 8.7 years in children and 29.3 years in adults; male patients prevailed (59.2 %); increased intracranial pressure was the most frequent symptom in children (91.1 %), while headache was the most prevalent finding in adults (88.9 %); 94.8 % of the cysts were supratentorial; rupture of the cysts during the surgery was reported in 26.3 % of cases; postsurgical complications occurred in 67.1 % of patients; relapses developed in 25 % of cases; the outcome (either at 6 months or at 2 years) showed a fatality rate of 5.3 %.

Hydatidosis of the Spine and Spinal Cord

The first documented information regarding vertebro-medullary hydatidosis dates from the period 1862 to 1865, when Kalenderu reported two cases with vertebral cysts (detected in the dorsolumbar muscles) (quoted from Arseni et al. 1981). In 1898, Botescu communicated a case of hydatid cyst located in the pelvis, and Tzaicu reported in 1930 a case with medullary compression whose starting point was in the musculature and presented a secondary rachidian invasion (quoted from Arseni et al. 1981). In 1927, Jianu detected a case of vertebral hydatidosis and later a case of thoracolumbar involvement without neurological symptomatology (cases communicated

Table 4.2 Main epidemiological and clinical characteristics of patients with cranial and intracranial hydatidosis managed during 1935–1955 in a Neurosurgery Clinic in Bucharest (Arseni and Samitca 1957)

Feature	Relevant statistics	Percent of total cases
Gender	Male	58
Age	<30 years	73
Inhabitance area	Rural	64
Duration of symptoms	<1 year	78
Type of cyst	Unilocular	81
Symptomatology onset	Insidious	92
Symptoms	Headache	59
	Epilepsy	50
Outcome	Immediate postsurgical mortality	9
	Late mortality (>18 months)	13
	Without neurological sequels (% of surviving patients)	40

in 1957) (quoted from Arseni et al. 1981). In 1946, the case of a patient with an epidural hydatid cyst was presented by Cosacescu and Vereanu. Later, in 1956, Horvath and Sandor presented their study on 14 patients with vertebro-medullary invasion (Arseni et al. 1981).

During the period from 1935 to 1957, a total of 20 cases of vertebro-medullary involvement due to hydatid cysts were noted in the Neurosurgery Clinic in Bucharest (Arseni et al. 1960). They account for approximately 3 % of cases with rachidian and intrarachidian tumors and approximately 0.06 % of all cases managed during this period. These cases represented about half the number of cases with cerebral hydatidosis. In most of the patients (40 %), the lesions were found in the lumbar region. The youngest patient was 14 years old and the oldest 66 years old. Male patients represented 55 % of the study group, and 80 % of the cases were rural inhabitants. It has been noticed that a high prevalence (25 %) of patients belonged to the 11- to 20-year-old age group. Radicular pain was the initial clinical symptom in most of the patients (70 %). However, syndrome of spinal cord compression was the most common finding (75 %) upon admission. The time span from the onset of the disease until hospital admission ranged between 0 and 6 months in the majority of the cases (40 %). Out of 19 cases who underwent surgery, the outcome was fatal in a single case; of the remaining patients who were operated and survived, relapses occurred in approximately 44 % of cases.

Throughout the time, other cases were also detected, as follows: a report on ten cases with bone involvement (of which four cases with vertebral involvement were diagnosed in the Department of Orthopedics of Brancovenesc Hospital, Bucharest) is presented by Negrea in 1957; in the same year, Vereanu reported four cases of bone involvement (including one case with vertebral location and one with sacral); in 1971, Marinescu reported 30 cases of vertebral hydatidosis (quoted from Arseni et al. 1981).

Craniospinal Hydatidosis

Lupascu and Panaitescu (1968) gave an overview in 1968, in their valuable treatise on hydatid disease, of the data reported by the National Cantacuzino Institute regarding involvement of different organs and systems in this disorder. According to this source, craniocerebral cases occurred with a prevalence of 1.4 %, and vertebral lesions were diagnosed in 0.7 % of patients.

A major epidemiological study performed in the entire country of Romania during the period from 1987 to 1991 (Iacobiciu et al. 2005), including 3,072 cases (2,701 adults and 371 children), provides valuable data on cerebral and vertebromedullary involvement: 0.94 % of patients were diagnosed with the condition at first hospitalization, 0.16 % at the second admission, and 0.1 % at the third one (Table 4.3).

Further investigations in children up to 15 years old (407 patients, 1987–1992) indicated the following percentage of cerebral involvement according to age groups: 5.21 % (0–5 years), 5 % (6–10 years), and 1.8 % (11–15 years) (Iacobiciu et al. 2005). According to Gherman et al. (1991), the prevalence of cerebral hydatidosis was 1–2 % in 1991. In 1994, Stefanoiu and Vranceanu reported in their study a prevalence of 0.4 % for cerebral hydatidosis. In the same study, the prevalence of this condition was 4 % in 407

Table 4.3 Cerebral and vertebro-medullary involvement of hydatidosis in 3,072 patients hospitalized in all of the Romanian surgical sections between 1987 and 1991

Location of the hydatid cyst	Adults		Children		Total	
	No. of cases	% of adult cases (n=2,701)	No. of cases	% of children cases (n=371)	No. of cases	% of total cases (n=3,072)
First hospitalization						
Cerebral	11	0.41	15	4.04	26	0.85
Hepatic and vertebro-medullary	1	0.04	–	–	1	0.03
Thoracolumbar	1	0.04	–	–	1	0.03
Only vertebro-medullary	1	0.04	–	–	1	0.03
Total	14	0.53	15	4.04	29	0.94
Relapse, second hospitalization						
Cerebral	1	0.04	4	1.08	5	0.16
Relapse, third hospitalization						
Cerebral	–	–	3	0.81	3	0.1

For 1991, only partial data were available

pediatric cases (Stefanoiu and Vranceanu 1994; Iacobiciu 1999). A survey taken from 1994 to 1999 in a southern Romanian county (Dolj county) reported cerebral involvement in 1 out of 213 cases (0.5 %) (Iacobiciu et al. 2005).

In 2000, Plesamosca and his collaborators reported data on 14 pediatric cases of hydatidosis with less common locations. Of these cases, cerebral involvement coexisted with involvement of other organs in 14.3 % of patients (Iacobiciu et al. 2005). A major epidemiological survey of 1,004 cases with hydatidosis diagnosed between 1985 and 1997 in three southwestern Romanian counties (Timis, Arad, and Caras-Severin) indicated cerebral involvement in 0.1 % of the study group (Iacobiciu 1999). The most recent studies undertaken from 2004 to 2010 in Timis (182 patients) (Calma et al. 2011), Arad (79 patients) (Calma et al. 2012), Caras-Severin, and Hunedoara counties (190 patients) (Moldovan et al. 2012) detected no cases with CNS involvement.

Orbital Hydatidosis

Between 1883 and 1968, a total of 24 cases of orbital hydatidosis were reported in Romania (Arseni et al. 1981). More recently, in 2006, Ciurea et al. (2006b) described another two interesting pediatric cases in a 4-year-old boy and in a 15-year-old girl.

Hydatidosis in Former Yugoslavia and Countries Succeeding Former Yugoslavia

Yugoslavia

As reviewed in Arseni et al. (1981), in 1952, Stojanović and Vujadinović reported only a single case (2.3 %) with cerebral involvement out of 44 patients with hydatid disease (quoted from Arseni et al. 1981). Later, in 1957, Papo and Vrigisić found that of 200 cases in which patients underwent surgery, two patients (1 %) had hydatid cysts with cerebral location (quoted from Arseni et al. 1981). In the countries succeeding former Yugoslavia, data on cerebral echinococcosis are available for Serbia, Montenegro, Croatia, and Macedonia, whereas none are available for Slovenia and Bosnia and Herzegovina.

Serbia

Hydatidosis is a mandatory notifiable disease in Serbia, and consequently the relevant data on this topic are archived at the National Institute for Public Health (Tables 4.4 and 4.5). However, when comparing the official data to that published in the literature, it becomes obvious that cases are largely underreported to this institute. A clinical study on hepatic hydatidosis performed in the largest Serbian clinical center indicated

that 1,016 adult patients underwent surgery for this illness between 1963 and 2006. Of this number of cases, 376 patients were managed between 1997 and 2006 (Basara 2007).

Although there are no specific surveys regarding CNS involvement of hydatidosis, the abovementioned extensive study on adult patients (Basara 2007) as well as another study on 149 children who underwent surgery for hydatid disease between 1990 and 2006 (Djuricic et al. 2010) evidenced no cases of CNS involvement. This suggests that the condition is probably extremely rare in Serbia. Nevertheless, a study performed from 2000 to 2004 analyzed the brain and meningeal biopsy samples from 4,987 patients with craniotomy. The results showed that hydatidosis was detected in three patients (0.06 % of the total cases) out of 23 cases with parasitic diseases. Two of them were adults (each presenting only a solitary cyst), and the third patient was a 12-year-old boy (who had two cysts) (Gazibara 2005).

Table 4.4 Cases of hydatidosis registered in Serbia during the period 1991–2010

Year	Cases per 100,000 inhabitants	Number of cases	Gender distribution: male (%)
1991	0.12	10	NA
1992	0.07	6	NA
1993	0.12	8	NA
1994	0.09	7	NA
1995	0.25	20	NA
1996	0.16	13	NA
1997	0.21	17	NA
1998	0.36	29	NA
1999	0.32	26	NA
2000	0.30	24	NA
2001	0.45	35	44.4
2002	0.36	27	31.4
2003	0.53	40	18.5
2004	0.28	21	37.5
2005	0.63	47	19
2006	0.51	38	29.79
2007	0.34	25	31.58
2008	0.50	37	32
2009	0.43	32	37.8
2010	0.38	28	28.6
Mean	0.32	24.5 (total: 490)	31.06

All data refers to Serbia only (without Kosovo) for the entire period 1991 to 2010 (from Reports on Infectious Diseases in Serbia, published annually by the Institute for Public Health in Serbia)
Abbreviations: *NA* not available

Montenegro

The data available for this country indicates the following incidence rates of hydatidosis (cases per 100,000 inhabitants): 0.48 in 2006, 0.32 in 2007, and no cases in 2008 (WHO Regional Office for Europe 2011). A recent report described two cases of cerebral hydatidosis in Montenegro. The first patient was a 16-year-old boy who had three independent cysts that were surgically removed. The outcome was favorable in this case, and no relapses were noticed 8 years after the surgical intervention. The second patient was a 22-year-old man previously operated on for a liver hydatid cyst. At admission, he presented multiple cysts detected by CT and MRI in the lungs, mediastinum, heart (left atrium), and brain (with cerebral infarction). He declined any surgical intervention, and no further information about the outcome is available (Asanin et al. 2008).

Table 4.5 Age groups and gender distribution of the cases of hydatidosis registered in Serbia during the period 2001–2010

	Age groups						
	0–9	10–19	20–29	30–39	40–49	50–59	60+
No. of cases	9	10	30	34	48	83	116
%	2.7	3.0	9.1	10.3	14.5	25.1	35.1
Males (no. of cases)	4	7	10	12	10	22	38
Males (%)	44.4	70.0	33.3	35.3	20.8	26.5	32.8

All data refers to Serbia only (without Kosovo) for the entire period 1991–2010 (from Reports on Infectious Diseases in Serbia, published annually by the Institute for Public Health in Serbia)

Croatia

In the Croatian region of Dalmatia, considered an endemic area for hydatidosis, a decrease of over 70 % in the incidence of this disorder was registered from the mid-1950s until 1997. Nevertheless, the relative proportions according to age, gender, and professional status distribution remained constant (Morovic 1997). According to the available data, the incidence of the disease (cases per 100,000 inhabitants) varied during the period from 1997 to 2010 between 0.23 (in 2010) and 0.81 (in 2004) (WHO Regional Office for Europe 2011).

CNS hydatidosis was diagnosed during the period from 1990 to 2000 in three patients (two males, ages 10 and 50 years, and a 20-year-old female with symptoms of elevated intracranial pressure who underwent surgery in Zagreb) (Negovetic et al. 1990; Talan-Hranilovic et al. 2002; Rumboldt et al. 2003), as well as in a 27-year-old male patient with brain involvement who was diagnosed in Sibenik in 2005 (Aleksic-Shihabi and Vidolin 2008).

Macedonia

From 1993 until 2009, the incidence of hydatidosis varied in this country between 0.15 and 1.9 cases per 100,000 inhabitants (WHO Regional Office for Europe 2011). In 1995, a case of vertebral hydatidosis presenting as paraplegic syndrome was reported in Germany in a 16-year-old child originally from Macedonia. The histological examination revealed multilocular cystic lesions (Druschky et al. 1995).

Hydatidosis in Bulgaria

In Bulgaria, the average annual number of surgical cases of hydatidosis increased by 60 % from the period 1971 to 1982 until 1983 to 1995. At the same time, the incidence increased from 2 to 3.3 cases per 100,000 inhabitants (Golemanov et al. 2011). During the period of 1985 to 2010, the average incidence (cases per 100,000 inhabitants) was approximately 6 (range: 2.3 in 1985 and 9.3 in 2002) (WHO Regional Office for Europe 2011). According to Golemanov et al. (2011), in some regions of southern Bulgaria, the incidence varied between 15 and 27 cases per 100,000 inhabitants during 1991 to 2000.

In 1966, Philippov reported 69 cases with hydatidosis and brain involvement that occurred over a 25-year period (Philippov 1966; Arseni et al. 1981). In 1988, Todorov et al. (1988) described the case of a 48-year-old male who had eight hydatid cysts localized in frontal, temporal, and parieto-occipital brain areas. Clinically, the patient presented with convulsive seizures, loss of consciousness, and headache. He was treated with albendazole, and the outcome was favorable.

Hydatidosis in the Former Soviet Union and Russia

During 2006 and 2010, the incidence rates of hydatidosis (cases per 100,000 inhabitants) ranged between 0.35 (in 2006) and 0.4 (in 2010) in the Russian Federation (WHO Regional Office for Europe 2011). A historical overview of cases of hydatid disease with CNS involvement is shown in Table 4.6.

Hydatidosis in Poland

Hydatidosis was and continues to be a rare disease in Poland (Arseni et al. 1981; WHO Regional Office for Europe 2011). Human cases of alveolar echinococcosis were detected as follows: one case in 1951, another one in 1958, and 22 cases during the period from 1994 to 2003 (Myjak et al. 2003). The data available for the period from 1998 to 2010 shows low incidence rates (cases per 100,000 inhabitants) of hydatidosis that ranged between 0.06 (in 2004) and 0.17 (in 2006) (WHO Regional Office for Europe 2011).

Regarding neurohydatidosis, Sokolowski and Mempel reported in a 1962 survey that only three patients were diagnosed with this condition during a 100-year period (Arseni et al. 1981). One of the cysts, the size of a bean, was clogged in the foramen of Magendie (Arseni et al. 1981). Another case with multiple cysts located in the posterior cranial fossa and in the spinal cord

Table 4.6 Reports on CNS hydatidosis in the former Soviet Union and Russia

Year(s)	Author(s)	Cyst location	No. of cases	Specific comments	References
1844	Reported by Grimberg in 1964	CNS	1	–	Arseni et al. (1981)
1959	Veselitskii	Brain	1	AE	Isik et al. (2007), Veselitskii (1959)
1962	Nikolski	Brain (frontoparietal)	1	Giant and calcified cyst Successful surgical removal	Arseni et al. (1981)
1963	Ogleznev	Vertebro-medullary	36	–	Arseni et al. (1981), Ogleznev (1963)
1965	Martyshin	Posterior fossa	1	AE Female patient	Isik et al. (2007), Martyshin (1965)
1966	Arutunov, Subina	CNS	108	28 cases (26 %) of AE	Arseni et al. (1981)
1966	Shubina and Timofeeva	Brain (frontal)	1	AE Female patient presenting seizures and mental disorder	Isik et al. (2007), Shubina and Timofeeva (1967)
1969	Kutniakov and Mitrofanov	Brain, cerebellum	5	AE Of 70 patients, brain metastases were noticed in 4 cases (5.7 %) and cerebellar metastasis in one case (1.4 %)	Arseni et al. (1981), Kutniakov and Mitrofanov (1969)
1977	Peresedov and Morgunov	Brain	1	Patient with a history of general epileptic seizures Association between primary calcified hydatid cyst of the left frontal wall and aneurysm of the supraclinoid portion of the left internal carotid artery with rupture of its wall The outcome was fatal because of massive subarachnoid hemorrhage due to rupture of the aneurysm	Arseni et al. (1981), Peresedov and Morgunov (1977)
1984	Kasumov and Nikonov	Sella turcica	1	AE Female patient	Isik et al. (2007), Kasumov and Nikonov (1984)
2011	Potapov et al.	Brain, heart, and kidneys	1	CE Male patient Removal of seven cysts without their rupture from the left parieto-occipital and right parietal area. Favorable postsurgical outcome	Potapov et al. (2011)

Abbreviations: *AE* alveolar echinococcosis, *CE* cystic echinococcosis, *CNS* central nervous system

Table 4.7 Single case reports on CNS hydatidosis in Germany

Year(s)	Author(s)	Cyst location	Specific comments	References
1934	Nachmacher	Brain (intraparenchymal, 2 hydatid cysts)	54-year-old female patient Rapid evolution to death	Arseni et al. (1981)
1941	Stieda	Brain (left cerebral hemisphere)	7-year-old child	Arseni et al. (1981)
1969	Bonis	Brain (parietal area)	AE Female Bavarian patient Disease evolution with epileptic seizures	Bonis and Sturm (1969), Isik et al. (2007)
1984	Bauer	Brain	AE Middle-aged female patient	Bauer et al. (1984), Isik et al. (2007)
1999	Hagemann et al.	Brain (left frontotemporal area, 2 hydatid cysts)	42-year-old male patient Recurrent headaches for 7 years The patient developed a severe meningeal inflammatory reaction to antihelminthic therapy	Hagemann et al. (1999)
2008	Spies et al.	Lumbar spine	18-year-old male patient Favorable outcome 1 year after surgical intervention	Spies et al. (2008)
2011	Nell et al.	Lumbar spine and psoas muscle	AE 80-year-old male patient Favorable postsurgical outcome	Nell et al. (2011)

Abbreviations: *AE* alveolar echinococcosis

(with favorable postsurgical outcome) was reported in 1973 by Mempel and Grochowski (Mempel and Grochowski 1973; Arseni et al. 1981).

Hydatidosis in Slovakia

During the period from 2000 to 2010, between 0 and 7 human clinical cases of CE were reported annually in Slovakia (except for the year 2000 when 31 cases were registered). The average incidence (cases per 100,000 population) was 0.098 (range: 0–0.58) (Czarkowski et al. 2008; Štefancíková and Dubinský 2010; Turceková et al. 2009). This figure was similar to the incidence found in the neighboring country of Poland (0.096) during the last decade (Czarkowski et al. 2008). Of the above-reported cases, cerebral hydatidosis was found in only one patient. In 2004, following neurological examination and CT screening, CNS hydatidosis was diagnosed in a woman treated for chronic obstructive pulmonary disease (Kinceková et al. 2008).

The first evidence of *E. multilocularis* in Slovakia was recorded in 1999 in a red fox (Dubinský et al. 1999), and since 2000, 16 human cases of AE have been registered. The average incidence rate was 0.027 cases per 100,000 inhabitants (Kinceková et al. 2011). Fourteen of these occurred in three endemic regions for *E. multilocularis* situated in the northern part of the country, where environmental conditions facilitated the overgrowth of the fox population and the parasite circulation (Miterpáková and Dubinský 2011). CNS involvement was not detected in any of these cases.

Hydatidosis in Germany

During 1999 to 2009, the incidence rates (cases per 100,000 inhabitants) of hydatidosis in Germany ranged between zero (in 1999) and 0.15 (in 2006) (WHO Regional Office for Europe 2011). Many interesting cases of CNS hydatidosis were reported in this country over time. A historical overview of particular single cases is provided in Table 4.7.

Of interest also are the findings of a survey undertaken from 1936 to 1960 on 600 cases of AE originating in Germany and Russia. Cerebral involvement was detected in 37 cases (6 %) (Bensaid et al. 1994; Clement et al. 1974; Isik et al. 2007). A retrospective study performed between 1985 and 1989 in Bavaria (situated in southern Germany and considered one of the main endemic regions for hydatidosis in Germany) reported an overall incidence (cases per 100,000 inhabitants) of 1.9 (1.5 for CE and 1.1 for AE). Of the 58 cases of AE included in the analysis, cerebral involvement was noted in 5.2 % of them. By contrast, none of the 123 cases with CE had CNS involvement (Nothdurft et al. 1995a, b).

Hydatidosis in Austria

Between 1854 and 1990, 128 cases of human AE were documented in this country; the average incidence was 0.94 cases per 100,000 inhabitants. None of these cases had CNS involvement (Auer and Aspock 1991). During 1999 to 2010, hydatidosis incidence (cases per 100,000 inhabitants) in Austria ranged between 0.04 (in 2006) and 0.59 (in 1999) (WHO Regional Office for Europe 2011). During 1995 and 2010, two cases with neurohydatidosis were reported in the literature: a 28-year-old female patient (AE of the liver, lungs, and brain) (Schmid et al. 1995, 1998; Reittner et al. 1996) and a 6-year-old girl originally from Bulgaria (CE of the spine involving T8–T9 vertebrae) (Thaler et al. 2010).

Conclusion

Although rare in Central and Eastern Europe, hydatidosis of the CNS should never be overlooked. It should be considered in the differential diagnosis of any patient who presents with seizures, focal neurological deficits, and symptoms of increased intracranial pressure (headache, nausea, vomiting, and papilledema), especially if that person comes from a region with a high prevalence of hydatid disease. Therefore, healthcare professionals should be aware of the disease epidemiology in order to identify at-risk patients.

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Hydatidosis of the Skull

5

Zahed Hossain

Contents

Introduction

Cranial hydatid cyst is a relatively rare condition. In the world literature, many reports of cranial hydatid disease are available, but most of them are small series, and reports of skull hydatid cyst are very scarce. It is part of hydatidosis, which is a zoonotic disease. *Echinococcus granulosus* larva travels through systemic circulation from the gastric mucosa to the cranial cavity. Through this pathway it is filtered in the hepatic and pulmonary beds. Even after the pulmonary filtration, a few still make it to the systemic circulation and can lodge in almost any part of the body, including the brain, heart, and bones (Kovoor et al. 2007; Reddy 2009; Nemati et al. 2010). Cysts in the head and neck region, especially the skull base, can present with atypical clinical symptoms (Sureka et al. 2010). Intracranial extracerebral hydatid cysts are rare and may occur in three forms: (a) cranial, usually the bony spongiosa is the first to be involved; (b) cranial extradural, the extradural space may be infected by embolization of scolices or embryos via blood vessels, by extrusion of intracerebral cysts via healthy dura mater or by erosion of osseous hydatid into the extradural space; and (c) combined, there may be simultaneous intracerebral, extradural, and bony cysts. Of the three forms, extradural variety is extremely rare as the physiologic flow of blood to the brain is mainly through the internal carotid system, so the likelihood of the larvae traveling through the external carotid system is very low (Ravalji et al. 2006).

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Incidence

Although hydatid cyst can occur in any organ or tissue of the body including brain and orbit, the bone and brain are the fourth common sites of involvement after the liver, lungs, and peritoneum (Mumtaz et al. 2009). Only 2 % of the hydatid cysts are located in the skeleton, and of these only 3–4 % are in the skull (Behari et al. 1997; Raynham et al. 2009). Recently, it has been reported that skull hydatidosis was firstly described by Guesnard in 1836, with the cranial vault (68.5 %) being more commonly involved than the skull base (Limaiem et al 2009). Skull base hydatid disease is extremely rare. Raynham et al. (2009) reported three cases of hydatid cyst of the skull base, the first of them involved the anterior cranial fossa and paranasal sinuses. The second was located in the infratemporal fossa. The last involved the temporal bone and posterior cranial fossa. Sureka et al. (2010) reported a case presenting with lower cranial nerve paresis, such as palatal and vocal cord palsy, mimicking a malignant mass. In 1992, Turgut et al. reported only three cases of orbital hydatidosis from their clinic, where non-orbital hydatidoses are frequently encountered. In 2004, Turgut et al. reported 25 cases of orbital hydatidosis in entire Turkey from 1963 to 2001 where hydatidosis is still a serious public health problem. A summary of the 38 reported cases of hydatidosis of the skull published in the world literature to date is given in Table 5.1 (Arseni and Samitca 1957; Orman and Le Roux 1968; Kanaka et al. 1970; Teymoorian and Bagheri 1976; Gokalp et al. 1979; Ozgen et al. 1984; Kanpolat et al. 1988; Gedikoglu et al. 1989; Benmoussa et al. 1990; Aydin et al. 1992; Rivierez et al. 1992; el Khamlichi 1993; Pasaoglu et al. 1998; Ennouri et al. 2000; Abbassioun and Amirjamshidi 2001; Erman et al. 2001; Turgut 2001; el Kohen et al. 2003; Taghipour et al. 2005; Lath et al. 2007; Limaiem et al. 2009; Raynham et al. 2009; Hossain et al. 2010; Siddiqui et al. 2010; Sureka et al. 2010; Yazdani et al. 2010).

Young males are most commonly affected (Teymoorian and Bagheri 1976). Because of the restricted geographic distribution of the echinococcal worms, persons of certain races are affected more commonly than others; however, the parasite has the capability of infecting persons of all races equally. No sexual predilection is recognized (Dandan 2008).

Pathology

Cranial hydatid cyst may occur in the skull bones (intraosseous) and in the intracranial space. In the skull, it may involve the cranial vault and skull base and may spread to the paranasal sinuses and orbit. Primary hydatid disease of bone due to *E. granulosus* occurs when a blood-borne scolex settles in the bone (Limaiem et al. 2009). It initially invades the diploe, and as it grows it widens the diploic space, and subsequently it extends in both directions (Dharkar 1996). The wall of the cyst consists of an inner endocyst (germinal layer) and outer ectocyst (laminated layer) (Nemati et al. 2010). In bone involvement, pericyst formation does not occur, thereby allowing aggressive proliferation in an irregular branching fashion along the line of least resistance, especially the bone canals. The parasite replaces the osseous tissue between trabeculae due to the slow growth of multiple vesicles. With time, the parasite reaches and destroys the cortex, with subsequent spread of the disease to surrounding tissues (Limaiem et al. 2009). Early cases present as an expansile osteolytic lesion in the diploe. The more advanced forms manifest as multilocular or unilocular destructive lesions with adjacent soft tissue masses (Teymoorian and Bagheri 1976). As the cyst grows, the bone undergoes pressure atrophy, and the inner or outer table of the skull ruptures. The inner table of the skull frequently ruptures, and the vesicular larva passes into the epidural space inducing symptoms of increased intracranial pressure. Less frequently, cysts may rupture the outer table of the skull at many spots and involve the scalp to produce prominence on the head (Aydin et al. 1992; Limaiem et al. 2009). When both outer table and inner table are destroyed, intra-cranial and extra-cranial spaces become communicated with each other (Fig. 5.1).

Table 5.1 Summary of the 38 reported cases of hydatidosis of skull published in the world literature to date

Author(s)	Country	Year of publication	No. of cases	Site of involvement	Radiological study	Outcome
Arseni and Samitca	Romania	1957	1	Skull	X-ray	NS
Orman and Roux	South Africa	1968	2	Vault—frontal (1) and base (1)	X-ray and angiogram	NS
Kanaka et al.	India	1970	1	Vault	X-ray	Behavior improved, recurrence after 6 mos
Teymoorian and Bagheri	Iran	1976	4	Base	X-ray	Complete recovery (2), died at 4 mos (1), well up to 2 yrs (1)
Gokalp et al.	Turkey	1979	1	Vault—Lt temporoparietal	X-ray	Complete recovery at postop 3 mos
Ozgen et al.	Turkey	1984	1	Intrasellar	X-ray and CT	Complete recovery at postop 10 mos
Kanpolat et al.	Turkey	1988	1	Base—cavernous sinus	CT	Unchanged ocular movement restriction at postop 12 mos
Gedikoglu et al.	Turkey	1989	1	Parasellar	CT	Complete recovery at postop 3 mos
Benmoussa et al.	Morocco	1990	2	Vault—parietal (1), occipital (1)	CT	Good (1), recurrence (1)
Aydin et al.	Turkey	1992	1	Vault—intradiploic, parietal, and occipital	X-ray, CT	Died at early postop
Rivierez et al.	France	1992	1	Base—cavernous sinus	CT, MRI	NS
el Khamlichi	Morocco	1993	1	Base—cavernous sinus	X-ray and CT	NS
Pasaoglu et al.	Turkey	1998	1	Base—infratemporal fossa	CT	Complete removal, No follow-up
Ennouri et al.	Tunisia	2000	1	Vault—Lt temporal	CT and MRI	Well at early postop
Abbassioun and Amirjamshidi	Iran	2001	7	Vault and base	X-ray, CT, and MRI	Well
Erman et al.	Turkey	2001	1	Vault—Rt parietal	CT	Complete recovery
Turgut[a]	Turkey	2001	3	Base	X-ray and CT	Complete recovery (2), unchanged (1)
el-Kohen et al.	Morocco	2003	1	Base—Lt jugular foramen	CT and MRI	Chemotherapy followed by motor improvement
Taghipour et al.	Iran	2005	1	Base—foramen magnum	MRI	Complete recovery
Lath et al.	India	2007	1	Base	CT	Well
Limaiem et al.	Tunisia	2009	1	Vault—Rt frontal	CT	Recurrence requiring second operation
Raynham et al.	South Africa	2009	3	Base	CT	Complete recovery
Hossain et al.	Bangladesh	2010	1	Vault—Rt temporal	CT	Complete recovery
Sureka et al.	India	2010	1	Base—posterior fossa	CT and MRI	Well at early postop
Yazdani et al.	Iran	2010	1	Base and orbit	CT	Recurrence
Siddiqui et al.	India	2010	1	Vault and orbit	CT	Complete recovery

Abbreviations: *NS* not stated, *Rt* right, *Lt* left, *CT* computed tomography, *MRI* magnetic resonance imaging, *mos* months, *yr(s)* year(s), *postop* postoperative

[a]Note that the number of cases was given within the brackets

The cases reported by the author had already been described by Ozgen et al., Kanpolat et al., and Gedikoglu et al. earlier

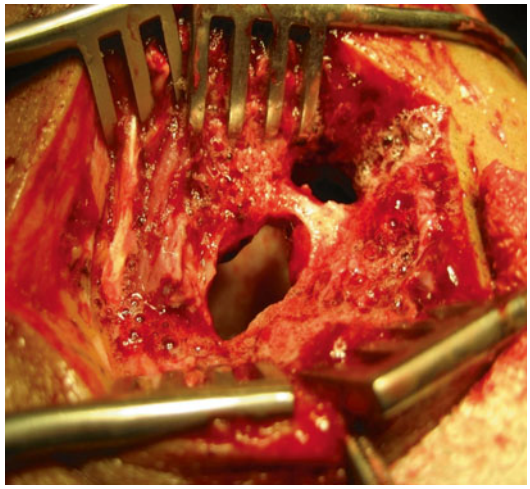

Fig. 5.1 Eroded bone seen perioperatively

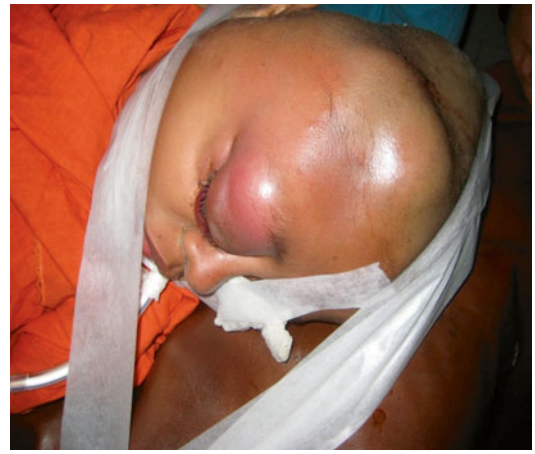

Fig. 5.2 Infected hydatid cyst (abscess) showing all the features of acute inflammation

Presentation

Cranial hydatid cysts present by their location in the skull. Nevertheless, if it ruptures, it may then show systemic features. Generally, four syndromes dominate the presenting clinical manifestations of cranial hydatid disease including increased intracranial pressure (48 %), skull deformity (48 %), cranial nerve palsies (42 %), and focal neurological disturbance (30 %) (Aydin et al. 1992; Limaiem et al. 2009).

When hydatid cyst involves the cranial vault, it may present with swelling on the head which causes the deformity of the head. It is usually painless and insidious in growth, but if it becomes infected, then it becomes painful. When frontal bone is involved, swelling is on the forehead and frontal region. When it involves the parietal bone, swelling will be on the parietal region. Accordingly, swelling may be on the temporal, occipital, or suboccipital region. The swelling is firm in consistency (Dharkar 1996). Scalp moves over the swelling if it is not ruptured externally. When it ruptures and involves the extra-calvarial soft tissues, swelling may be soft and cystic. If it becomes infected, all the features of acute inflammation may present in the form of swelling, redness, tenderness, and raised local temperature (Fig. 5.2).

Cranial hydatidosis may present with the features of intracranial space-occupying lesion. Presenting features may be classified as (a) features of raised intracranial pressure and (b) focal neurological signs. Intracranial pressure may increase due to its volume or it may obstruct the cerebrospinal fluid (CSF) pathway. These patients may also present with seizure (Al-Akayleh 2003). Features of raised intracranial pressure are headache, nausea and vomiting, papilledema, blurring of vision, gait disturbance/ataxia, vertigo, diplopia, bradycardia, and hypertension. In advanced conditions, respiratory irregularity and deterioration of level of consciousness may occur (Greenberg 2001). Focal neurological signs are according to the location of the cyst in the cranial vault, like hemiparesis, hemisensory deficit, cognitive disorder, and visual deficit. Diagnosis of a hydatid cyst can sometimes be confused with other space-occupying lesions of the brain, especially abscesses, neoplasms, and arachnoid cysts (Anvari et al. 2009; Bahloul et al. 2009; Nemati et al. 2010). Hydatid cyst in the skull base usually remains silent unless it involves the adjacent structures. It may involve the cranial nerves and may present with the features of cranial nerve palsies. Patient may present with anosmia if the cyst involves the olfactory nerve in the anterior cranial fossa at the cribriform plate. It may involve the optic nerve, and orbit

Fig. 5.3 Infected hydatid cyst involving orbit developing proptosis

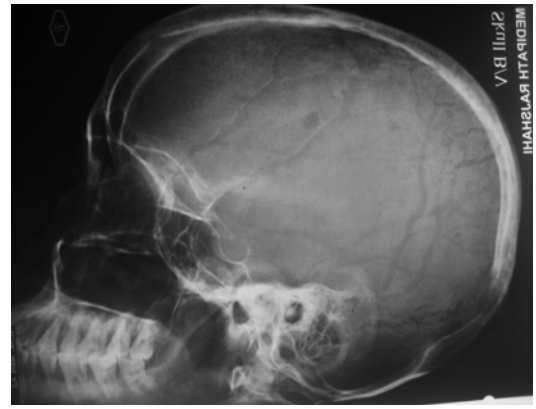

Fig. 5.4 Hydatid cyst involving the occipital bone

may present with visual impairment and proptosis (Fig. 5.3). Third, fourth, and sixth cranial nerves may be involved in the cavernous sinus or at their exit from the cranial cavity with diplopia and/or ophthalmoplegia. Hydatid cyst of the anterior cranial fossa enters into the paranasal air sinuses, which may precipitate development of sinusitis. Hydatid cyst of the middle cranial fossa may present with third, fourth, fifth, and sixth cranial nerve palsy. It may enter into the infratemporal fossa. Hydatid cyst of the posterior cranial fossa may present with features of (a) lower cranial nerve palsy like facial asymmetry, vertigo, impaired hearing, tinnitus and ringing in the ear, and regurgitation on swallowing; (b) long tract signs like weakness of one or both upper and lower limbs; and also (c) cerebellar signs like speech difficulty (dysarthria), gait disturbance, and ataxia. Raynham et al. (2009) reported three cases of skull base hydatid cyst, among them one involving the paranasal air sinus and presenting with complicated sinusitis; a second one involving the infratemporal fossa and presenting with painless right facial swelling, lateral displacement of ramus of the mandible, and sensory impairment of maxillary and mandibular division of the fifth cranial nerve; and a third one involving the left temporal bone and posterior cranial fossa and presenting with progressive weakness of legs, left arm, right face, and mixed sensorineural and conductive type of hearing loss.

Diagnosis

Diagnosis of echinococcosis is made by using imaging and serology techniques. Conventional radiography usually shows a variable-sized ill-delineated osteolysis (Figs. 5.4 and 5.5) without osteosclerosis (Limaiem et al. 2009). Computed tomography (CT) scan and magnetic resonance imaging (MRI) are valuable in the identification of cerebral and bone lesions and are helpful in surgical planning. CT scans obtained before and after contrast medium injection show the multivesicular pattern of the lesion and reveal its endo- and exocranial extensions (Ennouri et al. 2000; Limaiem et al. 2009) (Figs. 5.6, 5.7, and 5.8). Both CT and MRI are used frequently in diagnosing the cystic lesions (Tuzun and Hekimoglu 1998; Andronikou et al. 2002; el-Shamam et al. 2001; Ciurea et al. 2006; Kovoor et al. 2007; Anvari et al. 2009; Nemati et al. 2010). However, MRI is considered superior in demonstrating the cyst rim (Krajewski and Stelmasiak 1991; Tuzun and Hekimoðlu 1998; Altinörs et al. 2000; Pedrosa et al. 2001; Andronikou et al. 2002; Cavusoglu et al. 2009; Nemati et al. 2010). Contrast enhancement usually does not occur in cyst walls. But if cyst becomes infected, cyst wall may be enhanced faintly with contrast. Cyst fluid

shows density and intensity similar to CSF on computed tomography (CT) and magnetic resonance imaging (MRI), i.e., hypodense on CT and hypointense on T1WI and hyperintense on T2WI in MRI.

The differential diagnosis of intraosseous hydatid cyst may be difficult especially in cases of pure skull involvement. The association of the intracranial cystic lesion to osteolysis of the inner and outer tables is highly suggestive of hydatid cyst (Limaiem et al. 2009). Pericyst formation does not occur in bone, and the cyst has a much thinner wall. Because of this fact and the rigid nature of bone, the cyst cannot assume its typical shape (sphere). The

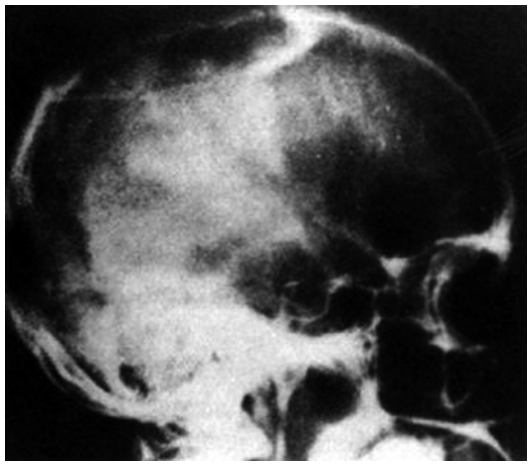

Fig. 5.5 Plain skull x-ray showing expansion of the parietal parasagittal bone due to an intradiploic hydatid cyst (Reproduced, with permission, from Abbassioun et al. 2003)

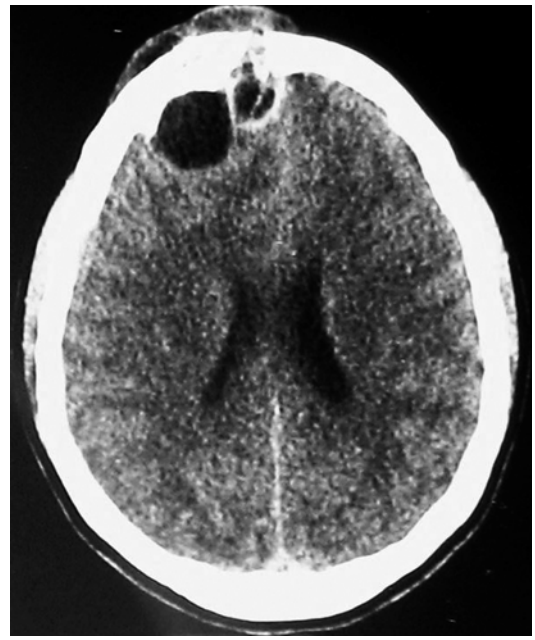

Fig. 5.7 Hydatid cyst of frontal bone on CT scan - axial view (Reproduced, with pemission, from Limaiem et al. 2009)

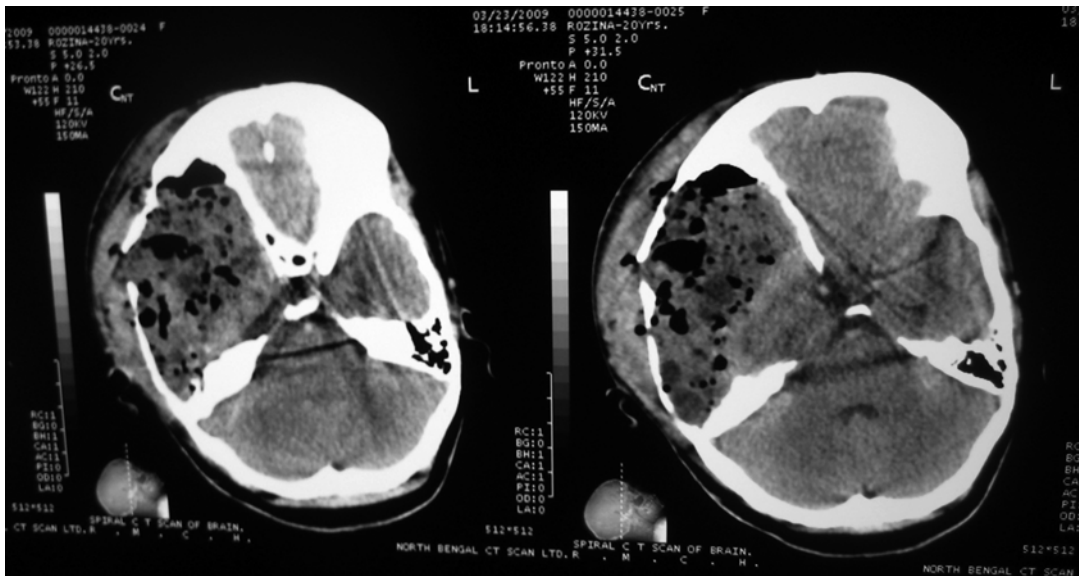

Fig. 5.6 Eroded bone with extracranial and intracranial extension of hydatid abscess seen on CT scan

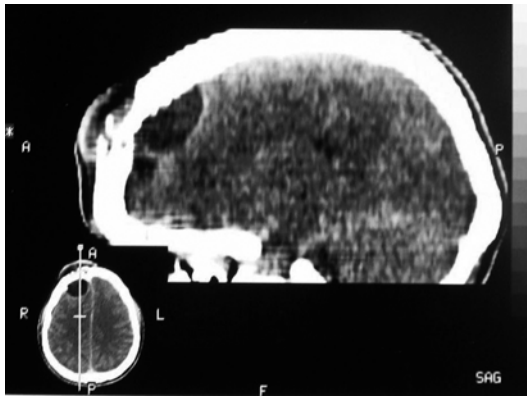

Fig. 5.8 Hydatid cyst of frontal bone on CT scan - sagittal view (Reproduced, with pemission, from Limaiem et al. 2009)

cyst enlarges in an irregular branching fashion along the path of least resistance. Over time, the parasite replaces the osseous tissue and destroys the cortex (Fig. 5.9a, b). Extraosseous hydatid cysts may calcify (Fig. 5.10), whereas intraosseous hydatid cysts rarely show calcification (Polat et al. 2003). Ringlike calcification of the cyst wall and extensive calcification in the cyst have also been reported (Dharkar 1996) (Fig. 5.11). Parasitized bone has heterogeneous medium to low signal intensity on T1-weighted MRIs and high signal intensity on T2-weighted images. CT demonstrates the calcification in extraosseous hydatid cysts (Polat et al. 2003). When hydatid cyst grows internally, it causes compression over the subjacent brain, but there will be no perilesional brain edema. If cyst becomes infected, there may be perilesional edema and cyst wall may take the contrast. Imaging has an important role in making a diagnosis of hydatid cyst. Hydatid cysts in unusual anatomical locations are difficult to diagnose on imaging, even in patients from endemic regions. Therefore, familiarity with imaging findings is crucial to make a preoperative diagnosis. On CT, this multiloculated cystic skull base lesion mimicked a malignant mass. MRI is a more useful imaging modality when a complex cystic head and neck lesion is present. A cystic lesion with multivesiculated "bunch of grapes" appearance, a peripheral T_2 hypointense rim ("rim sign"),

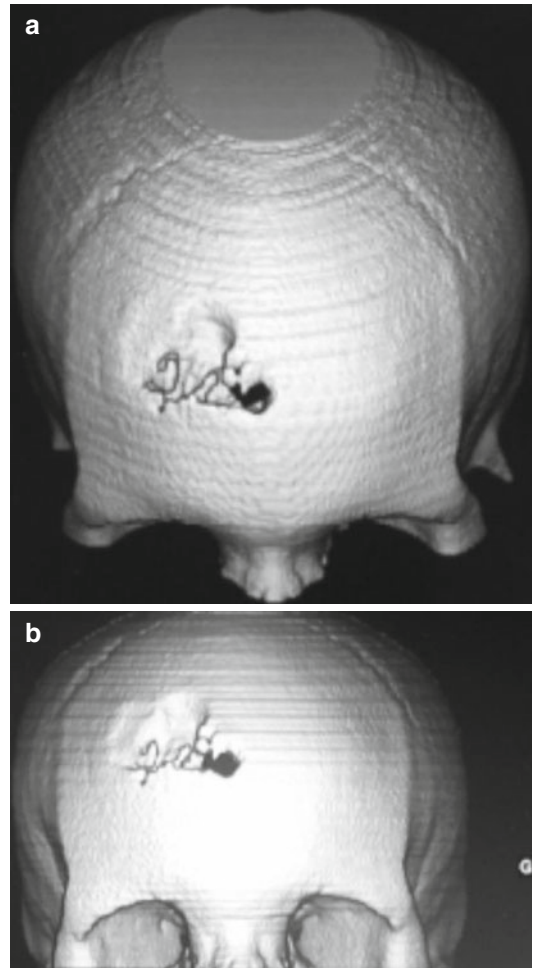

Fig. 5.9 (**a**, **b**) 3-D CT picture of hydatidosis of the cranial vault (Courtesy of F. Limaiem, MD)

and separated collapsed membranes as irregular low-signal-intensity linear floating structures ("serpent sign") were considered diagnostic for hydatid disease (Sureka et al. 2010).

Bone and brain tissue evokes minimal or no immunological response to hydatidosis. The peripheral blood and cerebrospinal fluid eosinophilia tests may be helpful for the diagnosis of hydatid disease (Erman et al. 2001; Limaiem et al. 2009). Serologic tests are valuable when they are positive, but they are usually false negative for osseous hydatidosis (Arazi et al. 2005; Limaiem et al. 2009). The Casoni and Weinberg tests, indirect hemagglutination, eosinophilia, and ELISA are used in diagnosing hydatid cysts,

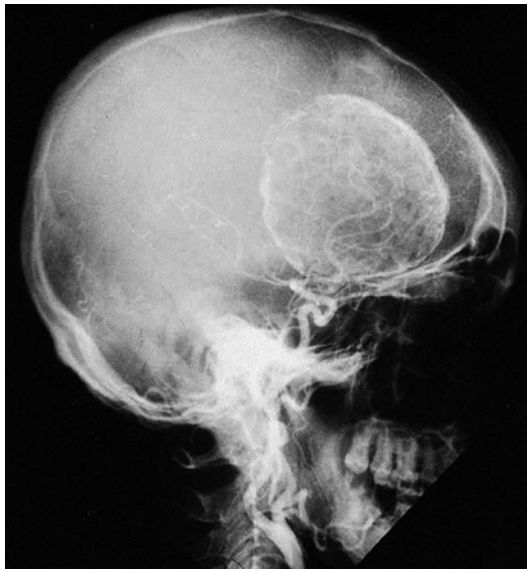

Fig. 5.10 Calcified hydatid cyst

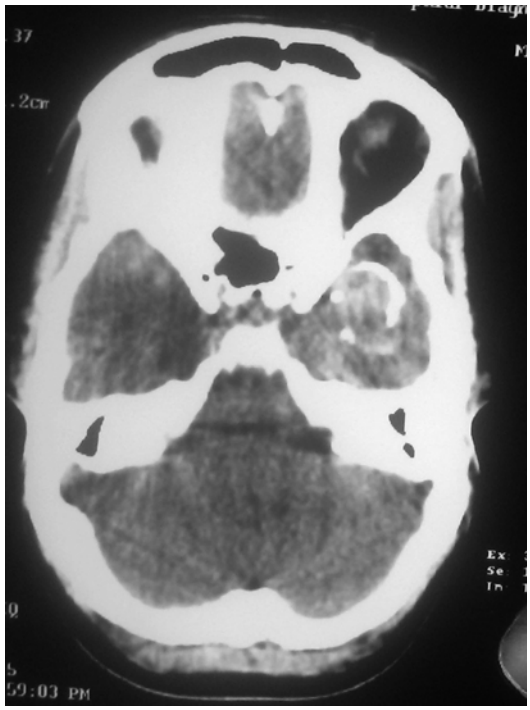

Fig. 5.11 Calcified cyst in the base of the skull (temporal)

but usually results tend to be false negatives (Khaldi et al. 2000; Andronikou et al. 2002; Cavusoglu et al. 2009; Reddy 2009; Nemati et al. 2010).

Differential Diagnosis

In particular, eosinophilic granuloma, cystic fibrous dysplasia, and calvarial epidermoid tumor/cyst must be considered in the differential diagnosis of intraosseous hydatid cyst. Eosinophilic granuloma is usually solitary and involves the diploe. CT scanning demonstrates a sharply marginated lytic skull defect more frequently involving the outer table than the inner table. The cystic form of fibrous dysplasia is usually homogeneously hypodense and typically has a smooth sclerotic border. An epidermoid tumor or cyst of the calvarium has a sclerotic rim and lacks inner trabeculae. Less likely considerations include solitary metastasis, brown tumor, and plasmacytoma. Metastases and brown tumors are rarely solitary, and they are characteristically poorly marginated. Plasmacytoma may be solitary; it usually has a septated, bubbly, and irregularly marginated appearance (Erman et al. 2001). Hydatid cyst growing internally causing compression over the brain can sometimes be confused with other space-occupying lesions of the brain, especially abscesses, neoplasms, and arachnoid cysts.

Treatment

Treatment of skull hydatid cyst should be aimed at the treatment of hydatidosis and skull defect caused by the cyst and treatment for the cyst (craniectomy). Both medical and surgical treatments are advocated for cranial hydatid disease. Medical therapy for small hydatid cysts has been promising. Albendazole alone or in combination with other compounds, such as praziquantel, has been reported with favorable results as an adjunct and, in certain circumstances, as the primary mode of treatment (Davis et al. 1989; Singounas et al. 1992; Todorov et al. 1992; Reddy 2009; Nemati et al. 2010). It is reported that albendazole results in the disappearance of up to 48 % of cysts and a substantial reduction in size of the cysts in another 28 % (Reddy 2009; Nemati et al. 2010). Albendazole therapy is given in a daily dose of 10 mg/kg, taken three times for 4 months (Al-Akayleh 2003).

The World Health Organization (WHO) recommendation on the duration of albendazole therapy is at least 3 months (Raynham et al. 2009). It is a broad-spectrum oral antihelminthic drug, which acts by blocking glucose uptake of the larva and adult worm. The glycogen storage is depleted, thereby decreasing the adenosine-5′-triphosphate formation resulting in death of the parasite (Al-Akayleh 2003).

Surgery is the mainstay of treatment for hydatid cyst of the skull. Total resection of the cyst along with the affected bone without rupture via the craniectomy is the recommended treatment; however, extradural hydatid cysts of intraosseous origin may be difficult to excise completely because of their adherence to dura and osseous trabeculae (Canbolat et al. 1994; Dharkar 1996; Erman et al. 2001; Limaiem et al. 2009). This, of course, is not possible when the disease affects the base of the skull (Dharkar 1996). During operation, the field of operation should be separated by hypertonic saline-soaked mop to minimize the spillage. After excision, the operative field should be generously irrigated with hypertonic saline solution. Chemotherapy should be continued postoperatively for 3–6 months (el Kohen et al. 2003; Raynham et al. 2009). Cysts in the base of the skull are aspirated by wide bore needle and injected with hypertonic saline or alcohol solution followed by partial or complete removal of the cyst. Then chemotherapy is continued for 3–6 months. Chemotherapy for hydatidosis of the central nervous system is discussed in Chap. 16.

Skull defect created by craniectomy is closed by cranioplasty with methyl methacrylate, i.e., bone cement or titanium plate. This can be done primarily if the surgeon is satisfied that the cyst is completely removed without any rupture or spillage. Steroids are helpful in relieving cranial nerve palsies (Dharkar 1996).

Complications

The most important complication of hydatid cyst is rupture with spillage of the hydatid fluid which is strongly immunogenic and may cause anaphylactic shock. This can happen during operation or due to head trauma which causes fracture of the skull bone. There has been repeated suggestion that coexistent bacterial infection of a liver hydatid cyst is possible, but suppuration of a hydatid cyst in the brain with daughter vesicles is an extremely rare occurrence. Erongun et al. (1994) found only two cases in the English literature from 1955 to 1991. Multiple infected cerebral hydatid cyst is uncommon entity and can be confused with other cystic brain lesions. Gana et al. (2008) described one case of infected hydatid cyst in the brain. Hossain et al. (2010) reported one case of abscess involving both intra- and extracranial spaces eroding the intervening bone. Complications of craniospinal hydatidosis are discussed in detail in Chaps. 17 and 18.

Conclusion

The following conclusions may be drawn from this chapter:

1. Hydatid disease of the skull is a rare entity.
2. Usually, it does not have any systemic sign unless it becomes ruptured or infected.
3. High index of clinical suspicion is required to diagnose the condition especially in the endemic areas. Painless swelling of the skull, unexplained features of raised intracranial pressure, focal neurological sign, or cranial nerve palsy should be investigated by CT scan or MRI as these are the most important tools for diagnosing the hydatidosis of the skull.
4. Bone and brain tissue evokes minimum or no immunological reaction to hydatidosis, so serologic tests are of little value in diagnosing the condition.
5. During operation, every effort should be made to prevent the spillage of the cyst fluid and to remove the cyst completely except in case of basal skull hydatidosis where complete removal of the cyst is not possible.

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Hydatidosis of the Brain

6

Faten Limaiem and Nidhameddine Kchir

Contents

Primary and Secondary Hydatidosis

Hydatid disease of the brain is a rare parasitic infestation which constitutes only 1–2 % of all intracranial space-occupying lesions (Mingde and Zheshang 1981; Micheli et al. 1987; Demir et al. 1991; Ciurea et al. 2006). Children are much more frequently affected than adults. In fact, 50–93 % of intracranial cysts are found in children younger than 17 years (Ciurea et al. 2006). In a previous study, this percentage was even higher, reaching 95.7 % (Ciurea et al. 2006). Characteristically, there is a predominance of males and children (Table 6.1) because these groups associate more closely with animals than do females and adults. In the meta-analysis of Turgut (2001), there were 67 male (56 %) and 52 female (44 %) patients. Conversely, in some series of brain hydatidosis (Tlili-Graiess et al. 2006; Ali et al. 2009), there was a slight female predominance. It has been suggested that an underlying ductus arteriosus patency during the neonatal period may be a cause of increased vulnerability of children by allowing passage of the parasites from the periphery to the brain (Lunardi et al. 1991; Onal et al. 2006).

In humans, intracranial hydatidosis can be associated with involvement of other organs such as liver or lung, or it may be an isolated infestation of the brain. Only embryos which succeed in passing through the filtering barrier systems in the liver and lung reach the brain by the systemic circulation. Once the hexacanth embryo has reached the brain, it will form a hydatid cyst

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Table 6.1 Epidemiological characteristics of brain hydatidosis reported in some series between 1999 and 2012

Author(s)	Year	Number of cases	Sex ratio (M:F)	Mean age (years)
Gupta et al.	1999	5	3:2	13.4
Khaldi et al.	2000	117	Slight male predominance	7.2
Bükte et al.	2004	18	2:1	20.3 (7–50 years)
Ciurea et al.	2006	76	45:31	Children: 8.7 Adults: 29.3
Tlili-Graiess et al.	2006	25	0.78	14 (30 months–56 years)
Ali et al.	2009	21	1:1.3	7.42 ± 3.2
Duishanbai et al.	2010	30	21:9	11
Basraoui et al.	2010	9	1:1	7.5
Mohindra et al.	2012	9	7:2	7 (4–44 years)

because of the ideal growth conditions (Turgut 2001). Although hydatid disease may be located anywhere in the brain, it most frequently involves the cerebral hemispheres (90–95 % of the cases) (Abbassioun and Amirjamshidi 2001). Other reported sites of intracranial hydatid cysts include subarachnoid space, ventricles, pons, cerebellum, aqueduct of Sylvius, extradural space, and diploic space of skull bones (Gokalp and Erdogan 1988; Cemil et al. 2009; Furtado et al. 2009).

Brain hydatid cysts are most often localized supratentorially in the distribution of the terminal branches of the middle cerebral artery, usually temporo-parieto-occipitally (Behari et al. 1997; Tuzun and Hekimoglu 1998). Left hemispheral predominance has been noted in several series in the literature and is explained by the emergence of the left common carotid artery directly from the aortic arch (Ciurea et al. 2006). Three forms of intracranial hydatid disease occur: intracerebral, intracranial extradural, and a combined form (Samiy and Zadey 1965; Ba'assiri and Haddad 1984; Canbolat et al. 1994; Cemil et al. 2009). Intracranial epidural hydatid disease is extremely rare because the physiologic flow of blood to the brain is mainly through the internal carotid system, so the likelihood of the larvae traveling through the external carotid system is very rare (Samiy and Zadey 1965; Ba'assiri and Haddad 1984; Canbolat et al. 1994).

Multiple hydatid cysts of the brain are very rare. Primary multiple cysts of the brain resulting from arterial embolism and without any radiological or clinical evidence of hydatid disease elsewhere in the body are extremely rare (Iplikcioğlu et al. 1989; Gupta et al. 1991; Mancuso et al. 1997; Ozkan et al. 2001; Karadağ et al. 2004). In a review of the literature related to primary multiple intracranial cerebral hydatid cysts, we were able to find only 19 cases (Table 6.2). Secondary multiple hydatid cysts of the brain can result from spontaneous, traumatic, or surgical rupture of a primary solitary cerebral cyst or as a consequence of a cyst rupture elsewhere and embolization of hydatids to the brain (Nurchi et al. 1992; Martin Oterino et al. 1996; Mancuso et al. 1997; Anvari et al. 2009). Multiple hydatid cysts resulting from the rupture of a primary cyst are acephaloceles; they are infertile and have no brood capsule and scolices (Lunardi et al. 1991; Ciurea et al. 2006; Onal et al. 2006).

Primary hydatid infestation caused by embryos which escaped hepatic and pulmonary barriers is generally single and fertile. On the other hand, secondary hydatidosis caused by scolices from ruptured fertile cysts is usually multiple and sterile. It is usually caused by myocardial cysts rupturing into the left ventricle. In a review of 112 children with cerebral hydatid cysts, Carcassone et al. (1973) found only four cases of multiple cysts in the brain (4 %). In the meta-analysis of Turgut (2001), there were 53 cases of multiple cysts (19 %), and the source of secondary multiple cysts was the left ventricle of the heart in two patients. For this reason, in such cases the heart must be carefully investigated as the source of the secondary multiple intracranial cysts. There is no consensus on the growth rate of

Table 6.2 Summary of the previously reported primary multiple cerebral hydatid cysts

Author(s), year(s)	Age/sex	Localization	Treatment	Outcome
Sharma et al. (1982)	9/F	5 cysts in the right supratentorial region	Surgery	Good
Todorov et al. (1988)	45/M	8 cysts in the frontal, temporal, parieto-occipital regions	Albendazole	Good
Paşaoğlu et al. (1989)	15/M	3 cysts in the left frontoparietal and 1 cyst in the left occipital regions	Surgery	Good
İplikcioğlu et al. (1989)	7/F	3 cysts in the right frontal, 2 cysts in the left occipital, 1 cyst in the left frontal regions	Surgery	Good
Cataltepe et al. (1991)	8/M	2 cysts in both parieto-occipital regions	Surgery	Good
Gupta et al. (1991)	18/M	Multiple cysts in both cerebral and left cerebellar hemispheres	Surgery	Died
Nurchi et al. (1992)	9/M	30 cysts in the right parietal and occipital regions	Surgery	Good
Bilge et al. (1993)	37/M	2 cysts in the left frontoparietal and occipital regions	Surgery	Good
Martin Oterino et al. 1996	69/F	Multiple cysts in both cerebellar and temporal regions	Albendazole	Died
Mancuso et al. (1997)	62/M	1 cyst in the right frontal and 1 cyst in the left frontal regions	Surgery	Good
Baysefer et al. (1998)	20/M	20 cysts in the left frontoparietal regions	Surgery	Good
Popli et al. (1998)	20, M	Multiple cysts in the left temporoparietal region	Surgery + albendazole	Good
Ozkan et al. (2001)	8, M	More than 25 cysts in the left temporo-parieto-occipital region	Surgery	Good
Nowak et al. (2002)	46, F	2 cysts in the cerebral and cerebellar regions	Albendazole	Good
Karadağ et al. (2004)	45, F	2 cysts in the right parietal region	Surgery	Good
Yurt et al. (2007)	19, F	24 cysts in both cerebral hemispheres	Surgery + albendazole	Good
Erkutlu et al. (2008)	15, M	2 cysts in the right parietal and occipital regions	Surgery	Good
Cavusoglu et al. (2009)	15, M	19 hydatid cysts in the right parieto-occipital region	Surgery	Died

the hydatid cyst of the brain and has been variably reported between 1.5 and 10 cm per year. Importantly, hydatid cyst has been shown to grow faster in the cerebrum than in the liver by a ratio of 3:1 revealing that brain like the lung tissue facilitates growth of the cyst as it is a compressible organ (Abbassioun and Amirjamshidi 2001; Andronikou et al. 2002). According to a review by Duishanbai et al. (2010), supratentorial hydatid cysts tend to be larger than the infratentorial counterparts when causing symptoms.

Diagnostic Approach

Quite independently of the hydatid cyst localization and the circumstances of its discovery, the diagnostic approach is always the same based on epidemiological, clinical, biological, imaging, and pathological arguments.

Epidemiological Data

Patients are usually from rural areas; they may have hydatid contact and live in canine environment. Children are in close contact with dogs. People are not practicing proper sanitary procedures and eating raw and uncooked or improperly cooked vegetables contaminated with *Echinococcus ova*.

Clinical Data

Intracranial hydatid cyst presents with a wide range of clinical manifestations which mainly depend on the location and size of a given hydatid cyst (Altinörs et al. 2000). Cysts develop insidiously, usually being asymptomatic initially, and present with protean clinical and imaging features (Ersahin et al. 1993). Headache

and vomiting due to raised intracranial tension are the most common presenting features (Carrea et al. 1975; Ersahin et al. 1993). Other manifestations of cerebral hydatid cysts are seizures, hemiparesis, visual disturbances, and ataxia. Papilledema is usually present at the time of presentation in children with cerebral hydatid cysts. Evidence of pyramidal tract dysfunction, appropriate to the location of the cyst, is noted in almost 90 % of patients. Mental changes are noted in 25 % of children and seizure activity in approximately 20 %. Other symptoms such as hemiparesis, seizures, visual field alteration, and gait disorders may vary with the location of the cyst (Paşaoğlu et al. 1989; Ozek 1994; Yuceer et al. 1998). According to some authors, clinical presentation of cerebral hydatidosis is somewhat different in children and adults (Micheli et al. 1987; Ersahin et al. 1993). Signs of increased intracranial pressure with papilledema dominate in the younger age group, whereas focal findings such as hemiparesis, speech disorders, and hemianopsia, sometimes associated with epileptic seizures, are more prevalent in the older age group (Micheli et al. 1987; Ersahin et al. 1993). The disparity between the size of the cyst and clinical presentation is an important feature of cranial hydatid cysts (Andronikou et al. 2002). In addition, duration time of symptoms is found to be an independent predictor of the outcome (Duishanbai et al. 2010).

Biological Diagnosis

Routine work-up of hydatid disease comprises blood investigations and serological tests. Blood investigations are abnormal in only few patients who demonstrate raised eosinophilic count. The serological tests are of little practical value in confirming the diagnosis of cerebral echinococcal disease (Popli and Khudale 1998). In systemic hydatidosis, serological test (Casoni skin test) is generally positive. However, in cerebral and intracranial hydatidosis, these serological tests are almost always negative (Baden and Elliot 2003).

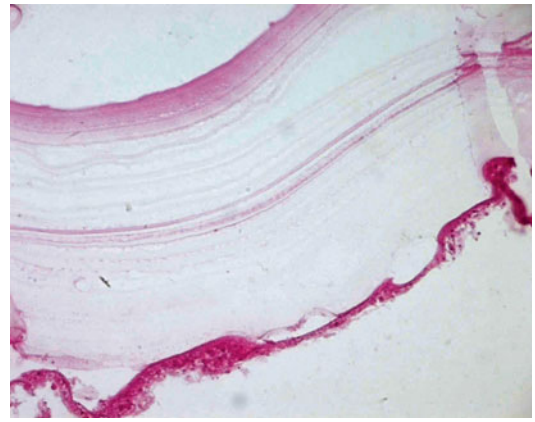

Fig. 6.1 Microscopic picture showing the laminated membrane and the germinal layer of the cyst (Haematoxylin and Eosin, magnification × 400)

Nonspecific Biology

The hemogram inconstantly shows hypereosinophilia.

Specific Biological Diagnosis of Hydatidosis

Direct Evidence of Parasitic Elements

Direct evidence of parasitic elements can be obtained from surgical samples. The parasitic elements to be sought are the cyst membranes, protoscolices, and hooklets. Although radiological investigations can be very helpful in identifying hydatid cysts preoperatively, their diagnosis is mainly based on histopathological examination (Figs. 6.1 and 6.2).

Histopathologically, the hydatid cyst has three layers: (a) First is the outer pericyst, composed of modified host cells. This layer is a dense fibrous zone in the liver and other organs. In the brain, however, there is only a shiny fine gliotic layer without any remarkable resistance surrounding the primary unruptured cysts. (b) The next layer is the middle laminated membrane which is acellular and allows the passage of nutrients. (c) The third is the inner germinal layer where the scolices (the larval stage of the parasite) and the laminated membrane are produced.

The middle laminated membrane and the germinal layer form the true wall of the cyst usually referred to as the endocyst. Daughter cysts are small spheres containing the protoscolices. The

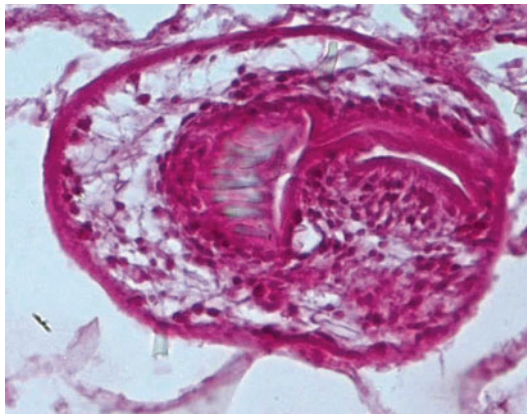

Fig. 6.2 Microscopic picture showing an enlarged view of a scolex. This section also includes the rostellar hooks (Haematoxylin and Eosin, magnification × 400)

innermost layer which is the germinative or fertile membrane performs two major functions: (a) production of the laminated membrane outward and (b) germination of a new generation of scolices inward. The formation of scolices takes place from the brood capsules attached to the germinative membrane. The pedicle of the brood cysts is very loosely attached to the germinal layer of the mother cyst. On gross examination, the vesicles resemble a bunch of grapes and may grow through the wall of the mother cyst. Cyst fluid, clear or pale yellow, has a neutral pH and contains sodium chloride, proteins, glucose, ions, and polysaccharides and is antigenic. When brood cysts and vesicles detach within the cyst, and pass into the cyst fluid, they form a white sediment known as "hydatid sand." Mild mononuclear cell infiltrates and occasional foreign body giant cells surround the cysts (Ameli and Abbassioun 1995).

Hydatid Serology

Serum is generally used for the detection of specific antibodies. Qualitative techniques include immunoelectrophoresis, electrosyneresis, and enzyme-linked immunoelectrodiffusion assay. Quantitative techniques include indirect hemagglutination and enzyme-linked immunosorbent assay, indirect immunofluorescence, and a review of the IgE level and of the immune complex.

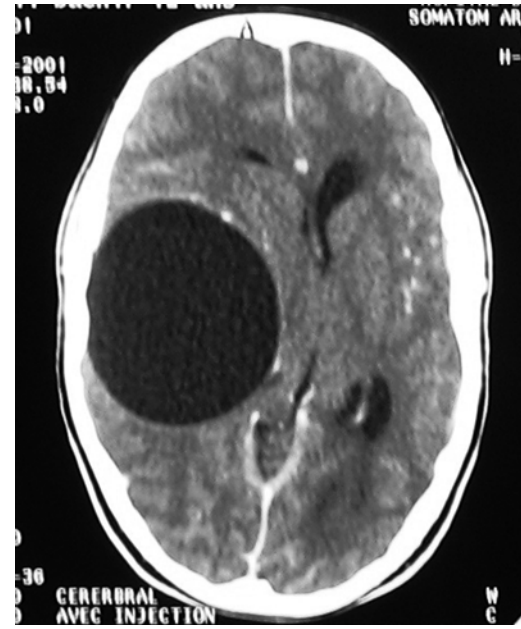

Fig. 6.3 Preoperative CT scan showing a right temporoparietal unilocular cyst with homogeneous fluid attenuation and midline shift toward left

Laboratory findings of patients with hydatidosis of central nervous system are discussed in Chap. 10.

Imaging Diagnosis

Imaging with CT and MRI are central to the diagnosis of cerebral hydatid cysts (Figs. 6.3, 6.4, 6.5, 6.6, 6.7, 6.8 and 6.9). Both are equally good for detection and localization of the cyst in brain. Whereas CT is better in demonstrating cyst wall calcification, MRI has an advantage in delineating the relationship of the cyst with adjacent structures (Bükte et al. 2004). Typical CT features of cerebral hydatid cyst include a spherical or oval homogenous fluid attenuation generally in the temporal and parietal lobes of cerebral hemispheres (Demir et al. 1991; Karak et al. 1992). Cystic lesion is usually large with significant mass effect in the form of ventricular compression and midline shift. Calcification in the cyst wall is very rare, seen in around 1 % of cases (McCorkell and Lewall 1985; Rudwan and Khaffaji 1988). No enhancement or perilesional

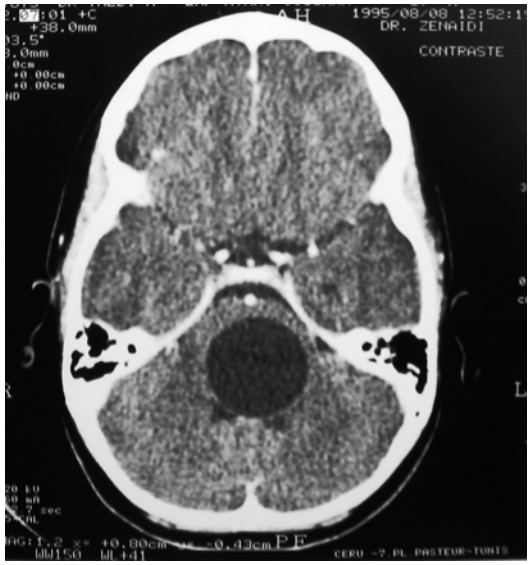

Fig. 6.4 Preoperative CT scan demonstrating a hydatid cyst of the brain stem with homogeneous fluid attenuation

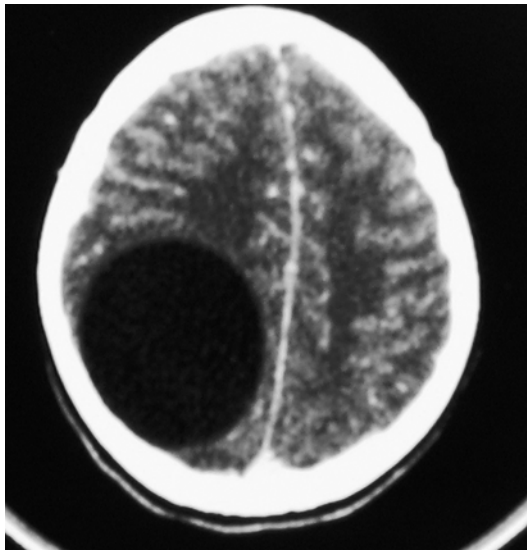

Fig. 6.5 Preoperative CT scan revealing a right univesicular occipitoparietal hydatid cyst

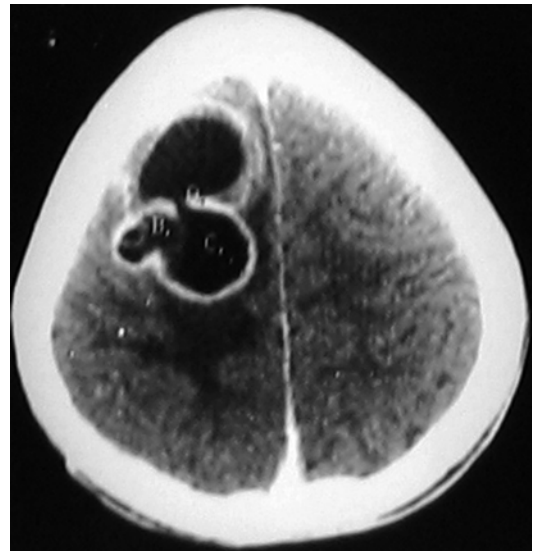

Fig. 6.6 Preoperative CT scan showing a thick-walled multivesicular, right frontal hydatid cyst

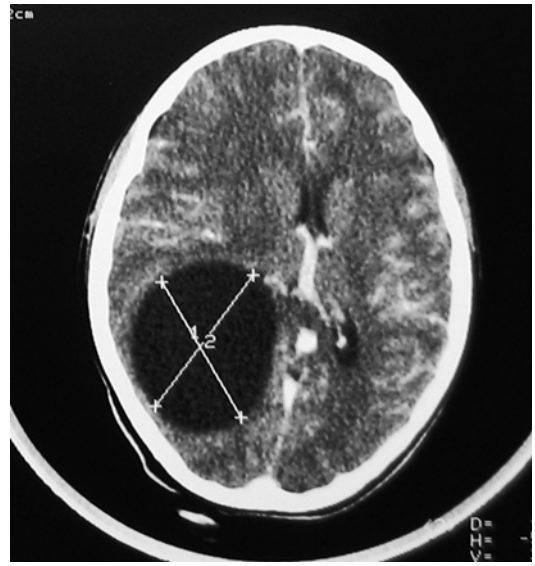

Fig. 6.7 Preoperative CT scan demonstrating a right parieto-occipital, spherical homogenous fluid attenuation mass with thin smooth wall and midline shift to left; no perilesional edema is seen. 1 and 2 are the two greatest diameters of the hydatid cyst

edema is seen in case of uncomplicated hydatid cysts. Enhancement of the cyst and perilesional edema in a case of cystic echinococcosis of brain indicates complications like rupture, hemorrhage, or infection in the cyst.

Although CT scan and MRI have greatly contributed to a correct early diagnosis, in a substantial number of cases, diagnosis is obtained postoperatively. A high index of suspicion, when a cystic mass is found on CT or MRI, is therefore required in endemic areas, but also in non-endemic areas, since migration and frequent traveling have changed

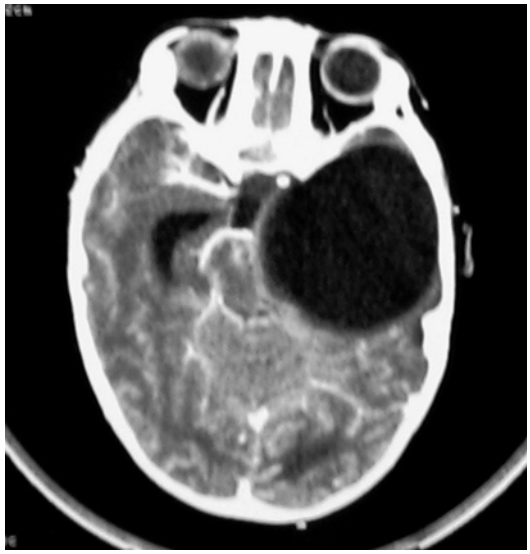

Fig. 6.8 Preoperative CT scan: unilocular left frontotemporal hydatid cyst with homogeneous fluid attenuation

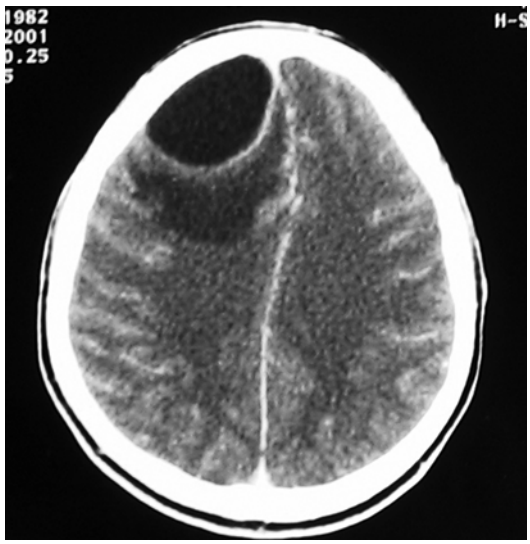

Fig. 6.9 Preoperative cerebral CT scan showing a right frontal univesicular hydatid cyst with perilesional edema

the worldwide occurrence. Newer imaging techniques, such as magnetic resonance spectroscopy and diffusion-weighted MRI, might further refine the diagnostic armamentarium (Ciurea et al. 2006).

The differential diagnosis of intracranial hydatid cysts includes cystic lesions such as porencephalic cyst, arachnoid cyst, cystic tumors of the brain, and pyogenic abscesses (Cataltepe et al. 1992; Sahin-Akyar 2002). In contrast to hydatid cysts, porencephalic cysts and arachnoid cysts are not spherical in shape and are not surrounded entirely by brain substance. Arachnoid cysts are extra-axial masses that may deform adjacent brain. Porencephalisc cysts result from insults to normal brain tissue and are lined by gliotic white matter that could easily be demonstrated with MRI (Topal et al. 1995; Tuzun et al. 2002).

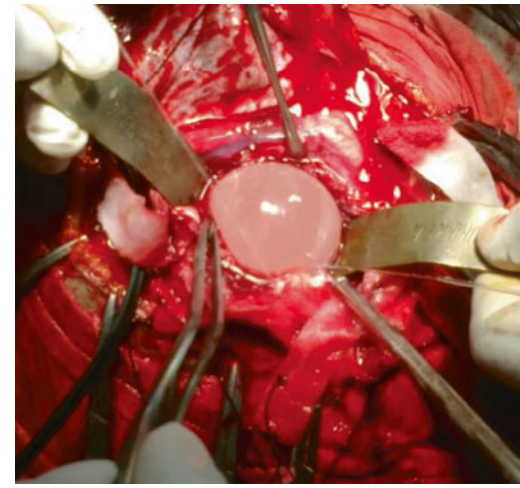

Fig. 6.10 Hydatid cyst being removed from brain (Courtesy of N. Khaled, M.D.)

Imaging of cerebral hydatid disease is discussed in detail in Chap. 11.

Treatment

In toto surgical removal of intracranial hydatid cysts remains the treatment of choice for cerebral hydatidosis (Figs. 6.10 and 6.11). The aim of surgery is to excise the cyst completely without rupture to prevent anaphylactic reaction and local recurrence. Preoperative diagnosis of cerebral hydatid cyst made on the basis of typical CT or MRI findings is an important component in the chain of events to prevent cyst rupture during surgery (Negovetic et al. 1990).

Subdural effusions and development of obstructive hydrocephalus are well-documented postoperative complications. Postoperative seizures (Abbassioun et al. 1978; Ersahin et al. 1993), development of porencephalic cysts, focal

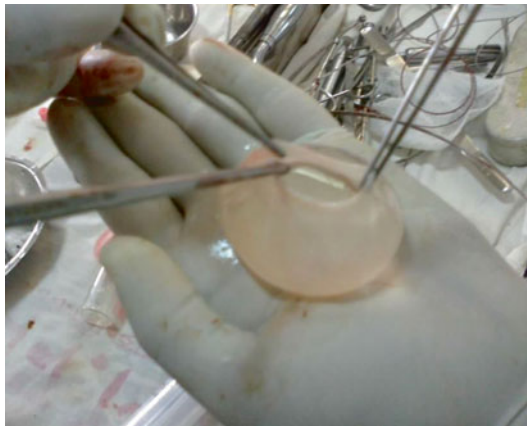

Fig. 6.11 Removed intact cyst being dissected (Courtesy of N. Khaled, M.D.)

signs (e.g., paresis), and nonbacterial meningitis have also been reported (Lunardi et al. 1991). Intraoperative rupture of the cyst may result in early death due to anaphylactic shock.

Chemotherapy is an adjunct treatment for patients with inoperable multiple cysts or deep-seated cysts and in those who are not good candidates for surgery or may be suffering from recurrent cysts (Yurt et al. 2007). Reported to be clinically effective, antihelminthic agents for the medical treatment of hydatid cyst are mebendazole and albendazole (Turgut 1998), but its effectiveness is still unclear.

Prognosis depends largely on accurate preoperative diagnosis, which is of extreme importance for the successful removal of an unruptured cyst. Long-term follow-up confirms that the outcome of intracranial hydatidosis without intraoperative cyst rupture remains excellent. Recurrence and multiplicity of cysts seem to be the most significant negative factors affecting the long-term outcome of patients with intracranial hydatid disease (Ciurea et al. 2006). Hydatid disease is generally a severe disease, with over 90 % mortality in untreated patients (Per et al. 2009).

Treatment of cerebral hydatid disease is discussed in detail in Chaps. 15 and 16.

Conclusion

Despite the introduction of modern surgical and pharmacological therapy, brain hydatid disease continues to be a substantial cause of morbidity and mortality in many parts of the world. New approaches to control and prevention of hydatidosis, including an effective livestock vaccine, potential dog vaccines against the tapeworm stage of *Echinococcus granulosus*, tailored educational programs, development of better diagnostics for definitive hosts and human beings (including dog coproantigen detection), more effective antiparasitic treatments, and the use of mathematical models to simulate best possible cost-effective interventions, will be expected to shorten the time of the attack phase and improve surveillance in the consolidation phase of hydatid control programs (Chabalgoity et al. 2000; McManus et al. 2003; Torgerson 2006).

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Intraventricular Hydatidosis

7

Sunil V. Furtado and Sumit Thakar

Contents

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Introduction

Epidemiology

Hydatid disease caused by ingestion of eggs of the cestode *Echinococcus granulosus* is endemic in the Middle East, Mediterranean region, South America, North Africa, India, and Australia (Onal et al. 1997). Intracranial hydatid disease, seen in 1–2 % of all patients with hydatidosis, accounts for 0.02–0.22 % of all intracranial space-occupying lesions (Rahimizadeh and Hadadian 1984; Mohindra et al. 2012). Their growth rate has been reported to vary between 1.5 and 10 cm/year (Gupta et al. 1999). An exclusive intraventricular occurrence of the disease is rare.

Classification

Intracranial hydatid cysts may be classified as primary or secondary. Primary cysts are due to direct infestation of the brain by larvae, and secondary cysts result from spontaneous, traumatic, or surgical rupture of a primary intracranial hydatid cyst. The latter variety is infertile and lacks brood capsules and scolices. In one of our patient, the smaller cysts were probably seeded by rupture of the larger primary cyst, which was compressing them anteriorly against the brainstem (Figs. 7.1 and 7.2).

Primary and secondary hydatidoses of the brain are discussed in Chap. 6.

M. Turgut (ed.), *Hydatidosis of the Central Nervous System: Diagnosis and Treatment*,
DOI 10.1007/978-3-642-54359-3_7,

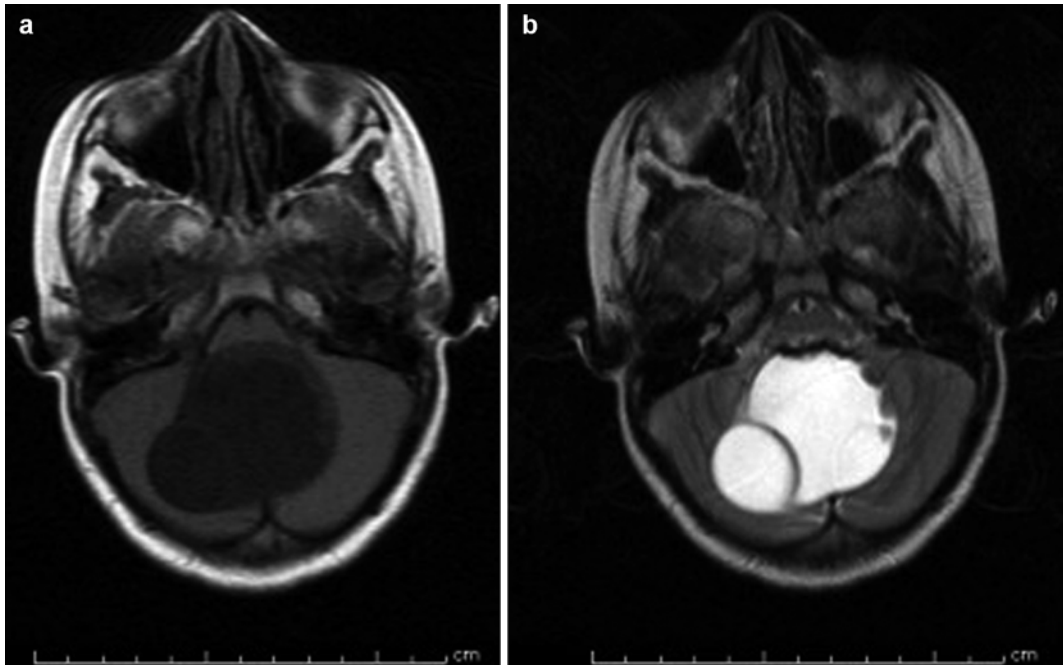

Fig. 7.1 (**a**) Axial T1-weighted image and (**b**) T2-weighted MRI showing two large hydatid cysts with the smaller cysts pushed anteriorly

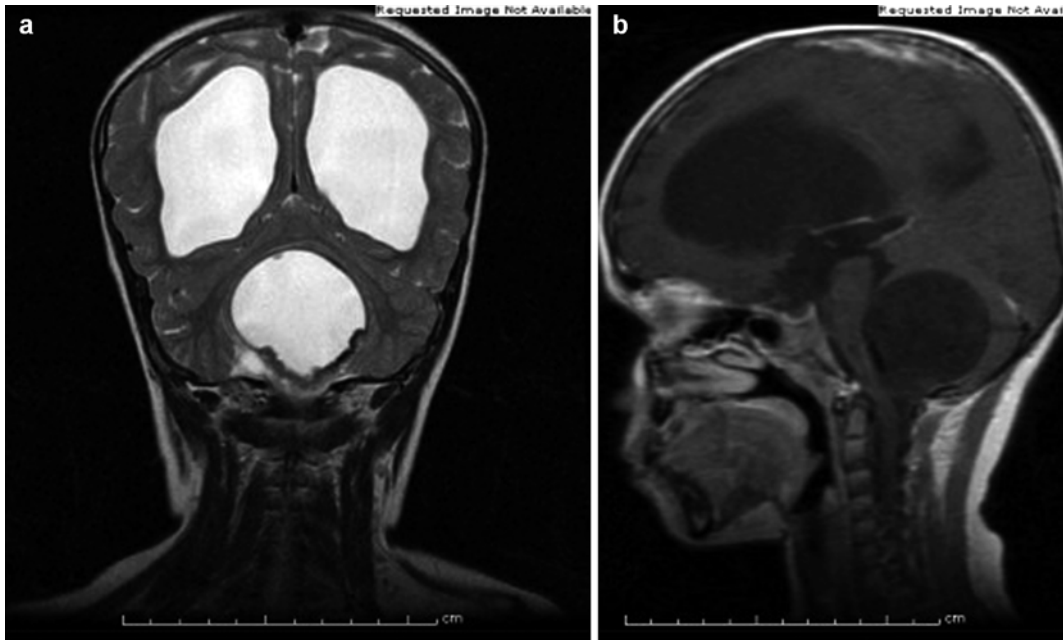

Fig. 7.2 (**a**) Coronal T2-weighted MRI showing a large cyst with daughter cysts filling the fourth ventricle. (**b**) Sagittal contrast image demonstrating no contrast enhancement

Intraventricular Hydatidosis

Multiple intracranial hydatid cysts are rare and are seen in about 10–15 % of intracranial hydatidosis (Ugur et al. 1998). Ruggiardo, in 1902, was the first to report the perforation of the ventricle by an intracerebral cyst (Valentino 1959). A literature search in PubMed revealed numerous reports of supratentorial intraventricular hydatid cysts (Negovetic et al. 1990; Lunardi et al. 1991; Peker et al. 1991; Cataltepe et al. 1992; Diren et al. 1993; Karadağ et al. 2004; Ciurea et al. 2006; Kamath et al. 2009; Mohindra et al. 2012) and only 9 reports of solitary cysts in the fourth ventricle (Rahimizadeh and Hadadian 1984; Pau et al. 1987; Gelabert Gonzalez et al. 1988; Singounas et al. 1992; Turgut 2001; Bukte et al. 2004; Furtado et al. 2009; Duishanbai et al. 2010; Mohindra et al. 2012). Turgut (2002) described a 13 % incidence of intraventricular hydatidosis based on a meta-analysis of all reported intracranial hydatidosis cases in the pediatric and adolescent group in Turkey. Table 7.1 provides a comprehensive list of all cases with intraventricular hydatidosis in indexed literature to date.

It has been postulated that oncospheres reach the ventricular cavity along the choroid plexus (Guzel et al. 2008). Another proposed mechanism is the spillage of ruptured primary cysts situated near the ependymal lining into the ventricle, causing multiple secondary cysts (Evliyaoglu and Keskil 2005). Like in other sites, surgery is the treatment of choice for intraventricular lesions, with cyst removal without spillage of fluid being the main prognostic factor (Altinörs et al. 2000; Furtado et al. 2009; Mohindra et al. 2012).

Presentation

Raised Intracranial Pressure

Intraventricular hydatidosis may either be asymptomatic or present with features of raised intracranial pressure, depending on the location of the cyst(s). Cysts in the posterior fossa, reportedly smaller than their supratentorial counterparts (Mohindra et al. 2012), and those in the posterior third ventricle or at the foramen of Monro are more likely to obstruct cerebrospinal fluid (CSF) pathways, causing hydrocephalus. All our patients reported headache and vomiting, while one patient with long-standing symptoms presented additionally with secondary optic atrophy and gait disturbances.

Incidental Pickups

In many cases, the lesions are incidentally picked up in the setting of multiple parenchymal cerebral lesions presenting with seizures or focal neurological deficits, or of systemic hydatidosis as seen in one of our patients with supernumerary seedling from a cardiac source with secondary intracranial cysts in the parenchyma and lateral and fourth ventricles (Fig. 7.3).

Unusual Symptoms

Location-specific symptoms include fluctuating signs of raised pressure like in one of our cases where the cyst was straddling the foramen of Monro, brainstem compression or cerebellar dysfunction like in one case involving the fourth ventricle (Figs. 7.1, 7.2, and 7.4), or third nerve paresis secondary to a trapped temporal horn (Choux et al. 1976; Onal et al. 1997; Evliyaoglu and Keskil 2005; Furtado et al. 2009; Mohindra et al. 2012).

Radiological Investigations

Computed Tomography Findings

Plain radiographs of the calvarium and cerebral angiography have lost their importance in the diagnosis of intracranial hydatidosis. On computed tomogram, unilocular cysts are often large, spherical, and homogenous lesions with sharply defined borders. There may be septations within the cysts, and these may occasionally be calcified. Less than 1 % of cases demonstrate calcification of the walls (Bukte et al. 2004). The thin

Table 7.1 Summary of selected cases with intraventricular hydatidosis published in indexed literature to date

Author(s)	Country	Year	Patient age (years), sex	Location	No. of cases/cysts	Presentation	Outcome
Filipov and Karag'ozov	Bulgaria	1955	NA	NA	NA	NA	NA
Djindjian and Porot	France	1957	NA	NA	NA	NA	NA
Valentino	Italy	1959	17, F	Lateral ventricle	1 case	Headache, vomiting	Favorable
Borne	France	1964	NA	NA	NA	NA	NA
Kaya et al.	Turkey	1975	21, F	Lateral ventricle	1 case	Headache, personality changes, papilledema	Multiple recurrences
	Turkey	1975	8, F	Lateral ventricle	1 case	Headache, papilledema, diplopia	Favorable
	Turkey	1975	12, M	Lateral ventricle	1 case	Headache, vomiting, papilledema	Favorable
	Turkey	1975	13, F	Lateral ventricle	1 case	Foster Kennedy syndrome, optic atrophy, seizure	Postoperative death
Rahimizadeh and Hadadian	Iran	1984	12, M	Fourth ventricle	1 case	Headache, vomiting, ataxia	Favorable
Pau et al.	Italy	1987	11, F	Lateral ventricle	Multiple	Hemiparesis	Favorable
	Italy	1987	58, M	Fourth ventricle	Multiple	Drowsiness, hemiparesis	Died
Gelabert Gonzalez et al.	Spain	1988	NA	Fourth ventricle	1 case	NA	A
Negovetic et al.	Yugoslavia	1990	20, F	Lateral ventricle	Multiple	Headache, seizure	Favorable
Peker et al.	Turkey	1991	15, M	Fourth ventricle and lateral ventricle	Multiple	Headache, nausea	Died
Cataltepe et al.[a]	Turkey	1992	NA	Lateral ventricle	12 cysts	NA	NA
	Turkey	1992	NA	Fourth ventricle	3 cysts	NA	NA
	Turkey	1992	NA	Aqueduct of Sylvius	1 cyst	NA	NA
	Turkey	1992	NA	Third ventricle	3 cysts	NA	NA
Copley et al.	South Africa	1992	12, F	Lateral ventricle	Multiple	Headache, dizziness	Favorable
	South Africa	1992	7, M	Lateral ventricle	1 case	Proptosis	Favorable

Singounas et al.	Greece	1992	33, F	Fourth ventricle	1 case	Headache, seizure	Favorable
Diren et al.	Turkey	1993	10, F	Lateral ventricle	1 case	Headache, visual deterioration	No follow-up
Altinörs et al.	Turkey	2000	NA	Intra- or periventricular	9 cases	NA	NA
	Turkey	2000	NA	Aqueduct of Sylvius	1 case	NA	NA
Onal et al.	Turkey	2001	NA	NA	5 cases	NA	NA
Turgut [b]	Turkey	2001	NA	Lateral ventricle	14 cases	NA	NA
	Turkey	2001	NA	Third ventricle	4 cases	NA	NA
	Turkey	2001	NA	Fourth ventricle	3 cases	NA	NA
	Turkey	2001	NA	Aqueduct of Sylvius	2 cases	NA	NA
	Turkey	2001	NA	Not specified	4 cases	NA	NA
Aydin et al.	Turkey	2002	18, M	Lateral ventricle	Multiple	Headache, blurred vision	Favorable
Karadag et al.	Turkey	2004	45, F	Lateral ventricle	2 cysts	Seizure	Favorable
Sherwani et al.	India	2003	10, F	Lateral ventricle	1 case	Headache, seizure	Favorable
Bukte et al.	Turkey	2004	7, F	Fourth ventricle	1 case	Cerebellar signs, ataxia	Favorable
Evliyaoglu and Keskil	Turkey	2005	7, F	Lateral ventricle	1 case	Headache, nausea, spasticity, cerebellar signs	Favorable
Iyigun et al.	Turkey	2004	2, M	Lateral ventricle	Multiple	Focal neurological deficit	Favorable
Ciurea et al.	Romania	2006	NA	Not specified	1 case	Raised intracranial pressure	Favorable
Guzel et al.	Turkey	2008	10, F	Lateral ventricle	1 case	Raised intracranial pressure	Favorable
Kamath et al.	India	2009	6, M	Lateral ventricle	1 case	Hemiparesis, headache	Favorable
Duishanbai et al.	China	2010	6, M	Fourth ventricle	1 case	Ataxia	Favorable
	China	2010	8, M	Fourth ventricle	1 case	Ataxia	Favorable
Guvenc et al.	Turkey	2011	33, F	Lateral ventricle	1 case	Headache, vomiting	Favorable

(continued)

Table 7.1 (continued)

Author(s)	Country	Year	Patient age (years), sex	Location	No. of cases/cysts	Presentation	Outcome
Mohindra et al.	India	2012	6, F	Lateral ventricle	1 case	Seizure	Favorable
	India	2012	5, M	Lateral ventricle	1 case	Increase in head size	Favorable
	India	2012	7, M	Lateral ventricle	3 cases	Headache, vomiting	Favorable
	India	2012	44, F	Fourth ventricle	4 cases	Headache, vomiting	Favorable
Majumdar et al.	India	2013	7, F	Lateral ventricle	1 case	Headache, vomiting	Favorable
Present series	India	2012	8, F	Fourth ventricle	Multiple	Headache, spasticity, visual disturbance, cerebellar signs	Favorable
	India	2012	9, M	Lateral ventricle and fourth ventricle	Multiple	Raised intracranial pressure	Recurrence

Abbreviations: *F* female, *M* male, *NA* not available data

[a]One of the cases reported by the authors had already been described by Peker et al. (1991)

[b]The cases reported by the author had already been described by Kaya et al. (1975), Peker et al. (1991), Cataltepe et al. (1992), and Diren et al. (1993)

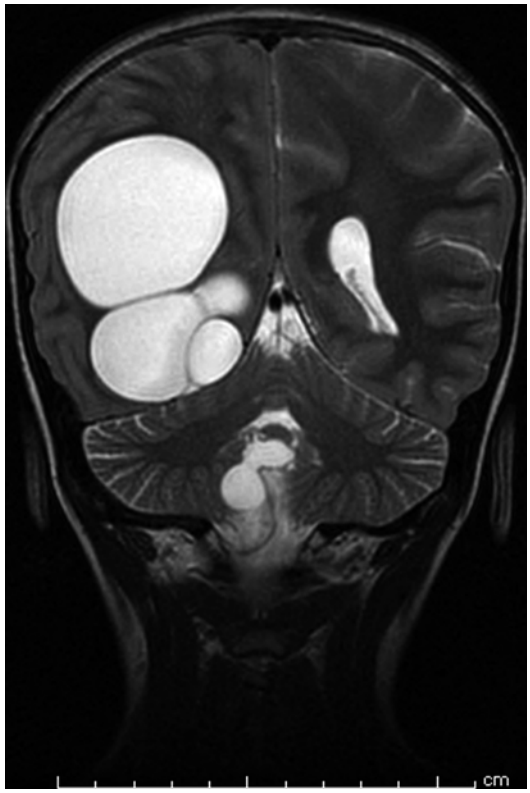

Fig. 7.3 Coronal T2-weighted MRI showing multiple cysts in the right occipital horn and fourth ventricle, extending outward through foramen of Luschka

membranes lining the cysts cannot be visualized as their density is similar to that of the adjacent brain tissue. Circular contrast enhancement and perifocal edema seen in multilocular cysts may result from active inflammation and must be differentiated from similar hallmarks of a brain abscess (Fig. 7.4) (Demir et al. 1991; Evliyaoglu and Keskil 2005).

Magnetic Resonance Imaging Findings

On magnetic resonance imaging (MRI), the lesions demonstrate CSF intensity with minimal or no enhancement in the simple cysts (Figs. 7.1, 7.2 and 7.3). Complicated cysts, viz., those with pericyst inflammation due to leakage of cyst content or infection, reveal intense contrast-enhancing rims with significant perilesional edema on T2-weighted images (Mohindra et al. 2012). Proton MR spectroscopy supplements diagnosis of these metabolically active lesions, with the cysts characteristically demonstrating elevated pyruvate, elevated succinate, acetate and alanine peaks, and a lipid-lactate peak at 1.33 ppm (Sreedhar 2006; Gupta et al. 2008).

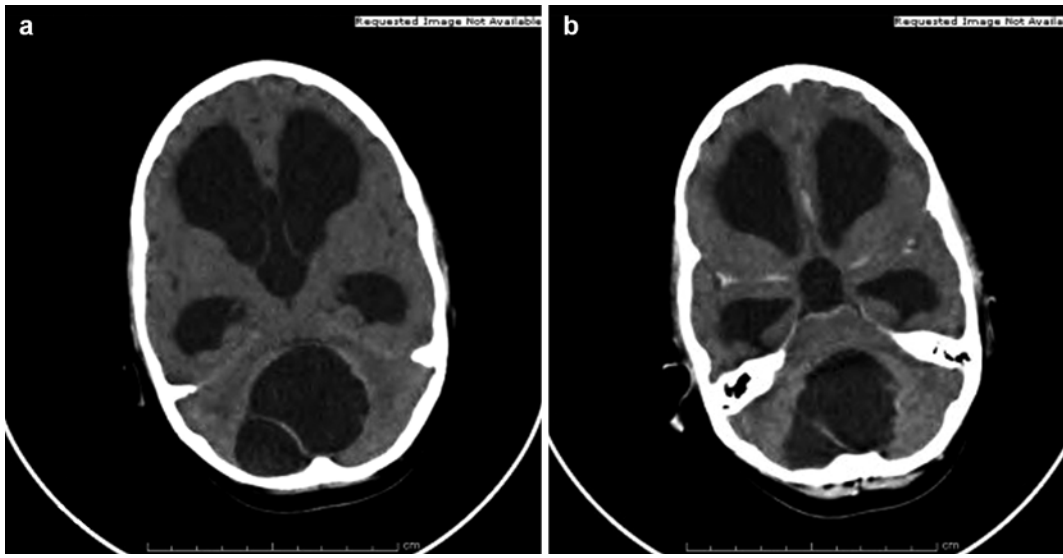

Fig. 7.4 (**a**) Plain and (**b**) contrast CT images of the cyst demonstrating no contrast enhancement with an added impression of septation

Differential Diagnoses

The radiological picture may be rendered complex by the presence of certain atypical features like intralesional nodular projections as seen in one of our patients (Figs. 7.1 and 7.2). In this case, the typical CSF signal intensities and lack of enhancement ruled out an astrocytoma, while the absence of preceding subarachnoid hemorrhage, infection, or congenital anomalies ruled out a trapped fourth ventricle (Zimmerman et al. 1978). Other close differentials that need exclusion are cysticercosis, arachnoid cysts, choroid plexus cysts, neoplastic cysts, infected or gliotic cysts, and colloid cysts (Handa et al. 1978; Zimmerman et al. 1978; Bukte et al. 2004). The final diagnosis, hence, is best arrived at by a combination of factors that include an appropriate clinical history, evidence of a primary hepatic focus, a high regional prevalence of hydatidosis, and laboratory findings.

Surgery

General Principles

In all cases, adequate anti-scolicidal measures need to be ensured by draping the brain with cotton strips soaked in scolicidal material like 10 % iodine or 1 % cetrimide (Altinörs et al. 2000; Furtado et al. 2009; Mohindra et al. 2012). Puncturing and aspiration of a large hydatid cyst followed by irrigation of the cyst with hypertonic solution and resection of the wall (puncture-aspiration-injection-reaspiration [PAIR] method) is not advisable because of the possibility of dissemination of cyst contents through the ventricular system (Altinörs et al. 2000). Complications that need to be anticipated with cyst rupture are the development of multiple daughter cysts, anaphylactic reaction, chemical meningitis, or ventriculitis induced by spillage of intracystic fluid (Altinörs et al. 2000).

Operative Technique

In the supratentorial compartment, a large frontoparietal craniotomy and a transcallosal transforaminal approach are used to deliver cysts at or near the foramen of Monro. A Cottonoid should be used at the foramen of Monro to prevent inferior migration of the cyst. Posterior fossa intraventricular cysts are approached by a midline suboccipital craniotomy in prone position with mild head elevation. We noticed that in these cases, the cerebral aqueduct, like the upper fourth ventricle, was enlarged by virtue of the proximal distension of ventricular system affected by the cyst. Care should thus be taken to prevent migration of the cyst into the third ventricle through an enlarged aqueduct (Fig. 7.5). This can be prevented again by the passage of Cottonoids under the cyst wall toward the aqueduct as the cyst is delivered (Fig. 7.6a). This prevents migration of smaller-sized primary and secondary cysts across the enlarged ventricular foramina. Cysts can be removed using the Dowling-Orlando water dissection technique through the foramen of Magendie. We used saline irrigation via a malleable ventricular catheter to prevent inadvertent cyst rupture and slow advancement of Cottonoids along with a Valsalva maneuver to deliver the cysts from the ventricle (Fig. 7.6b) (Furtado et al. 2009). These techniques and precautions facilitate the delivery of sizable unruptured ventricular cysts through narrow-sized foramina (Fig. 7.5).

Author's Experience and Case Studies

Of the two patients with intraventricular hydatid cysts we operated upon, the first (Figs. 7.1 and 7.2) was an 8-year-old girl from rural India who presented with occipital headache, vomiting, and deterioration of vision over a 1-year period. Her neurological deficits included secondary optic atrophy, poor visual acuity, coarse lateral gaze nystagmus, limb spasticity, and cerebellar dysfunction. At surgery via a midline suboccipital craniectomy, the vermis was found to be thinned out and the foramen of Magendie was enlarged. Three large and two small cysts were removed using Dowling's water dissection technique through the foramen. Abdominal MRI revealed a large hepatic hydatid cyst while MRI of the spine

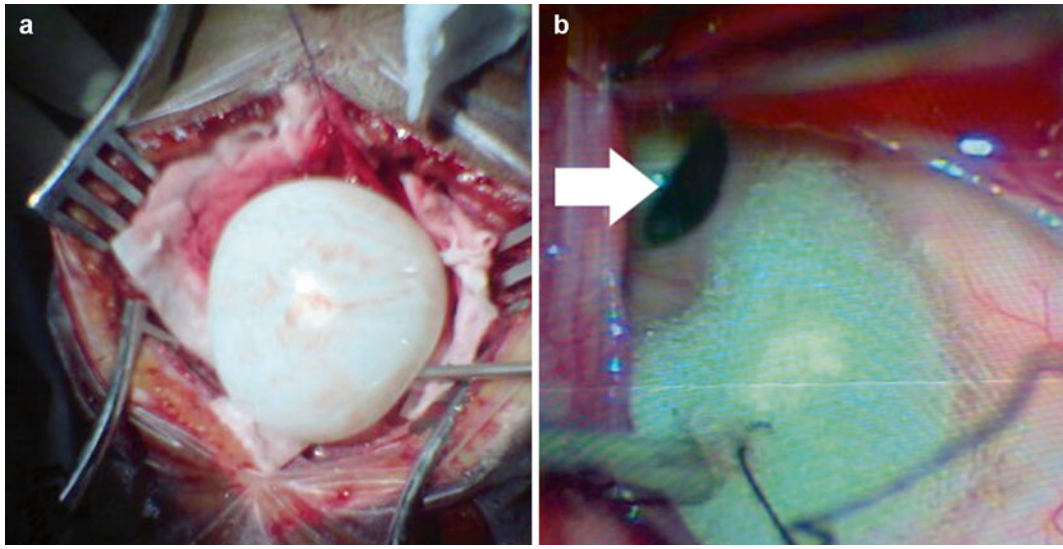

Fig. 7.5 (**a**) Large fourth ventricular cyst delivered in toto. (**b**) *Arrow* points to an enlarged cerebral aqueduct

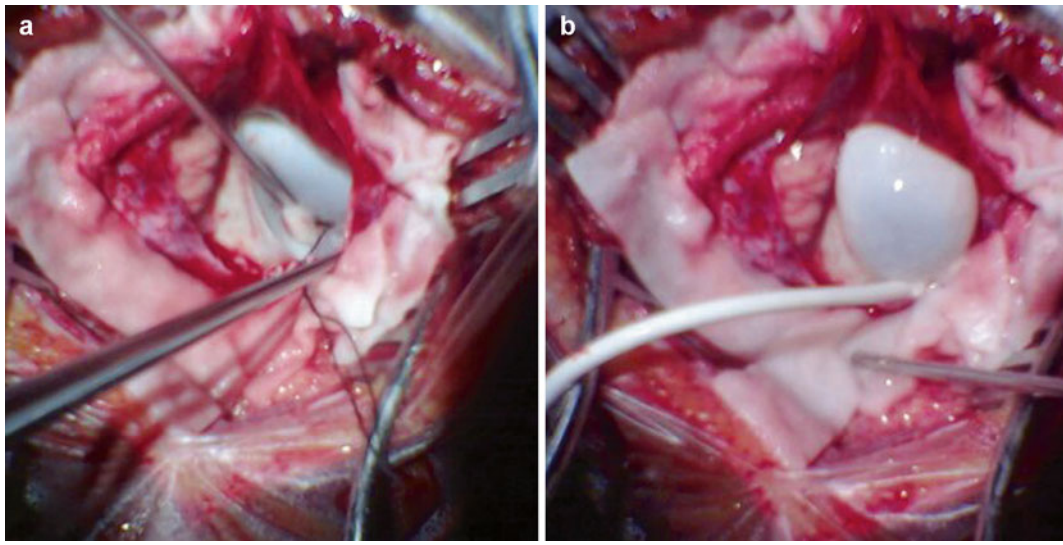

Fig. 7.6 (**a**) Cottonoids passed under the cyst wall toward the direction of the aqueduct. (**b**) Malleable ventricular catheter used to deliver the cyst

and heart were normal. Histopathological examination showed daughter cysts and a brood capsule within the large cyst. Hooklets were evident in the cytospin-prepared cyst fluid and absent in the smaller cysts (Furtado et al. 2009). At 1-year follow-up, she had no residual cyst(s) (Fig. 7.7) and her visual and cerebellar symptoms remained status quo.

The second case was a 9-year-old boy with holocranial (involving the whole head) episodic headache and vomiting of 3 months' duration (Fig. 7.3). Neurological examination revealed papilledema and a right sixth nerve palsy. He underwent bilateral parietal craniotomies and a midline suboccipital craniotomy for excision of multiple parenchymal, lateral ventricular cysts

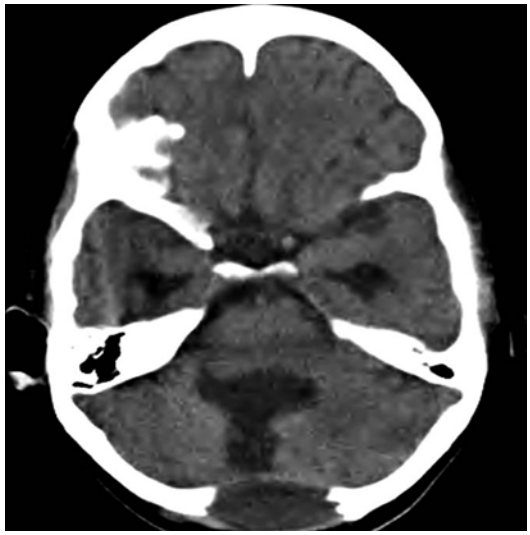

Fig. 7.7 Postoperative plain CT scan showing no residual cyst in the fourth ventricle

and fourth ventricular cysts, respectively. Postoperative imaging showed small residual parenchymal cysts which were treated with albendazole. He thereafter underwent cardiac surgery for removal of the cyst on the lateral wall of the left ventricle. These 2 representative cases were out of a total of 14 intracranial hydatid cysts operated over a 12-year period.

Endoscopy

Endoscopic removal of intraventricular hydatid cysts is an option which has to be weighed against the chances of complete removal of the cyst without spillage of contents. It has been performed in patients with an alternate diagnosis of colloid or arachnoid cysts, choroid plexus cysts, or neurocysticercosis (Husain et al. 2007).

Spillage of Cyst Contents

In case of spillage, irrigation with scolicidal agents such as 1 % cetrimide and 10 % formalin carries the risk of inducing ventriculitis (Furtado et al. 2009; Mohindra et al. 2012). A safer alternative is to administer antihelminthics like oral albendazole (10 mg/kg) for at least 2 months, a treatment regimen also indicated in cases of recurrence or systemic disease (Singounas et al. 1992; Gupta et al. 1999).

Postoperative Management

Based on the abdominal and cranial MRI findings, all our patients were administered albendazole (10 mg/kg per day) preoperatively and continued on the same postoperatively for a total duration of 2 months. Chemotherapy for hydatidosis of the central nervous system is discussed in Chap. 16.

Conclusion

Intraventricular hydatidosis can occur due to primary or secondary hydatid disease. A high index of suspicion is warranted for diagnosis especially when confronted with a smooth-walled, cystic intraventricular lesion of CSF intensity on MRI. This rare entity needs to be differentiated from cysts of gliotic, tumoral, or infective origins. Utmost caution needs to be exercised while delivering the cysts in order to prevent their rupture and subsequent dissemination, meningitis, or anaphylaxis.

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Hydatidosis of the Spinal Cord

8

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Introduction

Human echinococcosis, also known as hydatid (Greek for "watery cyst") disease or hydatidosis, is a rare but significant disease with a characteristic geographic distribution; it is mostly found in the sheep-raising regions of the world (Pamir et al. 1984; Morris and Richards 1992). Humans are infected with the larval form of the cyclozoonotic *Echinococcus* parasite, i.e., *Echinococcus granulosus* and less frequently *E. multilocularis*. Susceptibility of humans to infection varies, presumably because of individual differences in nutritional, immunologic, and genetic factors.

Etiology and Pathophysiology

Humans are incidental intermediate hosts. The infestation is mainly transmitted directly by contact with the infected animal or indirectly by feco-oral ingestion of the worm eggs from contaminated water or food (Prabhakar et al. 2005; Papanikolaou 2008). *E. granulosus* larvae develop slowly (usually over many years) into large unilocular, fluid-filled lesions—hydatid cysts. Incubation period may vary from months to years.

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Hydatidosis of the Spinal Cord

Involvement of the epidural space with sparing of the vertebral column is rare (Desai et al. 1999; Mohamed et al. 2004; Kaen et al. 2009). There are some reports from the literature describing massive affection of the epidural space without involvement of the vertebral column. Medjek et al. (1991) reported an intradural spinal hydatid cyst in the thoracic region and Akhan et al. (1991) one in a child. The intradural and extramedullary involvement is extremely rare, especially in non-endemic countries (Goçer et al. 1994; Kaen et al. 2009; Lakhdar et al. 2009). It appears only sporadically worldwide. Table 8.1 summarizes a total of 144 selected cases of spinal hydatidosis in the world literature to date (quoted from Deve 1928; Bertrand et al. 1956; Boixados 1961; Carrea and Murphy 1964; Pierini et al. 1965; Baurand et al. 1970; Karvounis et al. 1977; Bettaieb et al. 1978; San Martin Sánchez et al. 1980; Sharma et al. 1981; Pamir et al. 1984; Akhan et al. 1991; Medjek et al. 1991; Fahl et al 1994; Haddad and Bitar 1997; Turgut 1997; Islekel et al. 1998; Kabbaj-El Kouhen et al. 1999; Chat et al. 2000; Pushparaj et al. 2001; Chakir et al. 2002; Onbas et al. 2004; Kahilogullari et al. 2005; Layadi et al. 2005; Prabhakar et al. 2005; Charrada-Ben-Farhat et al. 2006; Sapkas et al. 2006; Kalkan et al. 2007; Kotil et al. 2007, 2010; Secer et al. 2008; Arif and Zaheer 2009; Jaiswal et al. 2009; Kaen et al. 2009; Lakhdar et al. 2009; Midyat et al. 2009; Turan Süslü et al. 2009; Celik et al. 2010; Thaler et al. 2010; Ediz et al. 2011).

The disease usually spreads to the spine by direct extension from pulmonary, abdominal, or pelvic infestation and less often begins primarily in the vertebral body, affecting predominantly the dorsal region of the spine (Bhojraj and Shetty 1999; Garcia-Vicuna et al. 2000; Govender et al. 2000; Hamdan and Al-Kaisy 2000; Schnepper and Johnson 2004; Herrera et al. 2005; Prabhakar et al. 2005; Sapkas et al. 2006; Papanikolaou 2008; Spies et al. 2008). When hydatidosis begins in the spine, it usually begins in the marrow of a vertebral body and may progress around the neural arch, through adjacent ribs, reaching the spinal canal or the intervertebral discs; thus, spinal involvement is believed to occur through direct portovertebral venous shunts (Morshed 1977; Fiennes and Thomas 1982). The extradural disease may spread through the neural foramen into the surrounding soft tissues as in the upper thoracic involvement by direct extension from a pulmonary lesion. However, the main mechanism for the intradural extramedullary involvement is not yet clear. Primary hematic dissemination is regarded as the most plausible mechanism, but dural tearing during surgery or during an aggressive invasion of spinal space, like lumbar puncture, may have a role in the etiology of the spreading of the infestation into the intradural space. This mechanism is well known for bacterial dissemination, but not for parasite spread.

Mortality/Morbidity

Spinal cord hydatidosis causes serious and disabling symptoms. Occasionally, deaths occur because of anaphylactic shock.

Race

No racial predilection has been observed.

Sex

In some endemic regions, females are affected more than males because their lifestyle habits and practices bring them into contact with the parasite.

Age

Individuals of all ages are affected. In some endemic countries, children have higher infection rates because they are most likely to play with dogs.

Table 8.1 Summary of 144 selected cases of spinal hydatidosis in the world literature to date

Author(s), year	Country	Age and gender	Localization	Neurological status	Neuroimaging	Outcome
Bartel (1928)	France	NA	Cervical	NA	NA	NA
Deve (1928)	France	NA	Cervical, ID, EM	NA	NA	NA
Rauzier (1928)	France	NA	Cervical	NA	NA	NA
Vallè (1928)	France	NA	Cervico-thoraco-lumbar	NA	NA	NA
Bertrand et al. (1956)	Morocco	25, F	T11-T12 ID, EM	Paraplegia	Myelography	Recurrence after 13 mos
Boixados (1961)	Spain	4, F	T5 ID, EM	Paraplegia	Myelography	Partial recovery
Carrea and Murphy (1964)	Argentina	9, F	T4–T5 ID, EM	Paraplegia	Myelography	Total recovery
Pierini et al. (1965)	Argentina	NA	Cervical, ID	NA	Myelography	NA
Baurand et al. (1970)	North Africa	35, F	T6 ID, EM	Paraplegia	Myelography	Total recovery
Karvounis et al. (1977)	Greece	37, F	L5–S1 ID, EM	Sciatica	Myelography	Total recovery
Bettaieb et al. (1978)	Tunisia	4, M	Upper thoracic, ID, EM	Paraplegia	CT-myelography	Total recovery
	Tunisia	8, M	Upper thoracic, ID, EM	Paraplegia	CT-myelography	Total recovery
	Tunisia	8, M	Middle thoracic, ID, EM	Paraplegia	CT-myelography	Total recovery
San Martin Sánchez et al. (1980)	Spain	62, F	L2, ID, EM	Paraplegia	Myelography	Total recovery
Sharma et al. (1981)	India	14, M	T6–T10, ID, EM	Paraplegia	Myelography	Partial recovery
Pamir et al. (1984)	Turkey	34, F	L2, ID, EM	Paraplegia	Myelography	No change
Akhan et al. (1991)	Turkey	6, M	T9–T11, ID, EM	Paraplegia	CT-myelography	NA
Medjek et al. (1991)	Algeria	21, F	T12–L1, ID, EM	Paraplegia	CT-myelography	Total recovery
Fahl et al. (1994)	Lebanon	55, F	T12–L1	Paraparesis	CT-myelography, MRI	NA
Haddad and Bitar (1997)[a]	Lebanon	46, M	L4–S1	Sciatica	CT	Recovery
Turgut (1997)[b,c] Islekel et al. (1998)	Lebanon	7, M, and 7, F	Cervical (2), thoracic (11), lumbar (4), sacral (1)	Pain (13), urinary incontinence, weakness (5), sciatica (2)	Myelography (7), CT (4), MRI (2)	Death (2), total recovery (2), no change (1)
	Turkey	61, M, and 23, F (mean age: NA)	Cervical (3), thoracic (35), thoracolumbar (3), lumbar (28), sacral (1), cervical and lumbar (1)	Paraplegia and paraparesis (61), cauda equine syndrome (27)	Myelography (56), MRI (8), CT (6), US (1)	Death (2), total recovery (5), recurrence (15)
	Turkey	19, M	L2–L4, ID, EM	Paraplegia	Myelography	Partial recovery

(continued)

Table 8.1 (continued)

Author(s), year	Country	Age and gender	Localization	Neurological status	Neuroimaging	Outcome
Kabbaj-El Kouhen et al. (1999)	Morocco	6, M	L1–L3, ID, EM	Paraplegia	CT-myelography	Partial recovery
Chat et al. (2000)	Morocco	13, F	T5–T11, L4–L5, ID, EM	Paraplegia	CT-myelography, MRI	Partial recovery
Pushparaj et al. (2001)	India	40, F	T10–T11, ID, EM	Paraplegia	MRI	Total recovery
Chakir et al. (2002)	Morocco	18, M	L1–L2, ID, EM	Paraplegia	MRI	Subtotal recovery
Onbas et al. (2004)	Turkey	48, M	Cervicothoracic, ID, EM	Paraparesis	MRI	Recurrence
Kahilogullari et al. (2005)	Turkey	32, F	L5–S2, ID, EM	Paraparesis	MRI	Total recovery
Layadi et al. (2005)	Morocco	35, M	Sacral, ED	Cauda equina syndrome	MRI	NA
Prabhakar et al. (2005)	India	3, M, and 1, F (mean age, 40 yr)	T8–T10	Paraplegia	Myelography	Without recovery
	India		T5–T6	Paraplegia	Myelography	Without recovery
	India		L5–S1	ASIA Grade C	Myelography, CT, MRI with contrast	Complete recovery after 1 yr
	India		L2–L5 ED, ID	Cauda equina syndrome	Myelography, CT, MRI with contrast	Complete recovery after 1 yr
Charrada-Ben-Farhat et al. (2006)	Tunisia	40, M	T7–T8, ED	Paraplegia	MRI	Total recovery after discharge
Sapkas et al. (2006)	Greece	62, M	ED	NA	NA	NA
Kalkan et al. (2007)	Turkey	8, M	T7–T8, ID, EM	Paraparesis	MRI	Total recovery after 4 mos
Kotil et al. (2007)	Turkey	34, F	T11 ED	Paraplegia	MRI	NA
Secer et al. (2008)	Turkey	35, M	T12, ID, EM	Paraplegia	MRI	Total recovery after 8 mos
Arif and Zaheer (2009)	India	9, M	L1–L4, ID, EM	Paraparesis	MRI	Complete recovery after 6 mos
Jaiswal et al. (2009)	India	21, F	T10, ED	Paraplegia	MRI	Partial recovery after discharge
Kaen et al. (2009)	Spain	59, M	T6, T10–T12, ID, EM	Paraparesis	MRI	Without recovery

Lakhdar et al. (2009)	Morocco	22, M	T11	Paraparesis	MRI	Total recovery after 15 mos
	Morocco	5, M	T12–L2	Paraparesis	MRI	Total recovery after 15 mos
	Morocco	10, F	L2–L5, ID, EM	Paraparesis	MRI	Total recovery after 18 mos
Midyat et al. (2009)	Turkey	13, F	ID, EM	Paraparesis	NA	NA
Salduz et al. (2009)	Turkey	41, F	ED	Sciatica	MRI	Total recovery after 5.5 yr
Turan Süslü et al. (2009)	Turkey	34, M	T10–T11, ID	Paraparesis	MRI	Total recovery after 1 yr
Celik et al. (2010)	Turkey	34, M	Thoracic, ED	Paraplegia	MRI	Total recovery after 2 mos
Kotil et al. (2010)	Turkey	30, F	L4–L5, ED	Sciatica	MRI	Total recovery after 7 mos
Thaler et al. (2010)	Austria	6, F	T8–T9, ED	Paraplegia	CT, MRI	Total recovery after 18 mos
Ediz et al. (2011)	Turkey	25, F	T7–T12, ED	Paraplegia	MRI	Partial recovery

Abbreviations: *M* male, *F* female, *C* cervical, *T* thoracic, *TC* thoracolumbar, *L* lumbar, *S* sacral, *IM* intramedullary, *EM* extramedullary, *ID* intradural, *ED* extradural, *CT* computed tomography, *MRI* magnetic resonance imaging, *US* ultrasonography, *mos* months, *yr* year, *NA* not available

[a]Out of the cases reported by the authors, two cases had already been described by Fahl et al. earlier

[b]Except for 13 patients, all had data suggestive of the exact location of the cysts in the spine

[c]Out of the cases reported by the author, two cases had already been described by Pamir et al. and Akhan et al. earlier

Classification

Morphologically, spinal involvement has been classified by Braithwaite and Lees (1981) into five types: (1) primary intramedullary hydatid cysts, (2) intradural extramedullary hydatid cysts, (3) extradural intraspinal hydatid cysts, (4) vertebral hydatidosis, and (5) paravertebral hydatidosis (Fig. 8.1).

Symptoms and Signs

Before an individual exhibits any symptoms and signs, many months or years may pass, during which the destiny of *E. granulosus* cysts is variable. Some cysts may grow to a certain size and then persist without noticeable change for many years, while other cysts may rupture spontaneously or collapse and completely disappear. After a variable incubation period, infestation may become symptomatic if cysts are growing and exerting pressure on adjacent tissue and inducing other pathologic findings. Sudden symptomatology is usually due to spontaneous or traumatic cyst rupture.

The clinical features of spinal cord hydatidosis are variable. The spectrum of symptoms depends on the following:

- Which part of the spinal cord has been involved
- Size of cysts and their sites within the affected spinal cord
- Interaction between the expanding cysts and adjacent structures

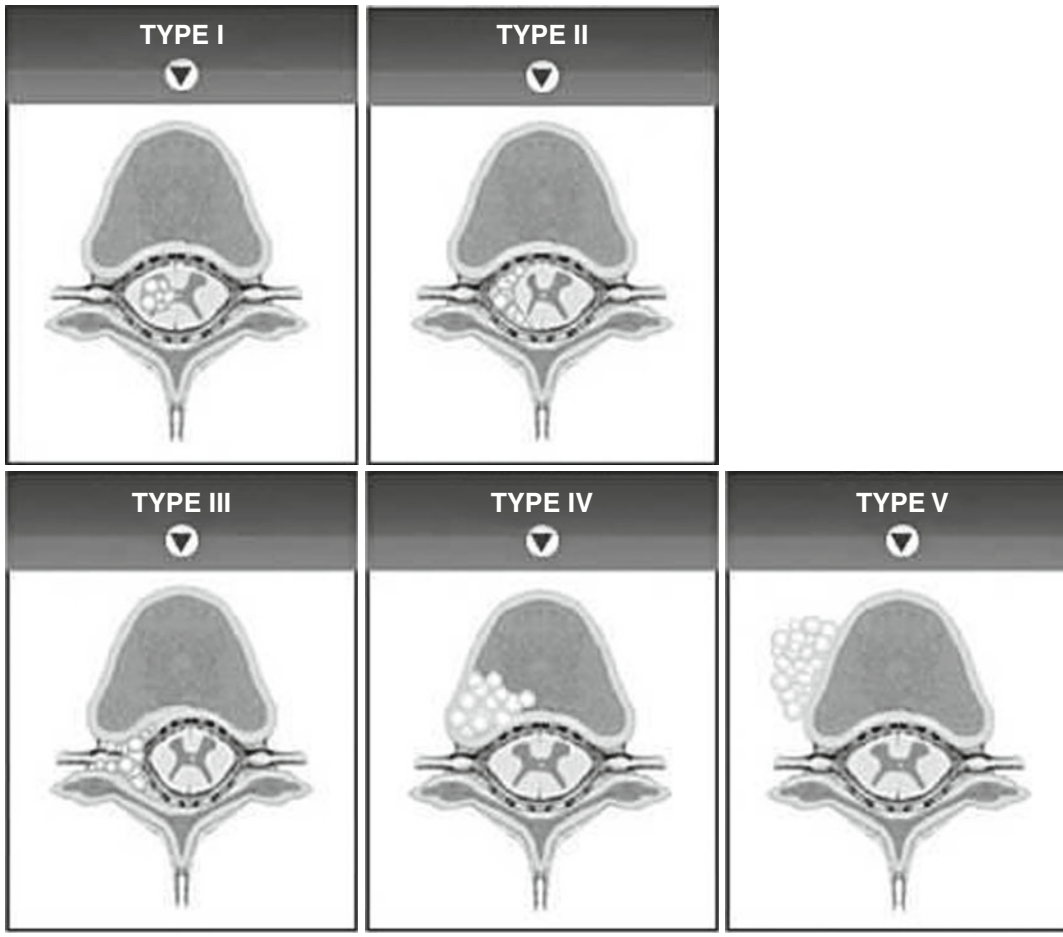

Fig. 8.1 Braithwaite and Lee's classification (Adapted from Braithwaite and Lees (1981))

- Complications caused by rupture of cysts
- Bacterial infection of cysts and spread of protoscolices and larval material into the blood vessels
- Immunologic reactions secondary to release of antigenic material

Physical

The initial clinical symptoms are usually nonspecific. In the beginning of the disease, the patient complaints of backache that lasts for a certain period of time (1–2 months). After disease-associated complications appear due to root and cord compression, the patients experience weakness in both lower limbs that gradually worsens, until the moment that the patients are unable to walk (Bilgic et al. 2009). The neurological complications are the result of invasive intradural and extradural growth of the cysts causing direct compression. This mixed picture poses a confusing picture for diagnosis and treatment planning.

Clinically, spinal cord echinococcosis manifests by radicular pain associated with objective sensory and motor disturbances. There are no pathognomonic signs and symptoms of this disease. For this reason it is often misdiagnosed initially as spinal tumor or disc herniation. The clinical presentation of spinal hydatidosis is variable, including paraparesis (62 %) or paraplegia (26 %), back pain or radicular pain (55 %), numbness or sensitivity loss (36 %), and sphincter disturbance (30 %) (Govender et al. 2000; Fares et al. 2003; Herrera et al. 2005; Papanikolaou 2008). The time period between the onset of the symptoms and medical consultation varies between 6 and 15 months (Khazim et al. 2003; Papanikolaou 2008).

Neurological Examination

Patients with spinal cord hydatidosis may present with one of three clinical syndromes: (1) a sensorimotor spinal tract syndrome, (2) a painful radicular spinal cord syndrome, or (3) rarely an intramedullary syringomyelic syndrome.

Sometimes, pain and stiffness of the back may antedate signs of spinal cord disease or dominate the clinical picture in some cases of extramedullary located cysts. The back pain usually worsens when the patient lies down and may be improved by sitting up. In the beginning, children experience severe back pain associated with spasm of paravertebral muscles; later in the course of the disease appear scoliosis and spastic weakness of the legs.

Sensorimotor Spinal Tract Syndrome

The signs of compression consist of (a) an asymmetrical spastic weakness of the arms and legs with cervical lesions and of the legs with thoracolumbar lesions, (b) reduced or lost sensory perception of pain and temperature below a certain level of the trunk, (c) signs of posterior column affection, and (d) a spastic bladder under weak voluntary control.

The onset of the compressive symptoms is usually gradual and the course progressive over a period of weeks and months, frequently with back pain. In patients with extradural cysts, paralysis usually develops over a period of days to several weeks, but the velocity of progression may vary. The initial disturbance may be motor or sensory and the distribution could be asymmetrical.

If the lesion is located in the low cervical segments and involves the anterior half of the spinal cord, the paralysis of the arms may be flaccid and areflexic in type and spastic of that of the legs. There is usually pain in the neck and shoulders and numbness of the hands; ataxia from posterior column lesions may accompany the paraparesis. In patients with cysts with high cervical location, a progressive syndrome of monoparesis, biparesis, and triparesis may be observed.

In thoracic lesions, one leg usually becomes weak and stiff before the other one. Subjective sensory symptoms of the dorsal column type (tingling paresthesias) may be present. Pain and thermal senses are more likely to be affected than tactile, vibration, and position senses.

The bladder and bowel usually become paralyzed coincident with the leg paralysis.

Radicular Spinal Cord Syndrome

Here, the syndrome of spinal cord compression is combined with radicular pain that is intensified by coughing or sneezing. It is described as knifelike or as a dull ache with superimposed sharp stabs of pain, which radiate in a distal direction. Besides the radicular pain, other usual symptoms include segmental sensory changes (paresthesias, impaired perception of pinprick and touch) and/or motor disturbances (cramp, atrophy, fascicular twitching, and loss of tendon reflexes) and an ache in the spine. Half of the patients experience tenderness of spinous processes over the growth by percussion. Sensory radicular symptoms often precede the signs of spinal cord compression by months.

Intramedullary Syringomyelic Syndrome

Intramedullary growths invade as well as compress and distort fasciculi in the spinal cord white matter. As the cord enlarges from the growing cyst, the free space around the cord is eventually consumed. No single symptom is unique to intramedullary cysts. Some degree of pain, sometimes minor, is common and is almost invariably present with lesions of the filum terminale. When the intramedullary cyst involves the central gray matter, a central cord or syringomyelic syndrome may result. The main symptoms are segmental or dissociated sensory loss, amyotrophy, early incontinence, and late corticospinal weakness. A sign of intramedullary lesion is a dissociation of thermal pain and tactile sensory loss over several segments on the trunk. Rarely, an extramedullary cyst may give rise to a syringomyelic syndrome, possibly by causing vascular insufficiency in the central portion of the cord.

Lesions at the level of the lowermost thoracic and the first lumbar vertebrae may result in mixed cauda equina and spinal cord symptoms. Positive Babinski sign indicates that the spinal cord is involved above the fifth lumbar segment. Lesions of the cauda equina alone, always difficult to separate from those of the lumbosacral plexuses and multiple nerves, are usually attended in the early stages by sciatic and other root pain and lumbar ache, which is variously combined with a bilaterally asymmetrical, atrophic, areflexic paralysis, radicular sensory loss, and sphincteric disorder. These must be distinguished from lesions of the conus medullaris, in which there are early disturbances of the bladder and bowel (urinary retention and constipation), back pain, symmetrical hypesthesia or anesthesia over the sacral dermatomes, a lax anal sphincter with loss of anal and bulbocavernosus reflexes, impotence, and sometimes weakness of leg muscles. Sensory abnormalities may precede motor and reflex changes by several months.

Complications

The primary cyst may contain daughter cyst and microruptures can give rise to secondary cysts. Spontaneous or traumatic cyst rupture and spillage of viable parasitic tissue during interventional procedures may result in secondary echinococcosis. Cysts may rupture into the blood vessels, leading to extraordinary manifestations and severe complications such as fever, urticaria, eosinophilia, and anaphylactic shock, as well as cyst dissemination.

Complications of spinal hydatidosis are discussed in detail in Chap. 18.

Diagnosis

Laboratory Studies

Routine laboratory tests should be obtained, but usually do not show specific values. Eosinophilia on cell blood count is absent or limited (<15 %). Indirect hemagglutination test and enzyme-linked immunosorbent assay are the most widely used methods for detection of anti-*Echinococcus* antibodies (immunoglobulin G). In spinal involvement, the serological sensitivity of antigens is 25 %, whereas it is 80–100 % in liver involvement (Kotil et al. 2007). Children aged 3–15 years may produce minimal serological reactions. No standard, highly sensitive, and specific serological test exists for cystic echinococcosis antibody detection.

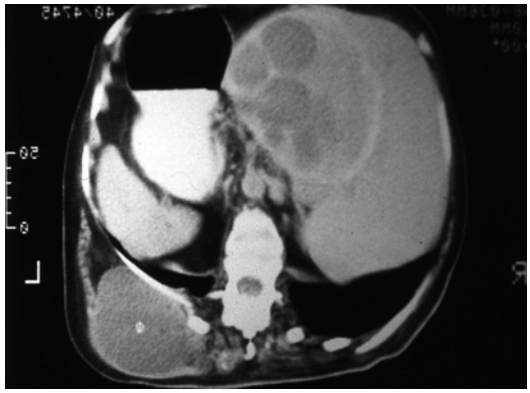

Fig. 8.2 Paravertebral hydatid cyst and hepatic cysts of a 49-year-old male patient with vertebral hydatid disease with destruction of two vertebral bodies (T12–L1) and paraplegia of 8 months of evolution. The patient was in a severe general state with sepsis, with fatal evolution (Courtesy of A. Herrera, M.D., Ph.D.)

Neuroimaging Studies

Imaging techniques such as plain radiographs, computed tomography (CT), and magnetic resonance imaging (MRI) of the spine should be obtained. They may be pathognomonic if daughter cysts and hydatid sand (protoscolices and debris) are present, but simple hydatid cysts may be difficult to differentiate from simple benign cysts, abscesses, Pott's disease, or benign or malignant tumors (Fahl et al. 1994; Turgut 1997). Imaging of spinal hydatid disease is discussed in detail in Chap. 12.

Radiographic Studies

Radiographic examination is useful for detecting calcified cysts.

Computed Tomography Studies

CT scanning can detect and locate smaller cysts precisely and sometimes differentiate parasitic from nonparasitic cysts (Fig. 8.2). Measurement of cyst density appears to be an additional tool to differentiate parasitic from nonparasitic cysts and for follow-up studies during chemotherapy.

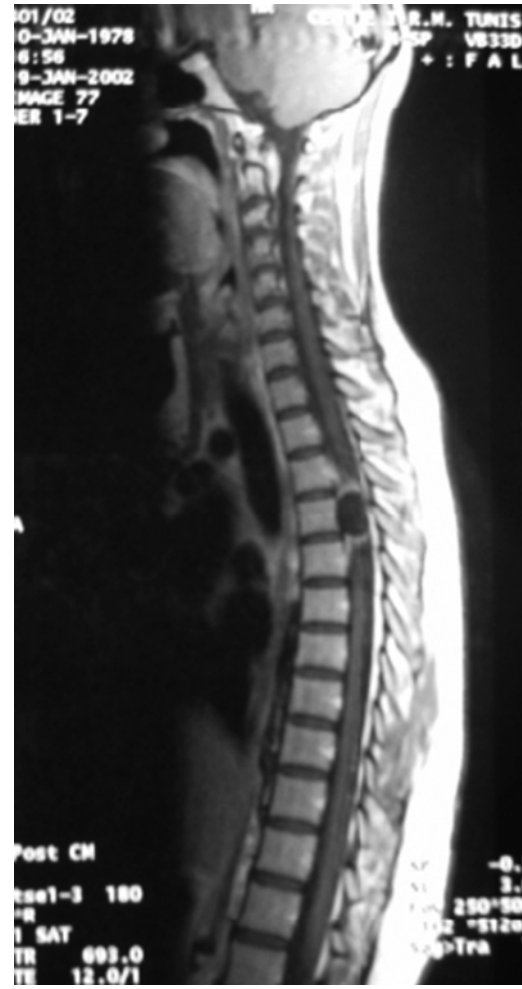

Fig. 8.3 MRI finding of a 24-year-old male patient showing extradural hydatid cyst at T4 vertebra corpus level (Courtesy of F. Limaiem, M.D.)

Magnetic Resonance Imaging Studies

MRI is the study of choice in the diagnosis of spinal echinococcosis since hydatid cysts have a unique appearance on MRI (Fahl et al. 1994; Mohamed et al. 2004; Lakhdar et al. 2009) (Fig. 8.3). Characteristic MRI findings of hydatid cysts are two dome-shaped ends, no debris in the lumen, and a "sausage-like" appearance with CSF-like signal intensities (Güneçs et al. 2009). The cysts are hypointense on T1W images. Intensity differences in T2W sequences of MRI can also determine the viability of the cyst (Jena et al. 1991). Viable cysts appear to contain a

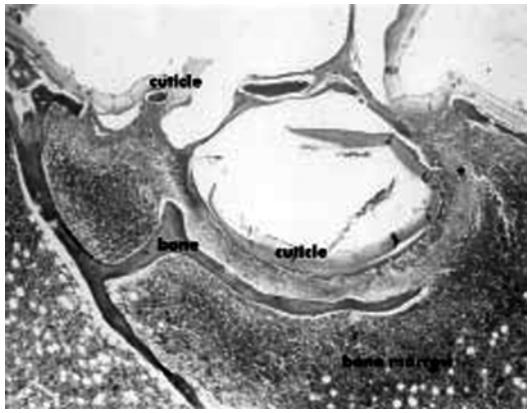

Fig. 8.4 Histopathological cross section of an excised hydatid cyst (Courtesy of A. Salduz, M.D.)

low-intensity fluid surrounded by an iso- to mildly hyperintense wall which on T2-weighted images appears as a low-intensity rim surrounding the high-signal cyst content (Tekkok and Benli 1993). Decrease in the intensity of the signal of the content and an increase of the signal of the cyst walls indicate a dying cyst. On T2W images they appear hyperintense with sharply defined, hypointense cyst wall which shows mild enhancement following intravenous gadolinium, reflecting the vascularity of the pericyst (Gupta et al. 2002).

Histopathological Diagnosis

The diagnosis can definitely be confirmed histopathologically by observing the allergic-type tissue reaction in the surrounding tissue and demonstration of the cyst wall histology and scolices (Salduz et al. 2009) (Fig. 8.4). Preoperative diagnosis is essential because the rupture and dissemination of cyst may result in anaphylaxis and recurrence.

Differential Diagnosis

The infection may be misdiagnosed initially as tuberculosis of the spine, which delays proper diagnosis and intervention. Other differential diagnostic possibilities include:

- Benign cysts
- Benign and malignant tumors
- Secondary tumors
- Abscesses
- Pyogenic infection of the spinal cord

Treatment

Despite the introduction of modern surgical and pharmacological therapy, the disease still continues to be difficult to cure and is highly prone to recurrence. Successful treatment of the spinal cord hydatidosis is challenging because of its invasiveness and its potentially severe complications.

Medical Care

The only antihelminthic agents that are effective against hydatidosis are albendazole and mebendazole (Turgut 1997; Brunetti et al. 2010). Praziquantel has recently been suggested; however, available data are limited (Bygott and Chiodini 2009). Medicamentous treatment should be applied before any surgical intervention in order to prevent the patient from a potentially lethal anaphylactic shock in case of a rupture of an active cyst (Hamdan and Al-Kaisy 2000). Chemotherapy for hydatidosis of the central nervous system is discussed in Chap. 16.

Surgical Treatment

Surgery is indicated if it is feasible, which depends on the size, location, and manifestation of the lesion (Prabhakar et al. 2005; Lakhdar et al. 2009; Salduz et al. 2009) (Figs. 8.4, 8.5, 8.6, 8.7, 8.8 and 8.9). Appropriate surgical treatment includes complete cyst resection without rupture of the wall (Bhojraj and Shetty 1999), appropriate decompression of the cord, correction of the deformity, and appropriate anterior and posterior instrumented stabilization techniques. Surgical treatment involves laminec-

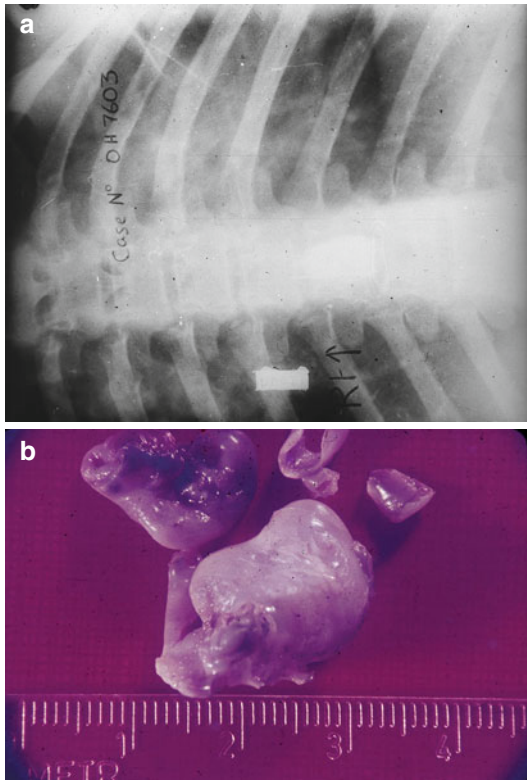

Fig. 8.5 Finding of spinal hydatidosis of a female patient, which did not recur (**a**, **b**) (Courtesy of F. S. Haddad, M.D.)

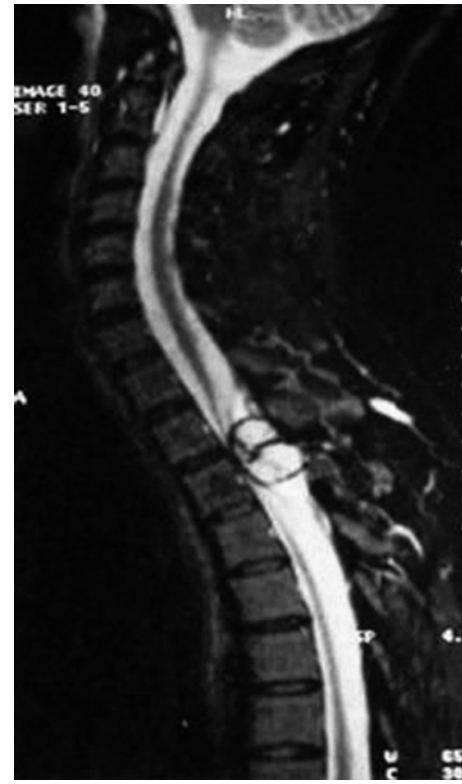

Fig. 8.6 Hydatidosis of L1. Anterior approach by thoracolaparotomy, extraction of cysts of the vertebral body (Courtesy of A. Herrera, M.D., Ph.D.)

tomy and decompression of the nerve elements/medulla. Difficulties in allocating of the intradural cyst(s) are due to the surrounding arachnoiditis, making them adhere to the arachnoid and difficult to remove. The principle is not to tear them apart in order to avoid spreading of the disease.

Generally, the patient should be in prone position, i.e., on the stomach, placed on a suitable bed or chair to release the abdomen that hangs freely in order to decrease the pressure in the paraspinal venous plexus to avoid excessive bleeding during the operation. Pillows are placed under the chest and both cristae spinae iliacae, or specially constructed frames, that support the chest and both cristae to release the abdomen.

Usually, the approach is made by a midline incision, along the line of the processus spinosus, at the appropriate level depending on the lesion localization. A standard procedure is applied to release the tendons of the paraspinal muscles and to display the rear aspects of spinous processes and lamina of the vertebrae. Laminectomy is performed at the levels of interest. Afterward, the dura is opened atraumatically in cases of intradural cysts; the surrounding operational area is coated with sterile material soaked with hypertonic 20 % NaCl for the isolation of the operative field (Turgut 1997). Then, the cysts are isolated from the surrounding nerve tissue (in cases of intradural extramedullary process). For intramedullary cysts, a medullotomy is carried out to open the medulla. This is performed with sharp instruments, such as diamond knife or microscissors, and the pia mater is cut in a substantial length (usually along the mid rear line of the medulla). Afterward, blunt microinstruments are used, usually two microdissectors. All procedures, starting from dura opening and finishing with its closure, are performed using an operating microscope.

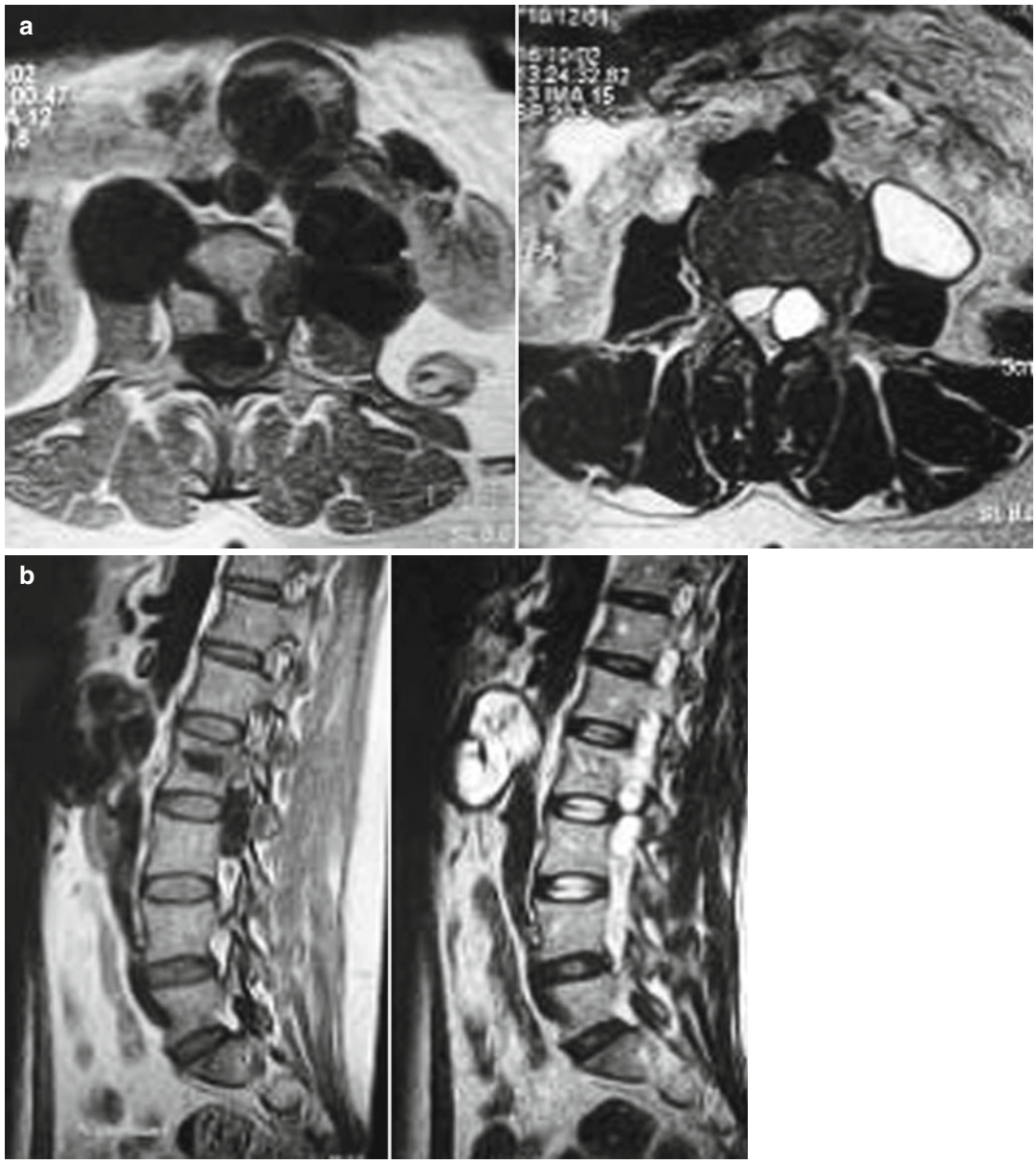

Fig. 8.7 Preoperative magnetic resonance images at (**a**) axial and (**b**) sagittal planes (Courtesy of A. Salduz, M.D.)

During the manipulation of the cyst(s), an irrigation with hypertonic 20 % NaCl solution and diluted Betadine is made (Turgut 1997). Some authors use 10 % formalin, but only when the dura is closed, never intradurally. Particular attention is made to avoid spreading of the disease intradurally or subarachnoidally and the surgeon has to avoid rupturing the cyst(s). For easier intraopera-

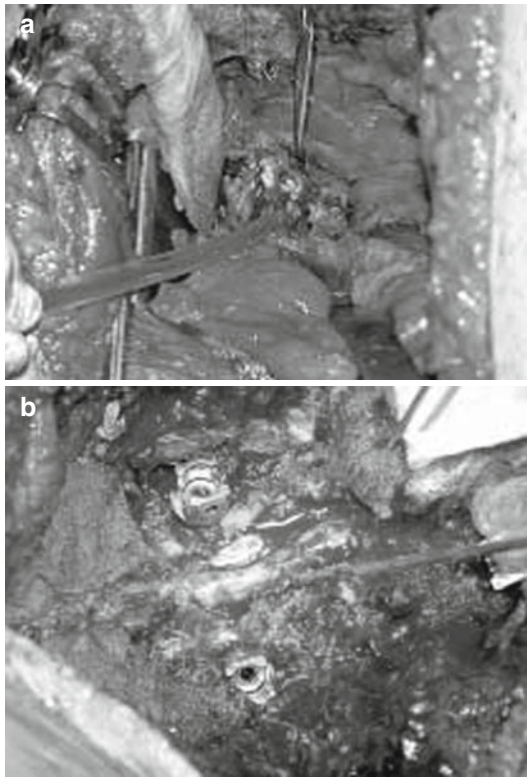

Fig. 8.8 (**a**) The image of the fistula at corpus of L2 vertebra extending posteriorly, (**b**) the image of the cyst after laminectomy (Courtesy of A. Salduz, M.D.)

tive navigation, it is possible to use intraoperative spinal monitoring with somatosensory and motor evoked potentials.

Complications related to intramedullary cysts removal are early (anaphylaxis, CSF fistula, wound infection, instability, delayed swelling of the medulla, and urinary tract infection) or late (dissemination of the cysts, instability of the spine, postsurgical myelopathy, postoperative syndrome of dysesthesia, and tethering of the spinal cord) (Turgut 1997).

Surgical treatment of spinal hydatidosis is discussed in detail in Chap. 14.

Conclusion

Hydatidosis of the spinal cord is a very serious condition with poor prognosis that has high morbidity and mortality. Long-term hydatidosis leads to persistent pain, secondary infections leading to sinuses and spinocutaneous fistulas, localized and remote recurrences, significant persistent neurological deficits, and spinal instability. Preventive measures should be taken in order to put the disease under control and eventually eradicate it, as has occurred in certain countries.

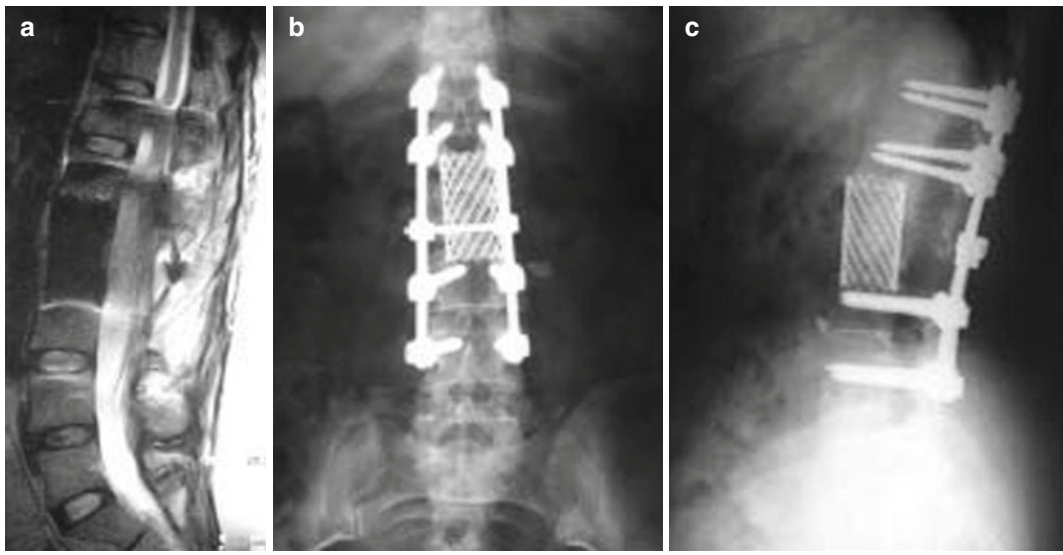

Fig. 8.9 (**a**–**c**) Magnetic resonance image and plain films after 5.5 years postoperatively (Courtesy of A. Salduz, M.D.)

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Hydatidosis of the Spine

9

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Introduction

Hydatidosis is a rare parasitic disease that is considered prevalent in Mediterranean countries, the Middle East, Oceania, South Africa, and South America (Murray and Haddad 1959; Gemmell et al. 1987; Szypryt et al. 1987; Kern et al. 2003; Romig 2009). The incidence of hydatid disease in the northern hemisphere ranges from 0.03 to 1.2 per 100,000 (Kern 2003; Romig 2009). In Spain, the incidence was 2.6 per 100,000 in 1987, but it fell to 0.55 per 100,000 in 2007 (Carmena et al. 2010). A small rise in incidence of the hydatid disease has occurred in European countries. According to some authors, it is linked to an increase in the fox population, as a result of the increase in rabbit population after myxomatosis decline (Deplazes 2006; Romig 2009). In Spain, the increase in the number of North African immigrants could explain this rise in incidence. Regardless of the sanitary control measures, it has been proposed to use a vaccine to eradicate the disease (Craig and Larrieu 2006). Currently this vaccine is being implemented in some countries (Tan et al. 2012). The epidemiology of hydatidosis in the world is discussed in Chaps. 2, 3 and 4.

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Bone involvement by hydatid disease is infrequent, ranging from 0.5 to 4 % of cases (Murray and Haddad 1959; Haddad and Bitar 1997; Merkle et al. 1997; Herrera and Martínez 2003; Bellil et al. 2009; Romig 2009). Spinal hydatidosis was first described by Chaussier in 1807 (Rayport et al. 1964). Vertebral bone location accounts for 50 % of cases of hydatid disease (Haddad and Bitar 1997; Turgut 1997; Govender et al. 2000; Martínez et al. 2001; Zlitni et al. 2001; Herrera and Martínez 2003; Herrera et al. 2005). The incidence of involvement in different areas of the spine varies from one author to another. By way of example, Rao et al. (1991) established that dorsal spine was involved in 50 % of cases, lumbar spine and sacrum in 20 % of cases, and cervical spine in 10 % of cases. Then, Haddad and Bitar (1997) found that multiple contagious vertebrae were affected in 11 of 14 cases with primary hydatid disease of the spine. In our experience, the lumbar spine is the most frequent location (34.61 %), followed by the dorsal spine (30.71 %), sacrum (26.9 %), and cervical spine (7.6 %). Nonetheless, these percentages vary widely.

Etiology

Several different species of *Echinococcus* have been described, but only two of them can parasitize humans: the *Echinococcus granulosus* species which causes cystic echinococcosis and the *E. multilocularis* species which causes alveolar echinococcosis. The *Echinococcus multilocularis* has a much lower incidence and never involves bone tissue (Szypryt et al. 1987). The *E. granulosus* species has been the etiologic agent in all of our cases. The species of *Echinococcus* are discussed in detail in Chap. 3.

Life Cycle

The life cycle of the tapeworm *Echinococcus* was not described until the nineteenth century (Lewis et al. 1975). Human hydatidosis is caused by the cystic (larval) stage of the tapeworm *E. granulosus*. Commonly, the intermediate host is sheep, and definitive hosts can be dogs, foxes, and other carnivores. Humans become the intermediate host by contact with an infected animal, usually a dog, or by eating vegetables contaminated by parasite eggs, which have come to them through the feces of an infected animal. Another source of infection is water pollution, a common vehicle in rural areas. The parasite passes through the intestinal wall and enters the portal circulation. It reaches the liver, which is the first filter, where most often it sets. The lung and the spleen may also be primarily colonized by the parasite. These primary visceral lesions behave as tumor nodes and transmit the parasite through the bloodstream to the bone tissue.

Pathogenesis

The larval parasite spreads through the circulatory system reaching the spine. The most usual site of infection is the metaphysis of a vertebral body, since this is the most vascularized area. A slower blood flow through the sinusoidal capillaries of the bone marrow and the fenestrations of the endothelium facilitate the deposition of the parasite.

Bone cysts in vertebral echinococcosis expand slowly with no development of the fibrous adventitious layer or pseudocapsule (pericyst) found in other locations (Fig. 9.1). On the contrary, the external layer (ectocyst) is an acellular membrane that allows the transfer of nutrients. The

Fig. 9.1 Cyst removed from a vertebral body

Fig. 9.2 Large open cyst with multiple daughter vesicles inside

internal layer, or germinal layer, usually shapes multiple compartments containing clear hydatid fluid and protoscoleces. These multiple vesicles remain attached to the germinal layer through a pedicle and resemble a bunch of grapes (Fig. 9.2). Sometimes these vesicles can grow through the external layer of the main cyst.

The clear, yellow hydatid fluid contains sodium chloride, proteins, lipids, polysaccharides, and ions, having a neutral pH. Breakage of a cyst can trigger an immunological reaction from the host, sometimes leading to an anaphylactic shock. Severe bone necrosis and inflammatory reaction may appear if bone lesions become infected, forming granulomas made up of lymphocytes, eosinophils, polymorphonuclears, and giant cells. Differential diagnosis with granulomatous infections might be very difficult.

Up until now it has been thought that disc space act as a barrier against infection. Colonization of several spinal levels at the same time, or spreading under the longitudinal ligaments from one vertebral body to the contiguous one, could explain the cases involving several spine levels. Nevertheless, Karantanas et al. (2003) have described a case of echinococcosis with cystic involvement of the disc space. Based on our experience with the hip joint, as well as the spread of the disease across the joint into the rib, our view is that the cartilage tissue is not an insuperable barrier against hydatid disease and parasite invasion through the joint surface is possible (Fig. 9.3).

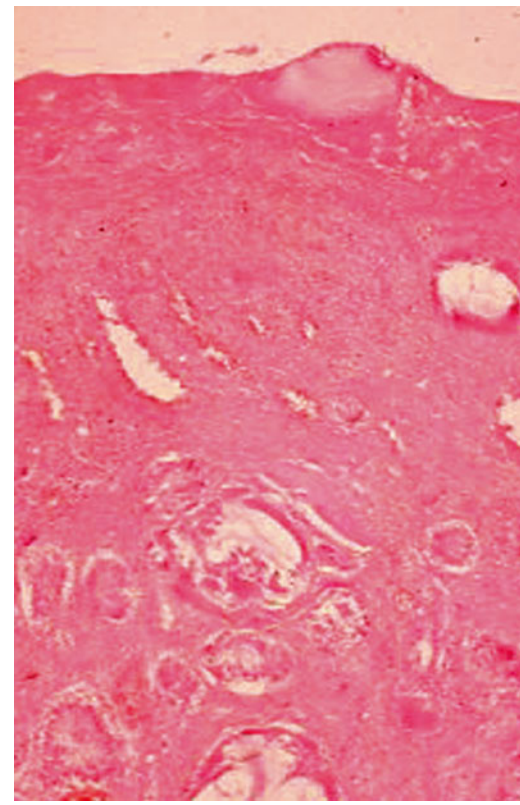

Fig. 9.3 Fibrous tissue on the surface of a femoral head. Hydatid membranes have replaced the cartilage

Bone cysts expand slowly and usually have a multilocular growth. Enlargement is achieved by local erosion of bone, and the pressure on the blood vessels of the marrow bone may result in a

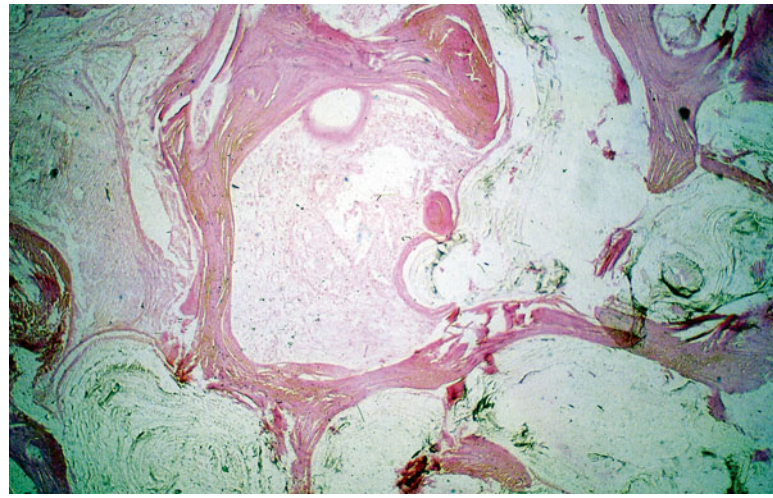

Fig. 9.4 Devitalized, eroded bone trabeculae by the growth of cysts

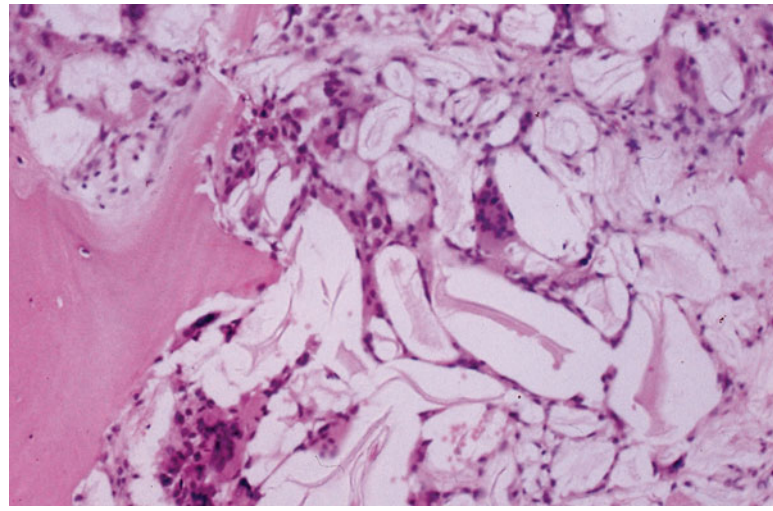

Fig. 9.5 Hydatid membranes with a giant-cell reaction next to an unstructured bone trabeculae

vascular necrosis (Fig. 9.4). Since trabecular destruction is complete (Fig. 9.5), infestation progresses toward the cortical bone and can spread through the anterolateral paravertebral area or into the spinal canal. Computed tomography (CT) scan or magnetic resonance imaging (MRI) may then show a pseudo-abscess (Fig. 9.6), and a differential diagnosis with spinal tuberculosis or vertebral pyogenic osteomyelitis is sometimes difficult.

Mechanical failure of the vertebrae can lead to compression fractures, even if cortical bone is preserved. The progression of the infection could lead to angular kyphosis and neural compression

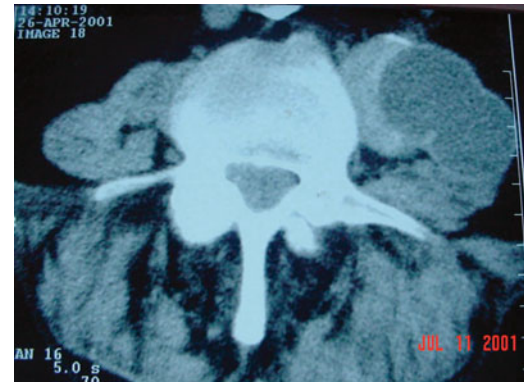

Fig. 9.6 CT: vertebral hydatidosis with large pseudo-extravertebral abscess

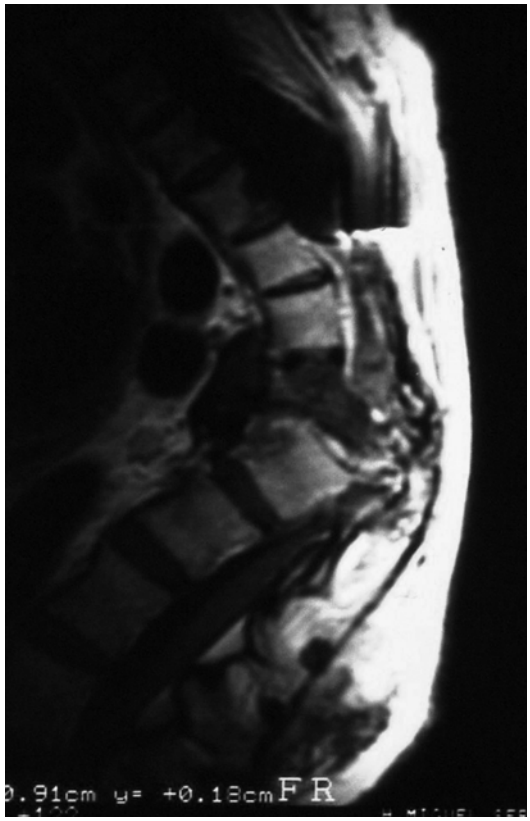

Fig. 9.7 Total destruction of two vertebrae producing severe kyphosis and cord compression

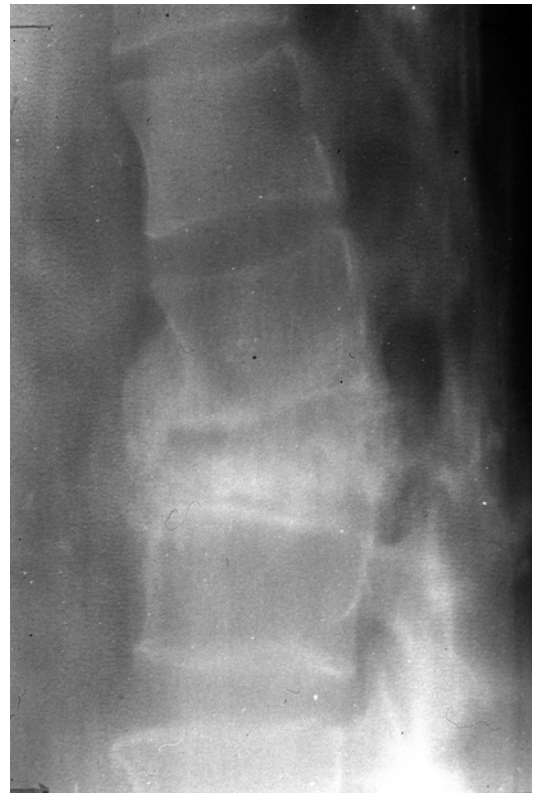

Fig. 9.8 Radiographic tomography: lumbar hydatidosis simulating a vertebral compression fracture

of the spinal cord (Fig. 9.7). In other cases, in which the infection progresses through the pedicles, the intervertebral foramina may be affected, and root compression symptoms could be present.

In this respect, the understanding of the mechanical strength properties of the vertebrae is necessary. Although the cortical bone is more resistant, cancellous bone plays a major role in the global mechanical strength of the spine, since its trabecular struts act as the internal scaffolding of the vertebral body. The damage to the cancellous bone leads to a loss of rigidity and to an initial loss of vertebral body height. If this damage progresses, the cortical bone remains as an empty eggshell, and it is not capable to withstand compressive loads, leading to a compression fracture (Fig. 9.8). If the infection involves also the cortical bone, the loss of resistance and the risk of fracture are then increased.

Clinical Presentation

Since 1807, when Chaussier described the first case of vertebral infection, there is a lack of published papers detailing accurately the clinical presentation of vertebral echinococcosis. This may be due to the unspecific presentation of the hydatid disease in the bone and to the long clinically silent period before the first symptoms (up to 40 years in some cases) (Murray and Haddad 1959; Zlitni et al. 2001; Song et al. 2007; Papanikolaou 2008). Echinococcosis in general, and that involving the spine in particular, is an adult disease, partly due to this long silent period. The youngest patient admitted to our service was 24 years old at the time of diagnosis, and the oldest one was 77 years old, with an average of 51.3 years at presentation.

Back pain is the most typical symptom of spinal hydatidosis, frequently associated with

neurological deficits. Trabecular and cortical bone are progressively destroyed as bone cysts expand, and vertebral compression fractures may appear. An angular kyphosis could be present especially when several levels are affected. In severe cases, bone sequestrums extruded into the spinal canal from vertebral bodies cause neural compression. Neural compression can also be produced by cysts invading the extradural space. Usually, both facts (extradural cystic invasion and destruction of the vertebral body) are present when echinococcosis brings about neurological deficits.

If infection progresses through the vertebral pedicles, involving the foramina, root compression symptoms could appear. When the hydatid cysts destroy the anterior vertebral cortex, the infection spreads through the anterolateral vertebral area. In these cases, the appearance of a pseudo-abscess may resemble a pyogenic osteomyelitis or a granulomatous infection such as spinal tuberculosis.

Back pain is associated with vertebral collapse and compression fractures, occurring when the vertebral destruction is advanced. Pain is typically severe at the thoracic and cervical levels and mild at the lumbar and sacral segments. All the patients treated in our hospital service reported moderate to severe back pain for several weeks. Neurological symptoms were present in a high percentage of cases at the time of diagnosis.

In our experience, the clinical course is relatively fast since pain appears, and a worsening of the symptoms coincides with the onset of neurological deficits in a high percentage of cases. The most frequent presentation is a spinal cord compression associated with paraplegia or tetraplegia. Another type of neurological complaint is a root compression syndrome with severe pain and sensory and motor deficits or sphincter dysfunction, depending on the level affected.

Superinfection of the hydatid lesion is possible, but it is not as frequent as other complications. If this happens, a large abscess may spontaneously drain to the surrounding tissues or outside the body, as we have seen in two cases. The course of sacrum involvement is usually asymptomatic, and in some cases, posterior soft tissues or retroperitoneal invasion may be present without previous neurological complaints. Two of our patients initially presented with a posterior sacral tumor and rectal symptoms as the early presentation of hydatid disease of the lower spine (Fig. 9.9).

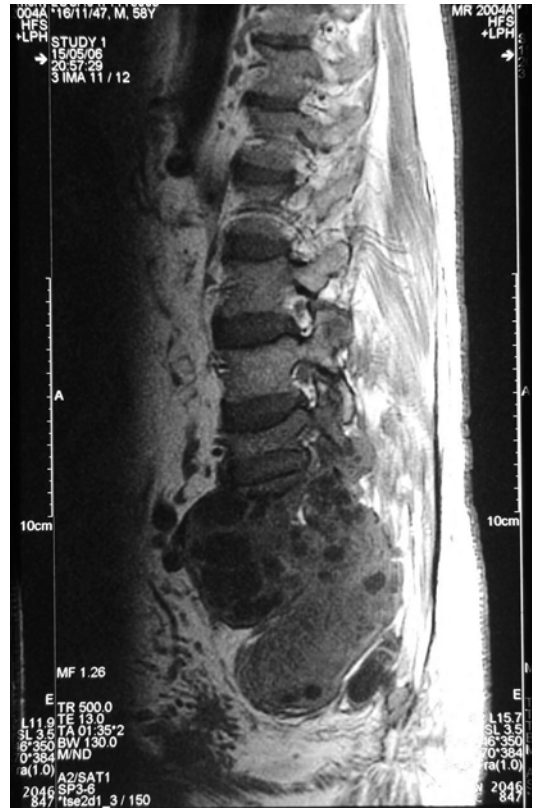

Fig. 9.9 Sacral hydatidosis with both extra- and intravertebral extensions

In conclusion, the clinical presentation of vertebral echinococcosis is totally unspecific and hardly suggests the diagnosis. Unfortunately, a progressive and severe back pain and the onset of neurological deficits are very common.

Complementary Tests

Imaging

Emergence of new imaging technologies has improved the diagnostic means of vertebral hydatidosis. CT was not available until the 1980s in

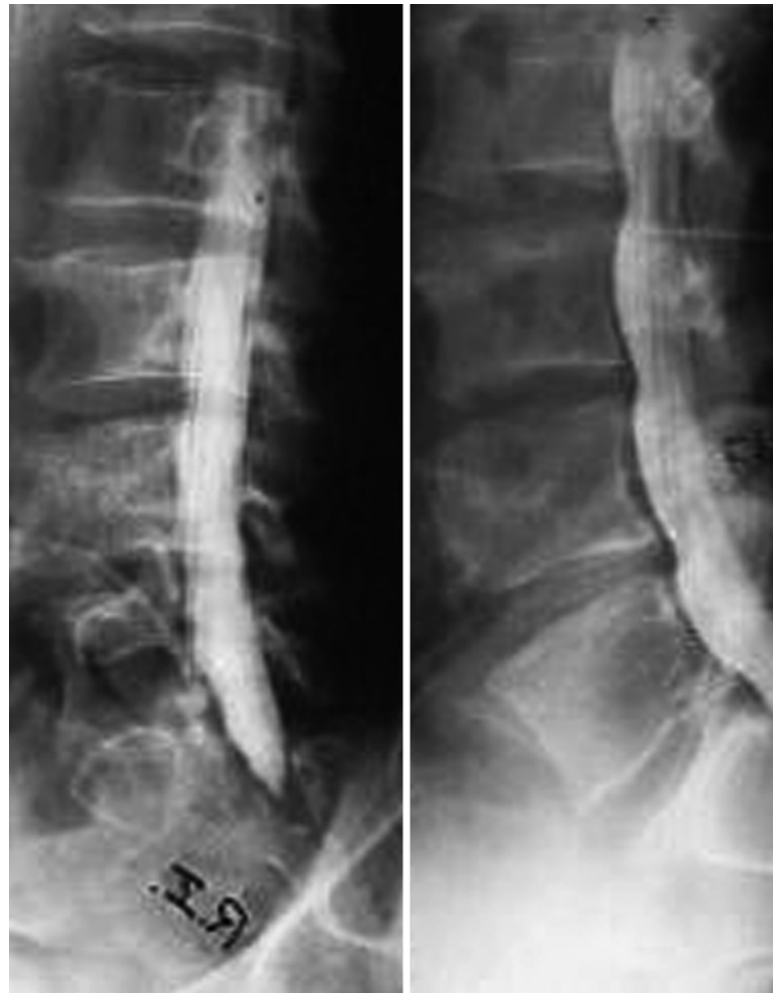

Fig. 9.10 Radiograph with contrast media

our hospital, and MRI was first used at the end of the same decade. MRI is the most reliable and useful method for diagnosis (Fahl et al. 1994; Işlekel et al. 1998; Singh et al. 1998) because it allows an excellent visualization of soft tissue injuries. Three-dimensional CT scan (3D CT) was also a breakthrough in identifying lesions and depicting its topography. Another technique ready to use is ultrasound, which has been applied to guide punctures of extravertebral injuries. But we consider most reliable, for this purpose, the CT-guided needle.

Taking advantage of modern methods of diagnosis, Braithwaite and Lees, in 1981, established five sets of column hydatid lesions which can lead to neurological problems: (a) primary intramedullary cyst, (b) intradural extramedullary cyst, (c) extradural intraspinal cyst, (d) hydatid disease of the vertebra, and (e) paravertebral hydatid disease. Currently, this classification is accepted by all the authors.

Our early experience with patients suffering from spinal hydatidosis began in the 1970s. At that time, the techniques at our disposal to diagnose neurological injuries were limited to conventional radiology and X-rays with contrast media (Fig. 9.10).

Images provided by conventional radiology are quite unspecific. Extensive osteolytic lesions affecting a vertebral body (Fig. 9.11) or the sacrum (Fig. 9.12) may be confused with tumor pathology. Likewise, plain radiography of a

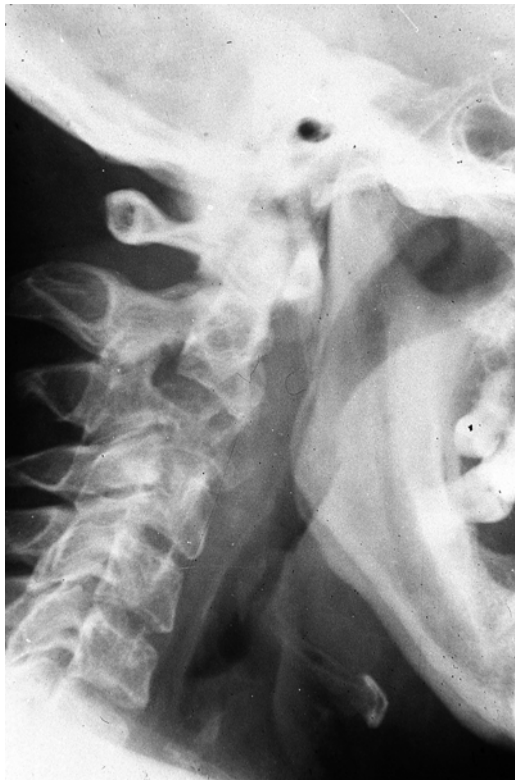

Fig. 9.11 Cervical hydatidosis: osteolysis of C3

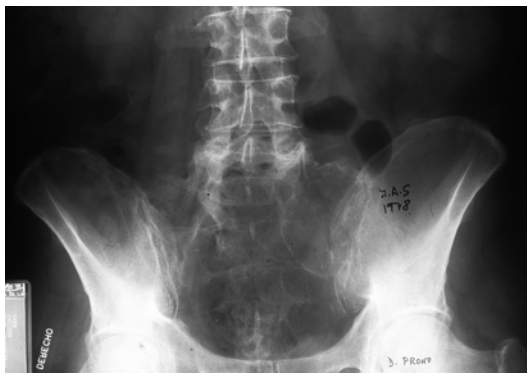

Fig. 9.12 Sacral hydatidosis: osteolytic lesion

crushed vertebral body (Fig. 9.13) may lead to the suspicion of a neoplastic etiology. In other cases, X-rays might suggest an infection of the spine, faced with reactive lesions simulating a vertebral osteomyelitis (Fig. 9.14). Only few skilled orthopedists or radiologists can suspect a hydatid injury on the basis of an X-ray, such as the case shown in Fig. 9.15, in which the diagnosis was suspected from an X-ray appearance showing little bony sequestrum, intervertebral disc integrity, and irregular osteolytic areas.

Radiographic tomography allows a more accurate identification of bone lesions. But its resolution is only slightly better than the X-ray; therefore, a tumor etiology is suspected in most cases. The introduction of CT scan in 1984 represented an inestimable help. It allowed us to establish which lesions are characteristic of hydatid disease in the vertebral body (Fig. 9.16): lytic lesions encircled with mild sclerosis, small bony sequestrum, and destruction of the cortex of the vertebra. In other cases, one may find an invaded spinal canal and vertebral pedicle destruction (Fig. 9.17) or small calcifications inside a lesion, which are typical of hydatid disease. The discovery of evident extravertebral, anterolateral lesions (Fig. 9.18), simulating a paravertebral abscess, should suggest a hydatid disease if they have a slight peripheral calcification. Other extra-spinal lesions can be located behind the spine (Fig. 9.19), resting on the rear face of the vertebral lamina. Sometimes, bony sequestrum fragments from the vertebral body might be seen occupying the spinal canal (Fig. 9.20). But most of these images can mislead to an infectious or tumor pathology. Therefore, knowledge of history, clinical signs, and laboratory tests of each patient must be the first step of the diagnostic process. CT scan may also lead to a false diagnosis in the cases when bone lesions resemble a neoplasm (aneurysmatic bone cysts) (Fig. 9.21). In short, CT scan has been a major contribution to the diagnostic process, but it should not be regarded as an infallible technique (Torricelli et al. 1990).

MRI and 3D CT scan allow a more refined diagnosis, particularly in the hands of a radiologist skilled in this disease and if one works in an area where vertebral hydatidosis is not unknown. MRI provides detailed pictures of both soft tissue and bone lesions. This technique usually gets an accurate identification of extravertebral cysts (Fig. 9.22), intravertebral lesions (Fig. 9.23), and extradural intraspinal cysts (Fig. 9.24). Sometimes, images may suggest a wrong infectious etiology. Careful observation will help rule

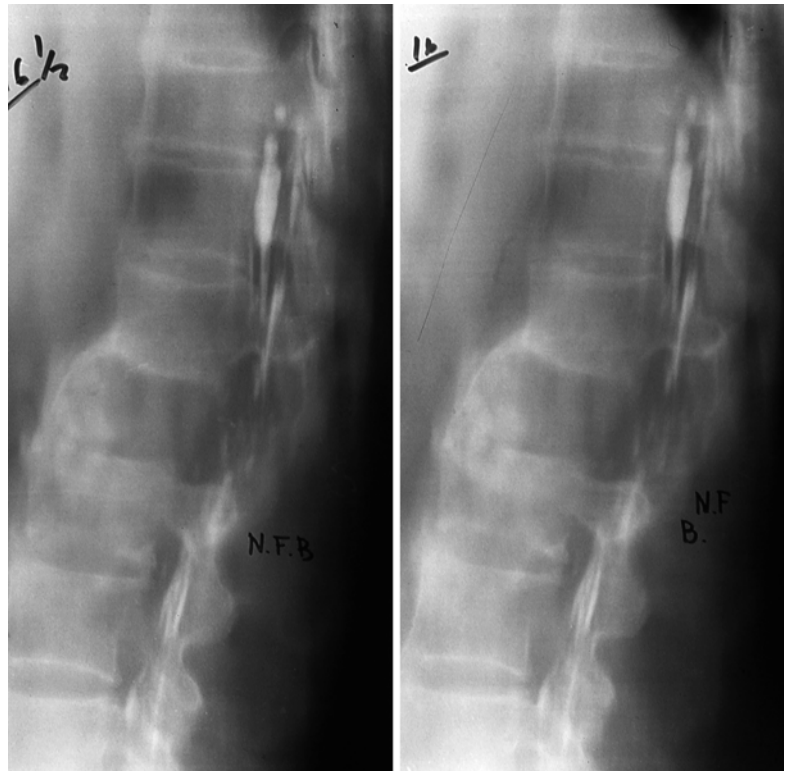

Fig. 9.13 Lumbar hydatidosis can be mistaken for tumor etiology

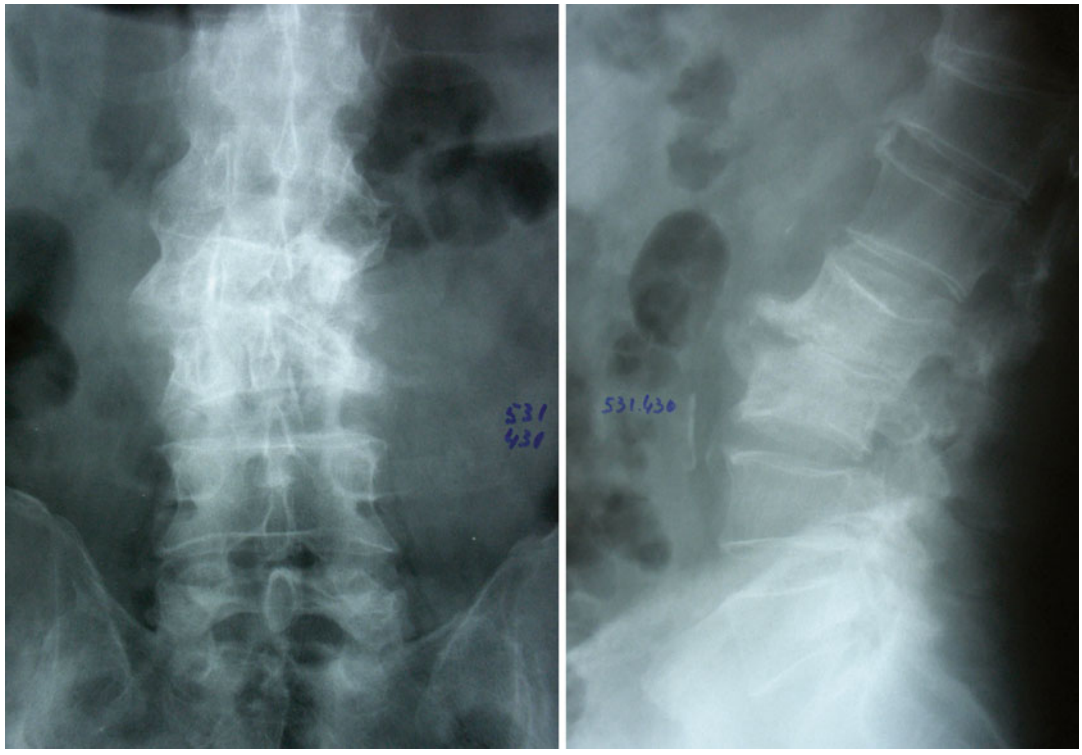

Fig. 9.14 (**a**, **b**) Radiographs of a lumbar hydatidosis can resemble a vertebral osteomyelitis

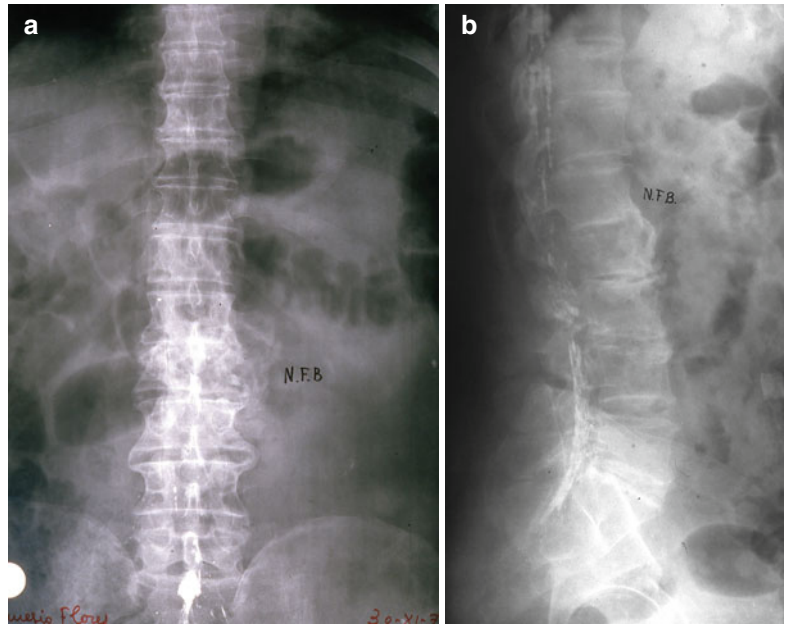

Fig. 9.15 (**a**, **b**) Lumbar hydatidosis

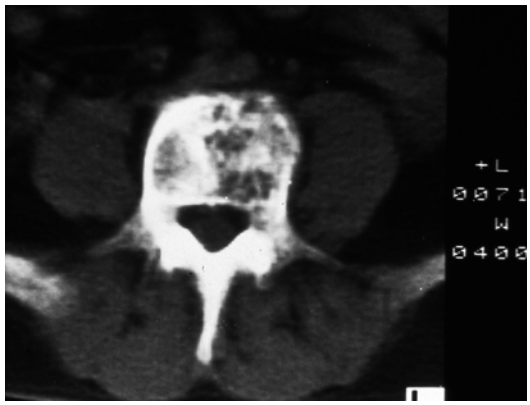

Fig. 9.16 CT: typical lesions of vertebral hydatidosis

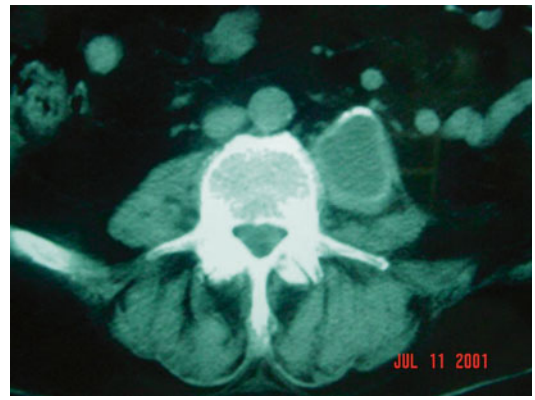

Fig. 9.18 CT: hydatid pseudo-abscess with peripheral calcification

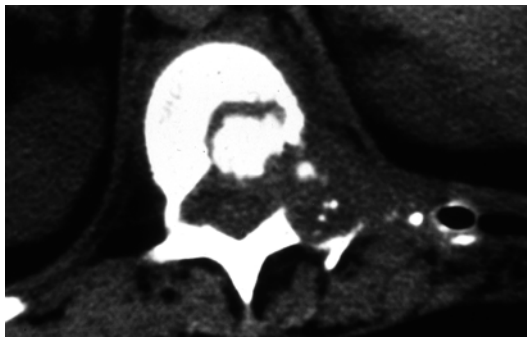

Fig. 9.17 CT: pedicle destruction and invasion of the spinal canal

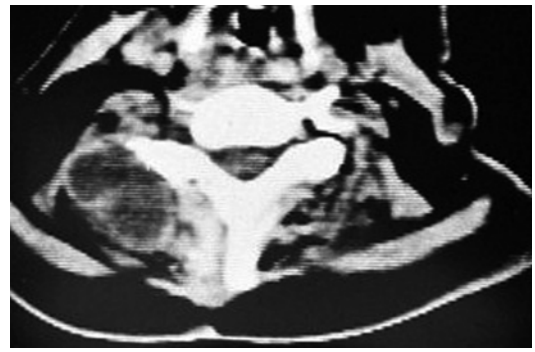

Fig. 9.19 Hydatid cysts on the rear face of a vertebral lamina

out a septic origin, based on the disc integrity and vertebral body images (Fig. 9.25). Another MRI possibility is the supervision of injuries evolution in patients undergoing medical or surgical treatment (Doganay and Kantarci 2009) (Fig. 9.26). 3D CT scan is another important aid in the diagnostic process, contributing to an accurate knowledge of the topography of the lesion (Fig. 9.27) and helping to determine the lesions etiology.

It may be concluded that the combination of different imaging techniques is essential for a diagnostic approach (Beggs 1985; von Sinner 1991), but we consider MRI as the most reliable mean. It is clear that modern imaging techniques have led to significant progresses in the diagnosis work-up, but accurate diagnosis of a lesion is not always possible. So, CT-guided puncture technique, or percutaneous biopsy technique guided by image intensifier or CT scan, is sometimes necessary to rule out different etiologies.

Laboratory Tests

Laboratory tests are useful tools in the diagnostic work. Some of these tests are not specific for

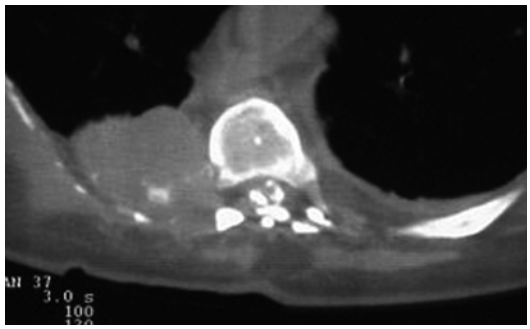

Fig. 9.20 Sequestrum fragments from the vertebral body occupying the spinal canal

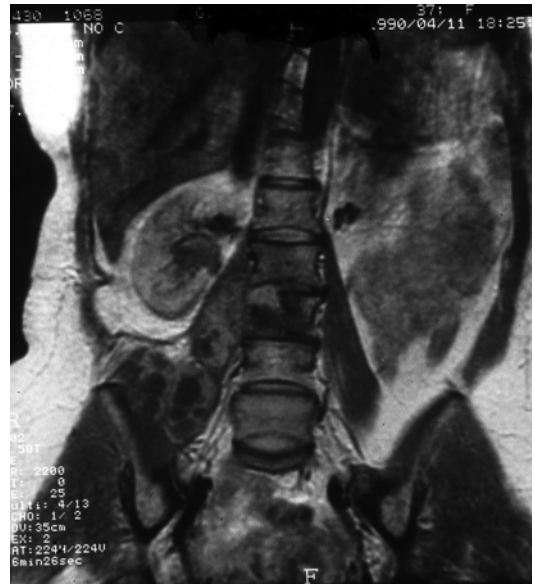

Fig. 9.22 MRI: extravertebral hydatid cysts in a lumbar hydatidosis

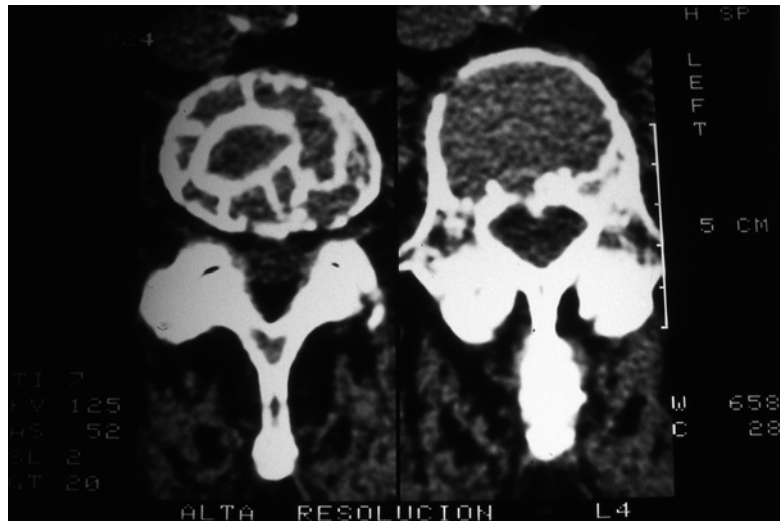

Fig. 9.21 CT: hydatid cyst simulating a vertebral aneurysmatic bone cyst

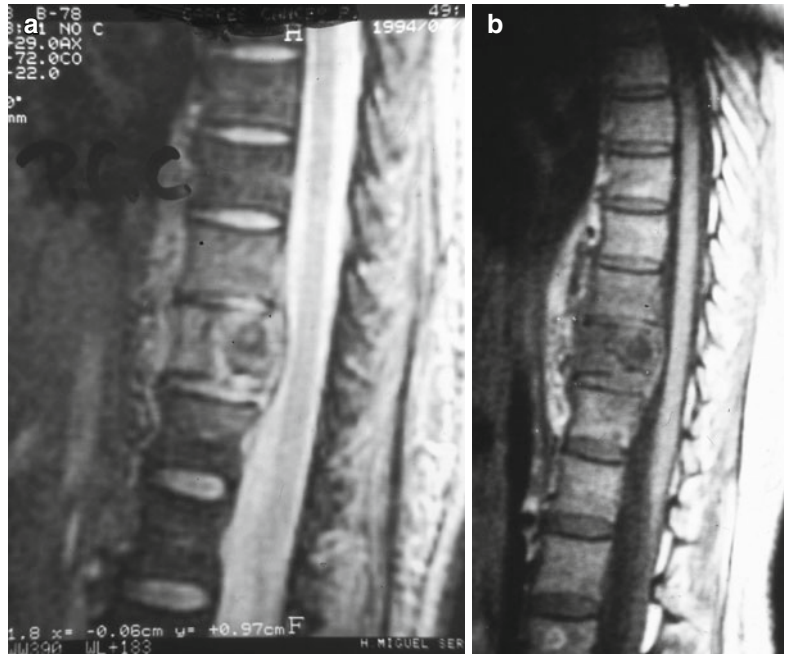

Fig. 9.23 Hydatid disease in a vertebral body: MRI images of thoracic spine in two planes (**a**, **b**)

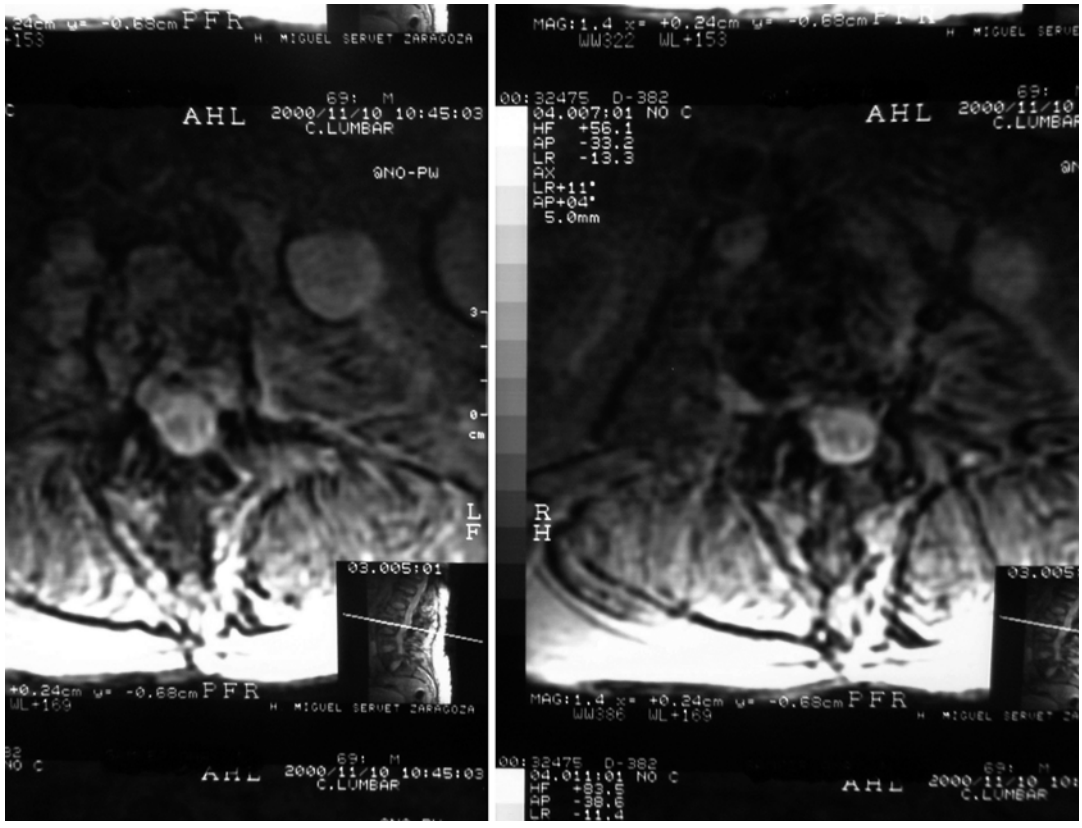

Fig. 9.24 Extradural intraspinal cysts

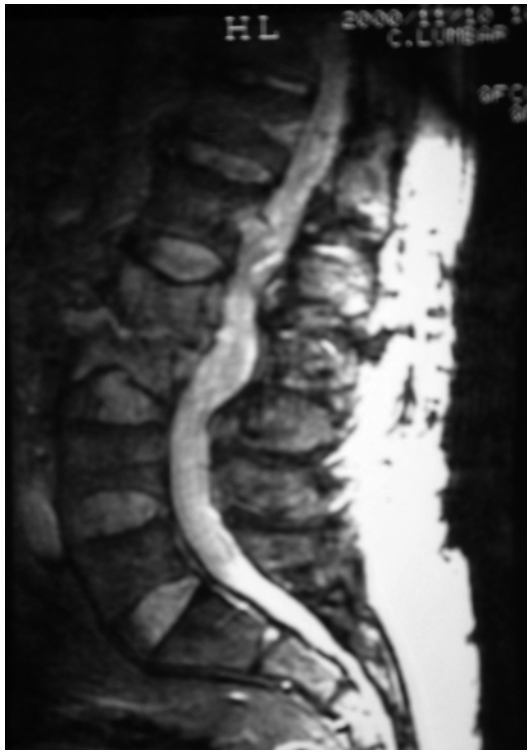

Fig. 9.25 Lumbar hydatidosis: involvement of two vertebral bodies, intraspinal cysts, and undamaged disc

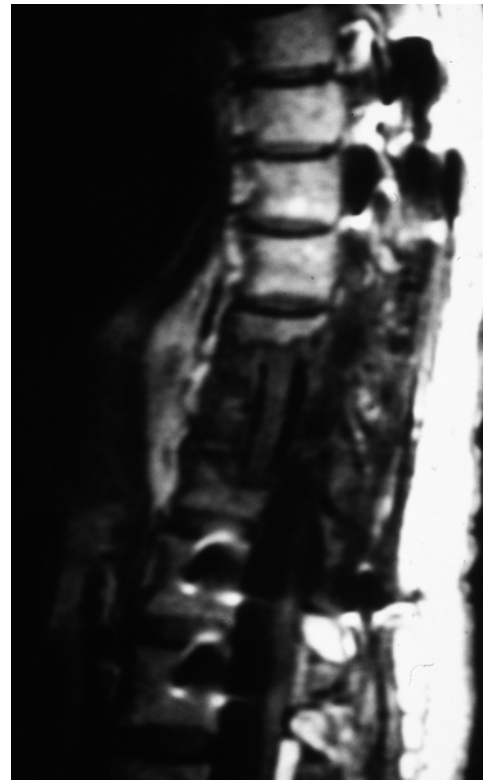

Fig. 9.26 MRI: follow-up in a case of partial corpectomy, bone graft, and posterior fixation

hydatidosis, but we use them routinely. White blood cell count is among these nonspecific tests. All of our patients had a slight leukocytosis, although a fair leukocytosis was found in two superinfection cases. Marked eosinophilia usually occurs in a high percentage of bone hydatid cases. In our experience, eosinophilia is found in 73.2 % of bone hydatidosis in any location and in 65.3 % of spine hydatidosis cases. All patients had an elevated erythrocyte sedimentation rate (ESR), ranging from 48 to73. ESR was higher in superinfection cases. The skin test, also known as Casoni's test, is clearly positive in a high percentage of cases, reaching an 88.7 % in our experience.

The application of enzyme-linked immunosorbent assay (ELISA) (Carmena et al. 2007) has been a breakthrough in the diagnostic process because of its greater precision and reliability. The most used technique is indirect ELISA. This test allows not only a qualitative diagnosis but also a quantitative one. Thus, the test can grade the intensity of the response and serves to determine the effectiveness of a surgical or medical treatment.

Significant levels of immunoglobulin G (IgG) can be detected using the purified antigen EM2 (Rausch et al. 1987). Likewise, high levels of IgG1 and IgG4 can be found using other antigens such as EM10 and Em18 (Wen and Craig 1994; Dreweck et al. 1997). We began using this test in the 1980s, and 82 % of our cases were positive. When the test was applied to monitoring the response to a surgery or chemotherapy treatment, a 40 % decline in total IgG values was detected. IgG2 determination was the most specific and better prognostic value test, which is consistent with the findings of Lawn et al. (2004). Laboratory findings of patients with hydatidosis of the central nervous system are discussed in Chap. 10.

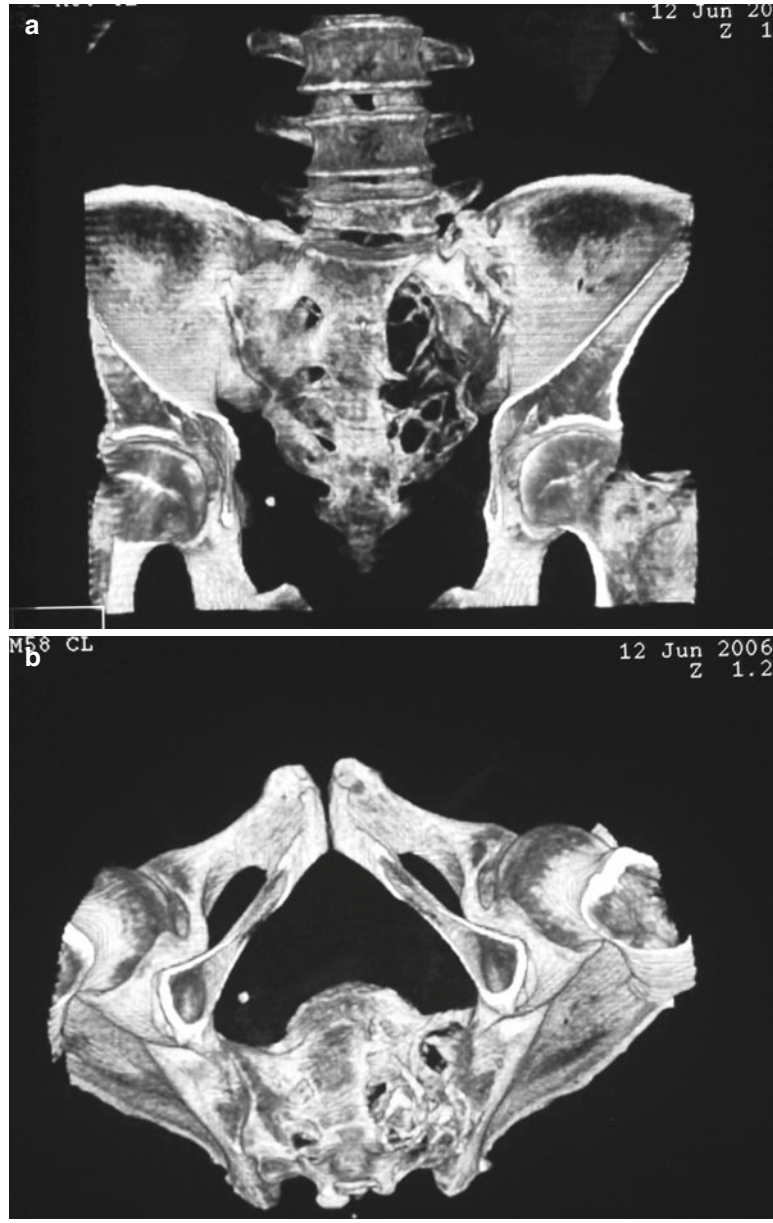

Fig. 9.27 (**a**, **b**) 3D CT of sacral hydatidosis

Diagnosis

The first step in the diagnosis is to suspect a vertebral echinococcosis in patients presenting with back pain, neurological deficits, and MRI or CT scan imaging findings suggesting spinal tumor or infection, especially in areas with high prevalence of hydatid disease. A detailed clinical interview is important, recording the medical history of the patient, region of origin, contact with farm or domestic animals or exposure to livestock, etc. History of echinococcal disease in other locations must be investigated. In our experience we found positive previous history of hydatid disease in 34.61 % of the patients with spinal echinococcosis. MRI and new laboratory tests

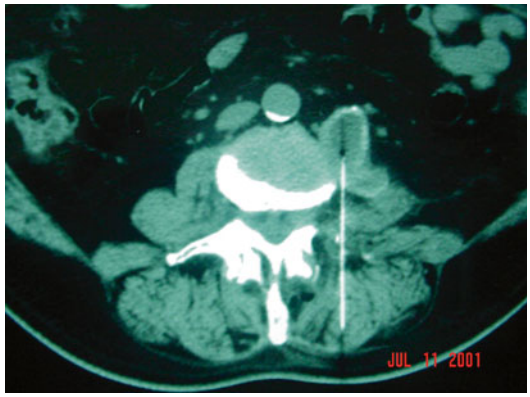

Fig. 9.28 CT-guided puncture of a hydatid pseudo-abscess

have provided a more precise diagnosis in the last years. CT scan images with 3D visualization of the spine can also be very helpful. In all cases under suspicion, we usually ask for a thoracoabdominal CT scan too.

While in the previous decades up to 40 % of the patients were diagnosed during the surgical procedure, nowadays 81.25 % of the diagnoses are made prior to the surgery. In our series, those cases resembling a vertebral pyogenic infection were the most challenging for the diagnosis. In two of them, we found a superinfection and the diagnosis was not made until the patients underwent surgery. In other two patients, a percutaneous CT scan-guided biopsy of a spinal abscess helped to clarify the diagnosis (Fig. 9.28).

Based on clinical findings, medical imaging, and laboratory tests, an early diagnosis must be made as an aid in surgical decision making, especially in patients with neurological deficit. The definitive diagnosis will be given by the surgical pathology analysis.

Treatment

Drug Treatment

Chemotherapy treatment of hydatid disease began in 1974 after the paper published by Heath and Chevis (1974). Within the benzimidazole drug group, mebendazole and albendazole have been the most widely used. We used mebendazole until 1986 with scarce effectiveness, possibly because of its poor absorption and subsequent low concentrations in serum and hydatid lesions (Bekhti et al. 1977). In 1986, we began to use albendazole, which has better absorption and achieves higher concentrations in serum by means of its active metabolite, albendazole sulfoxide (AlbSo) (Braithwaite and Lees 1981; Morris et al. 1983). Application rate of albendazole is 800 mg per day, in 28-day cycles, over a period of 6 months, with rest periods between cycles.

In our experience, chemotherapy can be considered as an adjunct to surgical treatment, but not as sole modality of treatment. Following the papers published at the end of the 1990s and early 2000 (Yasawy et al. 1993; Cobo et al. 1998; Urrea-Paris et al. 2000), we began to treat our patients with a combination of praziquantel, in doses between 25 and 50 mg/kg per day, and albendazole at 10 mg/kg per day. In our opinion, this association is more effective than albendazole alone, but the use of the combined chemotherapy has coincided with a more radical surgery, so it is difficult to assess the drug results. The fact is that we have treated several cases of spinal hydatidosis in recent years, and, currently, these patients are considered disease-free after a follow-up between 2 and 10 years post surgery. There were no major side effects, except for one patient with abnormal liver enzymes, who improved after discontinuation of therapy. Other drugs of the benzimidazole group have been used, such as oxfendazole and flubendazole (Morris and Gould 1982; Gavidia et al. 2010), but we have no experience with them. Other published studies talk about the use of substances that enhance the albendazole absorption or about the use of antimalarials such as mefloquine (Küster et al. 2011).

We believe that combined chemotherapy with praziquantel and albendazole is a good adjunct to surgical treatment. It is useful to limit the disease progression, but we don't believe that it must be

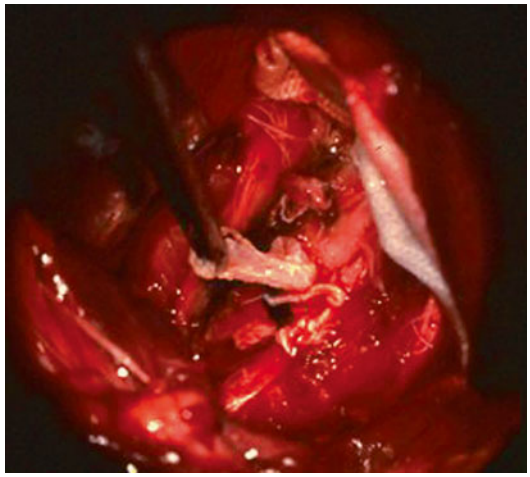

Fig.9.29 Removal of extradural cervical cysts

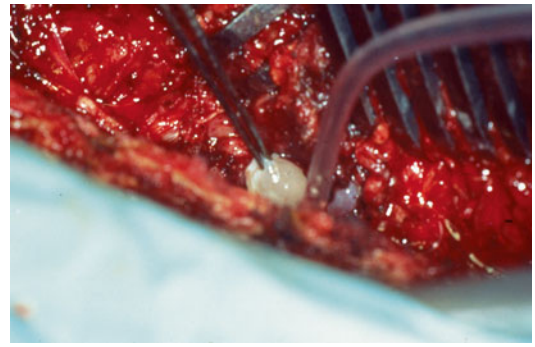

Fig. 9.30 Removal of extradural dorsal cyst

used as a sole treatment for bone hydatidosis. Our experience with two inoperable cases, located in the sacrum and the pelvis respectively, is that chemotherapy seems to stabilize the lesions. On the other hand, we do not take a month to complete one cycle of chemotherapy before spine hydatidosis surgery. Chemotherapy treatment is started if a firm diagnosis is available, and surgical treatment is carried out as soon as possible.

Surgical Treatment

An early surgical treatment is important when we suspect the diagnosis of vertebral echinococcosis. A delay in the diagnosis and treatment will result in a worse outcome of the surgery. In our hospital, which is the reference center for spine surgery in our region, a significant percentage of patients suffered of paraplegia or tetraplegia at the time of admission. Thirteen cases with spinal hydatid disease had severe neurological deficit. After surgery, although all patients improved, only one of them showed a complete neurological recovery.

Until the middle of the 1990s, the preferred operative treatment was an open debridement of the lesions and laminectomy with spinal cord decompression (Figs. 9.29 and 9.30). Continuous irrigation with hypertonic saline solution and formaldehyde was used during the surgery. This technique associated or not to an additional posterior fixation has been defended by many authors (Sami et al. 1996; Turgut 1997; Bhojraj and Shetty 1999; El Andaloussi et al. 2001). Nevertheless, in our experience, this surgical technique has shown suboptimal postoperative outcomes, especially a high percentage of infection recurrences.

From the 1990s onward, our approach to vertebral echinococcosis has become more aggressive, similar to that used for tumoral lesions (Herrera et al. 2005). When the infection is limited to the vertebral body, with or without involvement of the anterolateral aspect, we perform an excision of the cysts and a partial or complete corpectomy (Fig. 9.31) with anterior strut grafting (freeze-dried) through an anterior approach (Fig. 9.32). After that, a posterolateral spinal fusion is performed through a posterior approach (Figs. 9.33 and 9.34).

Sometimes the infestation spreads into the spinal canal through the extradural space. In these cases, when the cysts only affect the posterior aspect of the vertebral body or the pedicles, we use a posterior approach to perform a laminectomy, a

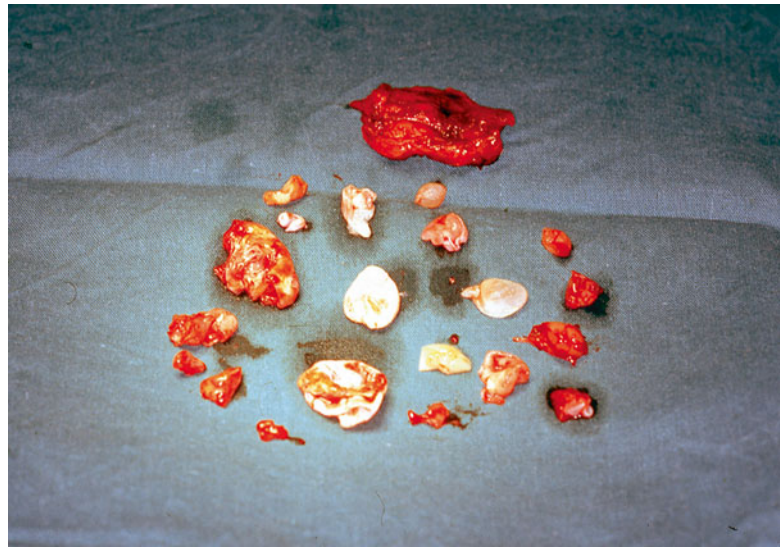

Fig. 9.31 Partial corpectomy: resected material

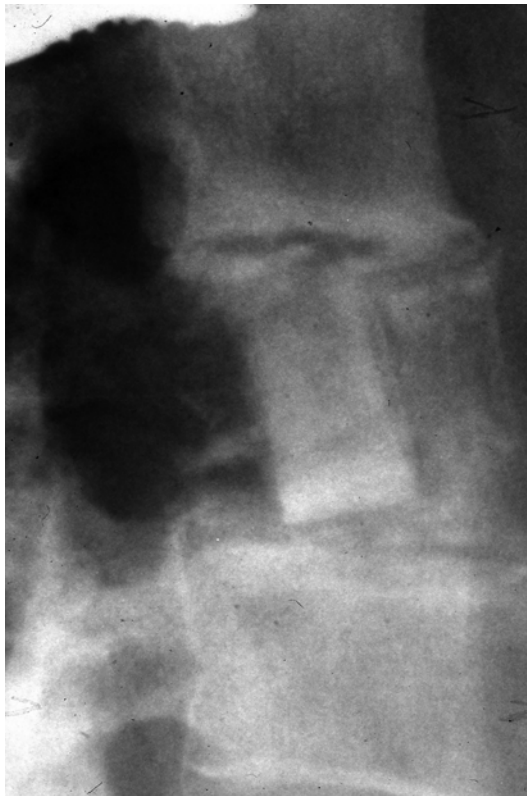

Fig. 9.32 Partial corpectomy: cryopreserved graft

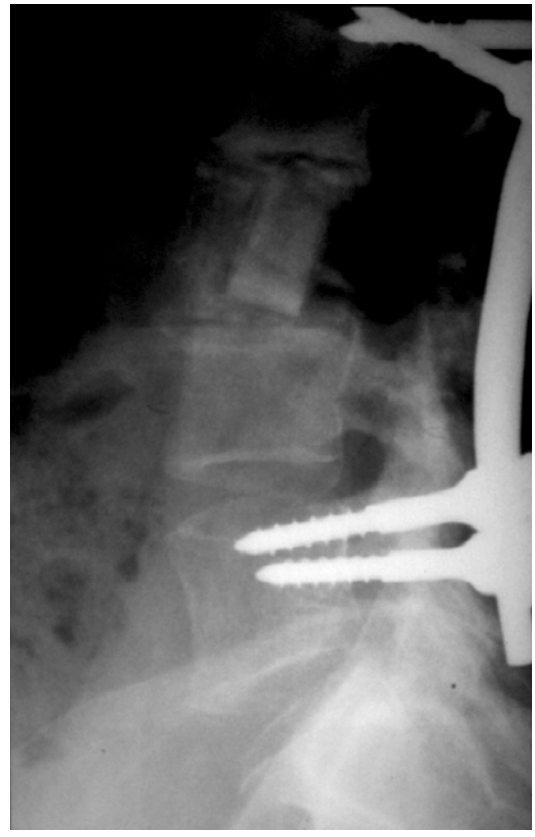

Fig. 9.33 Lateral radiograph: intersomatic graft and posterior fixation

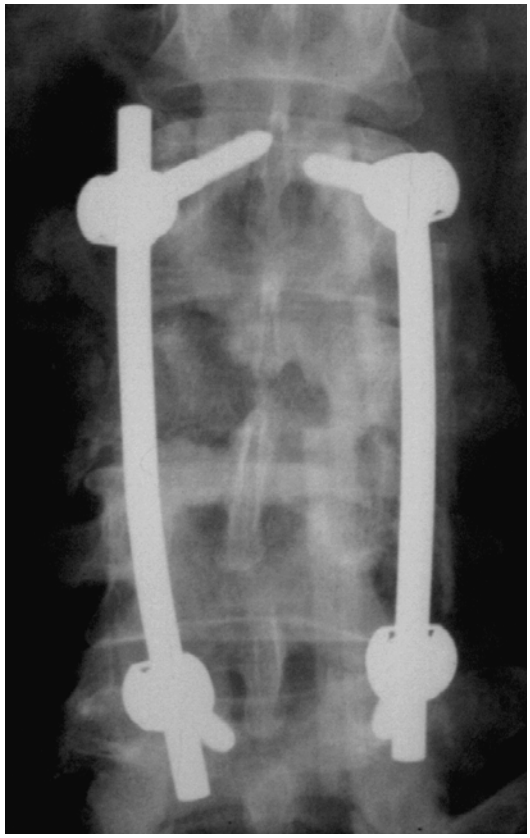

Fig. 9.34 AP radiograph of the case shown in Fig. 9.32

wide excision of the lesions, and a posterolateral instrumented fusion (Figs. 9.35 and 9.36).

But if the infection involves also the anterior part of the body, a combined approach will be necessary. We recommend performing first the decompression, curettage, and the instrumented posterior fixation through the posterior approach. Afterward, a partial or total corpectomy and grafting through the anterior approach are performed. With the combined radical surgery and a prolonged oral drug treatment, we have had good outcomes and absence of recurrences in the long-term follow-up in six of the eight patients treated with this protocol (Figs. 9.37 and 9.38). Those patients with paravertebral lesions or superinfection of the hydatid cysts had the worst outcomes, with the highest rates of recurrences that, in some cases, led to irresolvable infections. Surgical treatment of spinal hydatidosis is discussed in detail in Chap. 14.

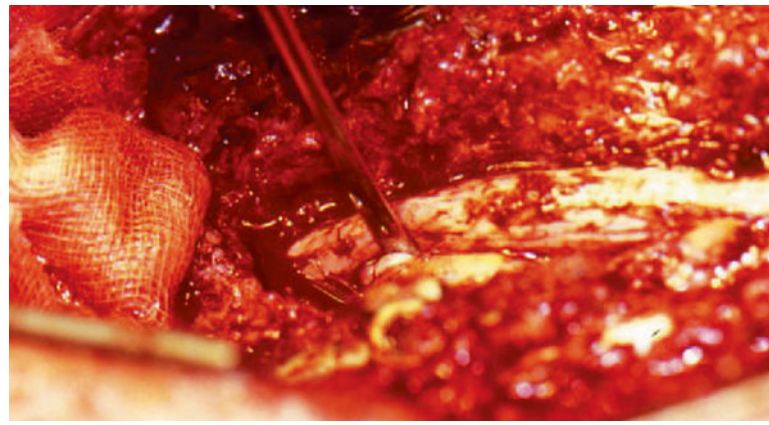

Fig. 9.35 Laminectomy and removal of extradural cysts

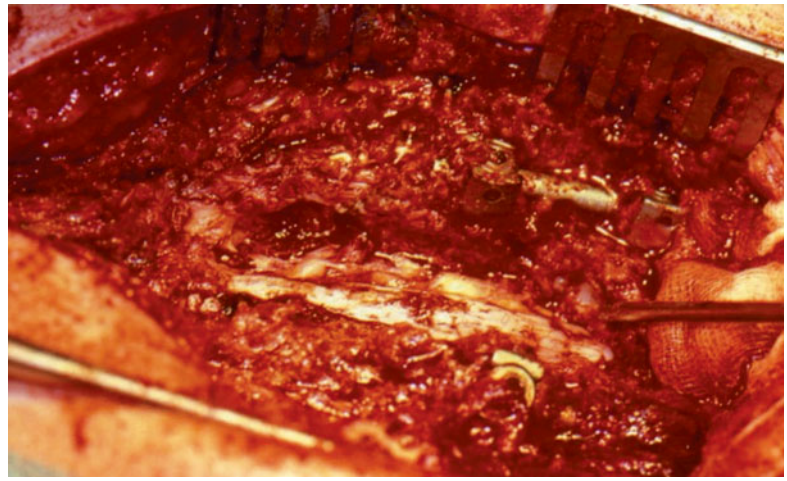

Fig. 9.36 Cyst removal in the case shown in Fig. 9.35. Note that pedicle screws placed

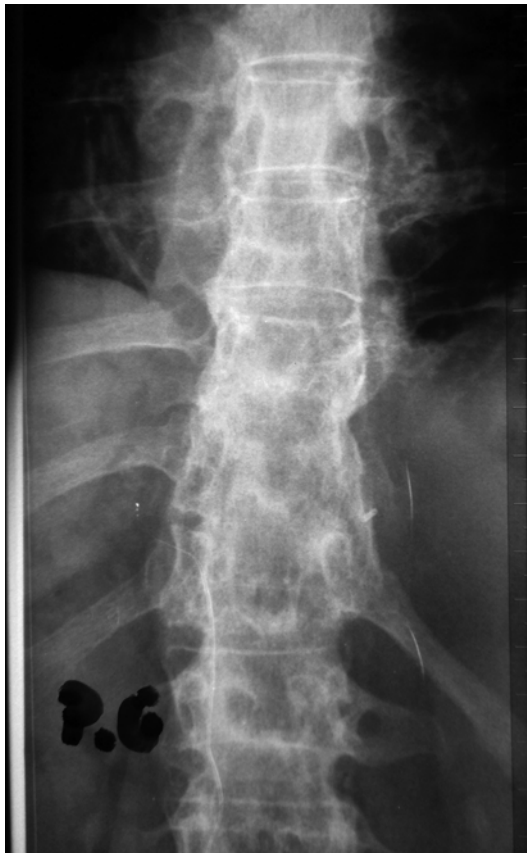

Fig. 9.37 AP radiograph at10-year follow-up: vertebral hydatidosis treated with partial corpectomy and posterior fixation. Note that the patient is disease-free

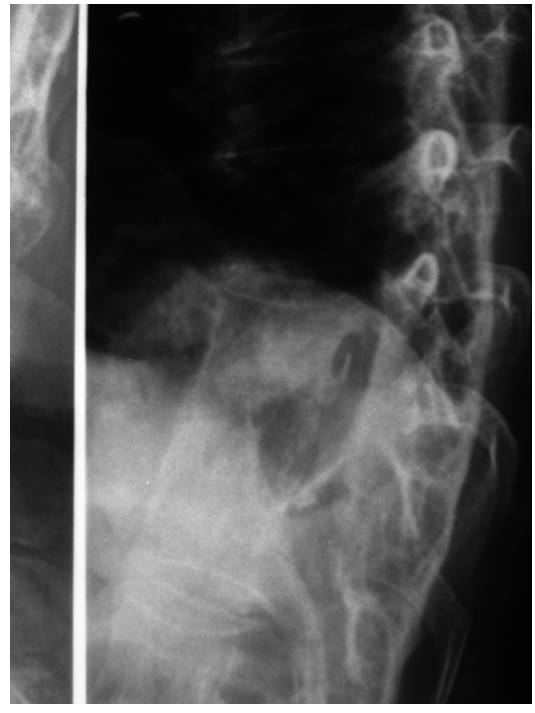

Fig. 9.38 Lateral radiograph of the same case shown in Fig. 9.37

Conclusion

Spinal echinococcosis is a severe disease with a technically demanding and challenging surgery. High migratory flows to the Western world might be associated with an upturn of

the incidence of infectious diseases like this, previously eradicated in our country. New imaging techniques, CT scan with 3D visualization and especially MRI, and laboratory tests (ELISA) have allowed an early diagnosis and treatment of hydatid spinal disease. In our experience, an aggressive surgical treatment associated with the use of prolonged chemotherapy (albendazole and praziquantel) has improved the outcomes for patients with vertebral echinococcosis.

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Laboratory Findings of Patients with Hydatidosis of the Central Nervous System

10

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Contents

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Introduction

The diagnosis of hydatidosis, caused by the larval stage of *Echinococcus granulosus* and *E. multilocularis*, respectively cystic echinococcosis (CE) and alveolar echinococcosis (AE), localized within different organs, including of the central nervous system (CNS), is very difficult to make during the primary stage of invasion because of the asymptomatic development until the appearance of morbid symptoms, which may not be specific. During the last three decades, new technologically acquired methods for diagnostic imaging, ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) have considerably facilitated the diagnostic process. Such diagnostic imaging requires expert diagnosis to differentiate benign and malignant tumors, nonparasitic cysts, and tuberculosis (Turgut 2002).

In practice, the parasitic nature of hydatidosis is established directly through laboratory diagnostic morphological methods (observation of protoscoleces, hooklets, parasitic cysts and their fragments, and histological preparations) or indirectly through immunologic methods which specify the parasitic nature of the disease in the primary stage; the findings are

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confirmed by diagnostic imaging (Taratuto and Venturiello 1997).

The clinical evaluation of laboratory information in the diagnosis of CNS hydatidosis is complex and is based on results from parasitological, histological, immunological, and other examinations. Specific clinicolaboratory examinations for the etiological diagnosis of this condition are unknown.

Hematologic Examinations

Clinicolaboratory hematologic tests for CNS hydatidosis are not specific in most cases, show considerable variation, and are not indicative of the disease. The reason is probably that the early appearance of serious clinical symptoms leads to seeking of early medical help (Turgut 2002).

In spite of that, hematological examinations are prescribed as a possibility for obtaining additional information for clinical diagnosis. Eosinophilia and leucocytosis in the full blood count, possibly anemia, and raised erythrocyte sedimentation rate (ESR) are kept under observation (Abbassioun and Amirjamshidi 2001a, b).

Eosinophilia

Examinations for eosinophilia in leucocytic formula (over 5 %) and in blood (exceeding 700/μL) should be conducted carefully, because they are signs of the pathological processes. Notwithstanding, this is not a permanent and reliable sign for diagnosis of CNS hydatidosis although it is accepted as an indication of live parasites. After death, calcification, or suppuration of hydatid cysts the hypereosinophilia disappears. It is found in one-third of patients and rarely reaches above 12 %, especially in multiple hydatidosis (Donovan et al. 1995; Turgut et al. 1997; Turgut 2002).

After successful surgical treatment the eosinophilia gradually returns to normal within a few months. If it remains elevated for more than 6 months, it is indicative of a postoperative recurrence or of residual cyst(s). The examination is a subsidiary method, very useful in the postoperative period (Reittner et al. 1996).

Leucocytosis, Anemia, Raised Erythrocyte Sedimentation Rate

Leucocytosis is usually observed in cases of suppuration, as well as necrosis in *E. multilocularis*. It has a subsidiary diagnostic meaning. Hypochromic anaemia is relatively rare (in up to 15 % of the patients) - the haemoglobin decreases to 60 %. The raised ESR is observed almost always in patients with hydatidosis (Herrera et al. 2005). These indexes – leucocytosis, anemia, and elevated ESR – are usually due to hydatic complications or to other accompanying diseases. Changes detected by clinical, laboratory, and hematologic examinations are infrequent and they are accepted only as additional indications. However, it is necessary to carry out these tests because, in many cases, they may help in specifying the diagnosis.

Examination of the Cerebrospinal Fluid

Examination of cerebrospinal fluid (CSF) obtained through lumbar puncture is important for the diagnosis of CNS hydatidosis. The most important contraindication is an increased intracranial pressure, which occurs in the course of the disease and should be checked in advance (Reittner et al. 1996; Turgut 2002). One looks for eosinophilic cells, hydatid protoscoleces, and hooklets in the CSF or, in case of unclear or negative results from the parasitological examination, an immunological examination should be made of the liquor for hydatidosis (Tappe et al. 2008).

Hydatid Protoscoleces

If fertile hydatid cysts rupture in the ventricles, parasitic scoleces and hooklets flood the CSF. These appear in the centrifuged CSF sediment

under the microscope at a magnification of 100× for the protoscoleces and 400× for the hooklets.

Eosinophilia in Cerebrospinal Fluid

An important diagnostic finding is the presence of eosinophilc cells in the centrifuged sediment of a CSF sample. This is best seen under Giemza staining. In CNS hydatidosis an abundant eosinophilic infiltrate collects around the cyst in the cerebral tissue. These cells penetrate the CSF channels. These cells are not always found in the CSF of patients suffering from CNS hydatidosis. In these cases the CSF reveals hyperproteinemia, with moderate pleocytosis, with a presence of eosinophilic cells.

Parasitological Morphodiagnostics

The most certain and precise diagnosis results from histopathological study of tissue removed at surgery.

Macroscopic Examination

A careful inspection of the presented operative material for presence of hydatid membranes, fragments of membrane, or daughter cysts is in order. The removed hydatid cyst is cut with sharp pointed scissors. The internal surface is scraped for "hydatid sand" (protoscoleces, hooklets, brood capsules) and small daughter cysts. These are removed and put into a glass container with water. The collected material is washed several times and is fixed in 70° ethanol and 10 % formalin for 1 h and is then kept in 70° ethanol.

Microscopic Examination

Protoscoleces

These are observed in native preparations. The collected hydatid fluid is centrifuged and a drop of sediment is put on a slide. The sediment is examined microscopically under a cover glass (magnification 100×). The protoscoleces have a characteristic structure and are agile. They have an oval form, sharply lined. Inside, a line of hooklets is observed, grouped around elongated axis in the middle of the protoscolex and forming a crown. Its dimensions are about 110/150 μm. From the sediment covering the slide a fixed stable preparation can be prepared for demonstration and training after Giemza staining.

Hooklets

Free hooklets can also be observed under the microscope in hydatid fluid sediment (magnification 400×). The hooklets of *E. multilocularis* are larger than those of *E. granulosus*. This comparison is possible when a single sample has hooklets from both species. They differ from one other in that the *E. granulosus* hooklets root has a bend while that of *E. multilocularis* has a more acute arc shaped bend (Vogel 1978).

Biological Method

The biological involves laboratory mice, inoculated with material suspected of hydatidosis.

Echinococcus granulosus

A specimen cyst, or fragments of it, should be washed with a saline solution and then placed into a laboratory conical glass container. After precipitation over 1 h the separated scolex sediment is washed several times with saline solution, drawn out into a syringe, and injected intraperitoneally into test animals. After 3–5 months an autopsy is performed. If in the examined material (hydatid cyst and hydatid fluid) there were viable scolices, new cysts are observed in the peritoneal cavity.

Echinococcus multilocularis

Cyst viability is investigated through test animals. Small pieces of surgically resected parasitic cysts are subjected to intraperitoneal or intrahepatic inoculation. If they do not increase in the animals, it is confirmed that the cysts are dead.

Determination of Protoscolex Vitality

This examination is particularly important to determine the prognosis by examining the operative specimen from *E. granulosus* cysts with protoscoleces, and for advice as far as non-recurrent conservative treatment is concerned. By heating the hydatid fluid (37–38 °C) the viable protoscoleces are desinvaginated, the crown with hooks comes out, and they begin to move actively. The staining method for determining the vitality of hydatid protoscoleces is easy. A hot, saturated methylene blue solution is used, which is put on a slide to obtaining an azure color. The solution is left to dry. For examination, a cover glass covered with protoscoleces is laid on the dye. The coloring agent penetrates only the dead protoscoleces and the viable ones do not absorb paint and remain unstained.

Morphological, Pathological, and Histological Examinations

Echinococcus granulosus

Primary localization of hydatid cysts in the CNS is rare. These cysts may be found in the hemispheres, ventricles, extradural and subcortical, and very rarely in the cerebellum and spinal cord. Children are more often and more severely affected and have an increased intracranial pressure. The hydatid cyst is normally single, spherical or oval, and filled with clear fluid (hydatid fluid). In some cases they appear as a "cluster." The pathological alterations in the surrounding tissues depend on the localization, size, and changes in the cyst itself: whether it is intact, ruptured, suppurated, or calcified (Abbassioun and Amirjamshidi 2001a, b; Haddad and Haddad 2005).

The appearance of the hydatid cyst is typical and it can be easily recognized visually. They consist of three layers: (1) an outer fibrous (adventitial) layer out of the real parasite, with different thicknesses and even absent – the pericyst; (2) an acellular (multilayered, laminated) membrane, easy to separate from the fibrous capsule and having a whitish color – the ectocyst; and (3) a very fine germinative membrane with numerous brood germinal capsules fastened to its internal surface – the endocyst. In larger cysts there can be "daughter cysts," swimming in hydatid fluid as well as "hydatid sand" in the sediment, formed from hydatid protoscoleces and hooklets which are visible under the microscope (Taratuto and Venturiello 1997).

The tissue reaction around the cyst is minimal, with infiltration of mononuclear cells. Degenerated and calcified cysts have similar infiltrates. In the case of bacterial infection there is a considerable inflammatory reaction with polynuclears, mainly eosinophils, and granulomatous inflammation with histocytes, giant cells, and connective tissue surrounding the cyst (Kars et al. 1982; Taghipour et al. 2008).

Histological diagnostics is best when made on material obtained by surgical operation or autopsy. All fragments from the obtained specimen have to be examined for laminated membranes, presence of daughter cysts, and viability. The dead cysts are necrotic, with semifluid content. The calcified cysts are also dead and they are removed surgically only if they are infected. In incompletely calcified cysts there are viable scolices. The viable cysts have the characteristic three-layer membrane (Kars et al. 1982; Özek et al 1993; Taratuto and Venturiello 1997).

The laminated membrane of the hydatid cyst is stained with the periodic acid (Schiff reaction), or PAS stain which is a histological marker for hydatid cyst. It is ten times thicker than the germinative layer which consists only of two cell layers. The protoscoleces are easily discernible with their characteristic hooklets; even if they are degenerated the hooklets remain (Taratuto and Venturiello 1997). Sediment from the hydatid fluid mixed with formalin is examined parasitologically; depend on where the sample is obtained, hooklets can be found as well as protoscoleces and fragments from laminated membrane. The hydatid cyst within bones (for example in the vertebral column) has no fibrous capsule, and in the intra-trabecular areas numerous small cysts develop. In the spinal cord the hydatidosis is a secondary invasion.

Echinococcus multilocularis

Clinically this looks like a malignant tumor, slowly increasing in size in the liver which can metastasize to the CNS: also occurs in the brain and, very rarely, in the orbit and spinal cord. The resected parasitical cysts look like a gray whitish mass, a conglomerate of small bladders connected with connective tissue. They have an exogenic growth and infiltrate the surrounding tissue (Craig 2003).

Around the cysts there is no fibrous layer and the germinative and laminated membrane of small cysts (2–3 mm) have a cellular appearance. They contain gelatinous material and only in some of them are protoscoleces found. (Taratuto and Venturiello 1997). The surrounding tissue reveals an inflammatory reaction, with infiltrates of polynuclears and many eosinophils, lymphocytes, histiocytes, and giant cells. The laminated membrane is stained for hydatidosis with PAS (Toussaint et al. 2001; Craig 2003; Yang et al. 2005).

Immunodiagnostics of Hydatidosis

Introduction

Early detection of the disease by immunodiagnostic methods is of considerable importance. It leads to early and adequate treatment and prevents the formation of serious complications, which can even lead to a fatal outcome.

Hydatid immunology investigations have developed considerably during the last few decades, but certain immunodiagnostic methods date from the very beginning of the last century: Gedhin, Weinberg test (1906, 1908), Casoni test (1911).

Characteristic of the *E. granulosus* antigen structure is the presence of heterogeneous antigens, which cross react with host antigens as well as with antigens of *E. multilocularis* and some other helminthes. As a result ,immunologic false results may be reported. False negative results are observed, too, in different organ localizations of hydatidosis, including the brain, orbit, as well as lungs, spleen, etc. Negative results are observed in new, small, dead, and calcified cysts.

False-positive and false-negative results are met less and less due to the introduction of new immunologic methods. They allow for an early diagnosis, because immune antibodies are detected 2–3 weeks after the primary invasion, even before clinical symptoms appear.

Evidences of Application

The immunological diagnosis of hydatidosis by different methods is used under the following circumstances.

Clinical Evidence

This is based on the detection of antibodies in the patient's blood, which are produced by the cysts while they are still very small – up to 1.0/1.5 cm. It differentiates hydatidosis from other diseases. Through repeated measurement it evaluates the efficiency of surgical treatment and of its successful outcome. In the case of decreasing specific antibody titers or negative diagnostic reaction, it reveals a good prognosis. In the case where the diagnostic titer remains at the same level or rises in level, this shows a postoperative recurrence. The clinical efficiency is evaluated by analogy to conservative therapy.

Epidemical and Prophylactic Evidences

Immunodiagnostic methods find application by large-scale diagnostic screening-seroepidemiologic surveys among the population at risk from different professional, social, and age groups. This is done for detection of epidemic foci, investigation of epidemiology, epizootiology, and infection risk degree. Of great importance here is the prophylactic diagnosis of family members of hydatidosis sick patient, where the diagnosis of so-called "family hydatidosis" is possible. Immunodiagnostic reactions by indirect hemagglutination (IHA) and enzyme-linked immunosorbent assay (ELISA) are suitable for large-scale investigations, in which reactions

are highly sensitive and very specific. There are preprepared immunodiagnostic preparations, suitable for differential diagnostics–specific for *E. granulosus* and *E. multilocularis* invasion, respectively.

Contemporary National Programs

Contemporary national programs for control of hydatidosis include the early diagnosis of asymptomatic forms as one of their basic measures. It is realized by making large-scale screening examinations as a first diagnostic means or combined with diagnostic imaging methods. The combination of two tests is recommended, for example ELISA and Western blot (Craig and Larrien 2006). Such examinations are carried in some endemic countries on different continents.

Immunity and Diagnostics

The *E. granulosus* species is genetically heterogeneous and consists of ten strains (G1 to G10), defined through molecular biological methods such as polymerase chain reaction (PCR) and differences in antigen content as well as in basic intermediate and end hosts. The most widespread is the sheep strain (G1). Because of antigen differences of the irregularly spread genotypes, it is recommended that antigens of *E. granulosus* isolates are used, which are specific for a particular geographic area (Eckert and Dephazes 2008; Rosenvit et al. 2006; Gihan et al. 2009). By chronic invasion of *E. granulosus* and *E. multilocularis*, the interaction between parasite and host leads to considerably expressed humoral and cellular immune response.

Humoral Immune Response

B lymphocytes produce specific antibodies – a process conditioned by antigens passing through the parasitic cyst membrane. The immune response is influenced by the cyst structures, individual genetic host differences, invasion duration, etc. In serum of hydatidosis sick patients specific antibodies of IgG, IgE, IgA, and IgM types may be detected.

Antibodies of IgG type: these immunoglobulins are basic antibody types, which are produced by *E. granulosus* invasion and consist of four subclasses, respectively IgG1 to IgG4. Having most expressed sensitivity and specificity are IgG1, cross reactions are mostly due to IgG2, those with protective functions are IgG3, and specific and without cross reactions are IgG4 (the last mentioned are detected only in two-thirds of the cases of invasion) (Ramzy et al. 1999).

Depending on organ localization, the humoral immune response differs in diagnostic value. Those by parasitic cysts in brain and orbits IgG antibodies are quite often specific. The immune response also depends on the parasite morphology. In injured cyst membrane it is elevated and in suppurated cysts it is reduced and can even be missing. In secondary echinococcosis the immune response is more elevated in comparison with primary echinococcosis. After successful treatment the immune antibodies decrease and eventually disappear.

Antibodies of IgE Class: these are involved with the pathogenesis of allergic reactions of the first type (IgE mediated reaction of hypersensitivity). The specific IgE are tissue antigens, liberated under the influence of parasitic metabolic products. In *E. granulosus* invasion they are detected in the serum specific IgE antibodies in 25–90 % of cases, but allergic reactions of a quick type appear very rarely in intact cysts. The reason is the presence of IgG4, which blocks the anaphylactic reactions. Fixed in the skin, antiparasitic IgE explains the Casoni test effect. The common and specific IgEs are present more in multiple hydatidosis and in the presence of daughter cysts, but their level depends on the organ localization. In calcified cysts the IgEs decrease gradually. After effective treatment for up to 1 year they are detected only in a half of the cases (Ortona et al. 2003).

Antibodies of IgA and IgM Class: these are rarely examined. Antiparasitic antibodies of these classes are detected in serum of low parasite content antibodies – IgA to 54 % and IgM to 37.5 %, but with high specificity –100 % and 95.7 % respectively. After effective treatment they persist for some years and are unsuitable

for evaluating post treatment tracing patients (Doiz et al. 2002).

Cell-Mediated Immune Response

T-lymphocytes decrease in the blood as does their functional activity. An immunosuppression develops as a result of cytotoxic effects of low molecular *E. granulosus* fractions, T-sub-spherical activation (CD8+), and unbalance between subpopulations Th1 and Th2 of T-helper cells (CD4+). In fertile cysts the activity of Th2 increases, becoming apparent with increased values of IL-4 and IL-10 and IFN-γ decreasing. After effective treatment the IL-4 and IL-10 generating decreases and IFN-γ increases. The examination results of these markers in various dynamics are indicative, but they are unsuitable for routine practice because of high cost and difficult execution (Ortona et al. 2003).

Now we will briefly discuss the basic routine immunodiagnostic tests, applied in practice as described below.

Routine Immunological Diagnostic Tests

According to the purpose of immunological tests in routine diagnostic practice, they are classified as either primary diagnostic and screening tests or secondary confirming tests, after WHO. Until now no absolutely specific and sensitive tests for hydatidosis diagnosis have been developed.

Primary Diagnostic and Screening Tests

Primary diagnostic and screening tests are of high sensitivity and limited specificity. The ELISA, IHA, latex agglutination test (LAT), and bentonite flocculation test (BFT) reactions and immunoelectrophoresis are the most often used in practice. It is recommended to use a minimum of two primary tests in each case under diagnosis.

Secondary Confirming Tests

Secondary confirming tests are usually less sensitive than the primary ones, but with higher specificity. These are the Western blot reactions, agar double-diffusion (DD5), and IgG subclass determination.

Antigens Used in Immunological Tests

Hydatid cyst liquid, which contains two important diagnostic antigens (Ag5 and AgB), is most often used for diagnosis (Biffin et al. 1993). Ag5 is a thermolabile lipoprotein complex which has two compound parts molecular masses of 57 and 67 kDa, respectively. It disintegrates into two fractions with molecular masses of 20/22 and 38/39 kDa (Gonsales-Sapiensa 2000). The second fraction can also be detected in healthy people. Cross reactions may occur with other helminthoses and in people with blood group antigen P1 (Gadea et al. 1999). AgB is a thermostable lipoprotein with a molecular mass of 120/160 kDa and is detected by all four Echinococcus species. Five forms of AgB with five different genes are detected in different strains. Basic, purified, and recombinant antigens are used in scientific investigations (Ortona et al. 2000). Besides hydatid liquid antigens, larva extracts as well as histological cuts of protoscolices are used in immunological reactions, being subjected to fluorescent antibody tests.

Immunological Methods Proving the Anti-Echinococcus IgG

Complement Fixation (CF, Weinberg–Ghedini Test)

Complement fixation was first used in Echinococcus diagnosis by Ghedini in 1906 and improved by M. Weinberg in 1908. Its sensitivity reaches 60–70 %. It is applied in parallel with the fluorescent antibody test (FAT) and indirect hemagglutination assay (IHA). The serological titer decreases quickly after successful therapy. However, if it remains elevated for 6–12 months this indicates a recurrence. This test is not very specific – it is complicated in execution and has now almost fell into disuse as a routine practice (Kagan 1968).

Agglutination Reactions

Agglutination reactions as immunological methods providing the anti-Echinococcus IgG are described below.

Indirect Hemagglutination Assay (IHA): introduced in 1957 and is still often used in practice. Erythrocytes loaded with Echinococcus antigens are used. The reaction sensitivity varies from 62 to 100 % and the specificity from 92 to 100 % depending on the diagnostic kit quality. It gives cross reactions with other helminthoses as well as nonparasitic diseases (Kagan 1968; Zhang and McManus 2006).

Latex Agglutination Test (LAT): introduced in 1960. Latex particles loaded with Echinococcus antigens are used. The sensitivity is between 50 and 92 % and the specificity is 95 %. Cross reactions are also observed in 10 % of cases (Kagan 1968). The test is easy and rapid in execution and suitable for the practice.

Bentonite Flocculation Test (BFT): applied for echinococcosis in 1959 by Norman, Sadun, and Allain. Inert bentonite particles loaded with parasitic antigens are used. The test sensitivity is 70–100 % and the specificity 94 %. Cross reactions with other diseases are observed in 3–27 % of cases (Kagan 1968).

Precipitation Reactions

Precipitation reactions as immunological methods providing the anti-Echinococcus IgG are described below.

Scolex Precipitation: first used by Schulz and Ismailov, 1962. Rarefied scolices are used in saline solution. On adding serum of patient, microscopic precipitates are observed on the scolex cuticular surface. The sensitivity is very high, 82–94 % and the specificity is 88–100 %. This is not applied in routine practice because live scolices are used.

Double Diffusion Arc 5 (DD5): arc 5 fraction – which is identical to Ag5 – is found in echinococcic liquid (Porreti et al. 1999; Zhang and McManus 2006). It is an agar reaction and the immune complexes are observed on a precipitation strip. The sensitivity is 47 % and specificity 93–100 %. Cross reactions occur with alveococcosis and cysticercosis.

Immunoelectrophoresis: used especially for investigation of the composition of antigens in echinococcic liquid. Antibodies and antigens form in the electric field on an agar precipitation strip. The sensitivity is 63–80 % and specificity 97 % (Zhang et al. 2003). It is unsuitable for seroepidemiologic investigations and is only used in clinical diagnosis.

Reactions with Participation of Marked Antibodies

Reactions with participation of marked antibodies as immunological methods produced by the anti-Echinococcus IgG are described below.

Fluorescent Antibody Test (FAT): introduced for echinococcosis diagnosis in 1963. Antibodies are proved through indirect immunofluorescence. Hydatid protoscolices or histological slices containing the antibodies are fixed on a slide. On contact with serum the antibodies combine with the parasite antigens. The reaction is visualized by addition of anti-human antibodies, conjugated with fluorochrome, which fluoresces specifically under ultraviolet light. The sensitivity is high – 82–100 % (Kagan 1968). It is often applied in parallel with IHA.

Enzyme-Linked Immunosorbent Assay (ELISA): applied to echinococcosis in 1974. A total echinococcic liquid is used as antigen. Methods have been developed with purified antigens – Ag5, AgB, and recombinant antigens (Gonzalez Sapienza et al. 2000; Siles-Lucas and Gottstein 2001; Ortona et al. 2003). The reaction sensitivity is 44–100 % and specificity 65–100 %. In rarer echinococcosis localizations, such as in brain and orbit, the sensitivity is lower –25–56 %. Cross reactions with other helminthoses (fasciolosis, schistosomiasis) and some malignant diseases are rarely observed. It is also applied to diagnosis of *E. multilocularis* invasion and the antigen used is from a parasite larva secretion, purified and recombinant antigens.

Enzyme-Linked Immunoelectrotransfer Blot (Immunoblot, Western blot, EITB): different antigen fractions are used. They are divided by molecular mass through electrophoresis and are transferred on a membrane, which undergoes an immunoenzymatic reaction. The

presence of antibodies against antigen fractions is visualized as a strip with definite molecular mass. It is accepted that the 8/12 kDa fraction, which derives from AgB, is of diagnostic importance for the echinococcosis. The sensitivity is variable – 65–100 % – and the specificity is high – 94–100 %. Cross reactions with alveococcosis are met in 53–84 % of cases. The test is a reliable confirmatory diagnostic method with a high sensitivity and specificity index (Verastegui et al. 1992; Gadea et al. 1999; Porreti et al. 1999; Makni et al. 2007).

Immunological Tests for Investigation of Anti-Echinococcus IgE

Casoni Intradermal Test

This is a method for echicoccosis diagnosis and is applied "in vitro" and through allergic reaction. An echinoccocic liquid is injected intradermally and the erythema size is measured every 30 min. The use of unstandardized antigen often leads to false positive results. The sample sensitivity is 75–95 % and the specificity is low – 55–82 % (Kagan 1968). After a Casoni intradermal test the treatment efficiency cannot be determined with this test, because sensitization occurs, and remains positive so the humoral antibodies produced make the serological tests positive. At present it is not recommended by WHO because of the risk of serious allergic reactions and low specificity.

Basophil Degranulation Test

Concerns detection of anti-Echinococcus IgE, fixed on basophil cells. The developed degranulation test has a high sensitivity – 93% and specificity – 97–100 %.

Serologic Method

Recombinant antigens and monoclonal antibodies – called the Western blot – are investigated for IgE antibodies, which react with AgB. The sensitivity is low – 50–52 % – but the specificity is high – 95–100 %. The surveys for specific IgE are not enough and there are no diagnostic tests in routine practice. They are confirmatory tests because of their high specificity and low cross reactivity (Ortona et al. 2003).

Molecular Biological Method

The polymerase chain reaction (PCR) is used for species identification of *E. granulosus* and *E. multilocularis* in areas where both diseases are spread. By means of PCR a strain identification of *E. granulosus* is made from G1 to G10 (Weiss 1995; Yang et al. 2006).

Conclusion

The introduction of immunological methods and techniques in suitable combination leads to an optimal diagnostic conclusion. By means of other diagnostic possibilities such as imaging diagnostics and laboratory-clinical examinations it is possible to exclude other diseases. The use of at least two tests for routine immunological testing in hydatidosis of CNS, orbit, and spinal column is recommended. The suitable combinations are IHA with FAT as well as IHA with ELISA or ELISA with Western blot confirmation (Force et al. 1992; Doiz et al. 2001). In the post treatment period (surgical, conservative) we have accepted a minimum time limit of 5–10 years. Periodically we evaluate the antibody titer with immunological examination on ELISA and IHA. Following effective treatment it usually decreases progressively down to non-diagnostic values in 3–5 years. While FAT becomes negative quite quickly, the IHA remains positive for a long time (as long as one to two decades), but at low levels. High titers, as well as increasing after operation, indicate the presence of residual cysts or postoperative recurrences.

Figure 10.1 shows in bold characters the use of laboratory diagnostic methods on patients with hydatidosis of CNS.

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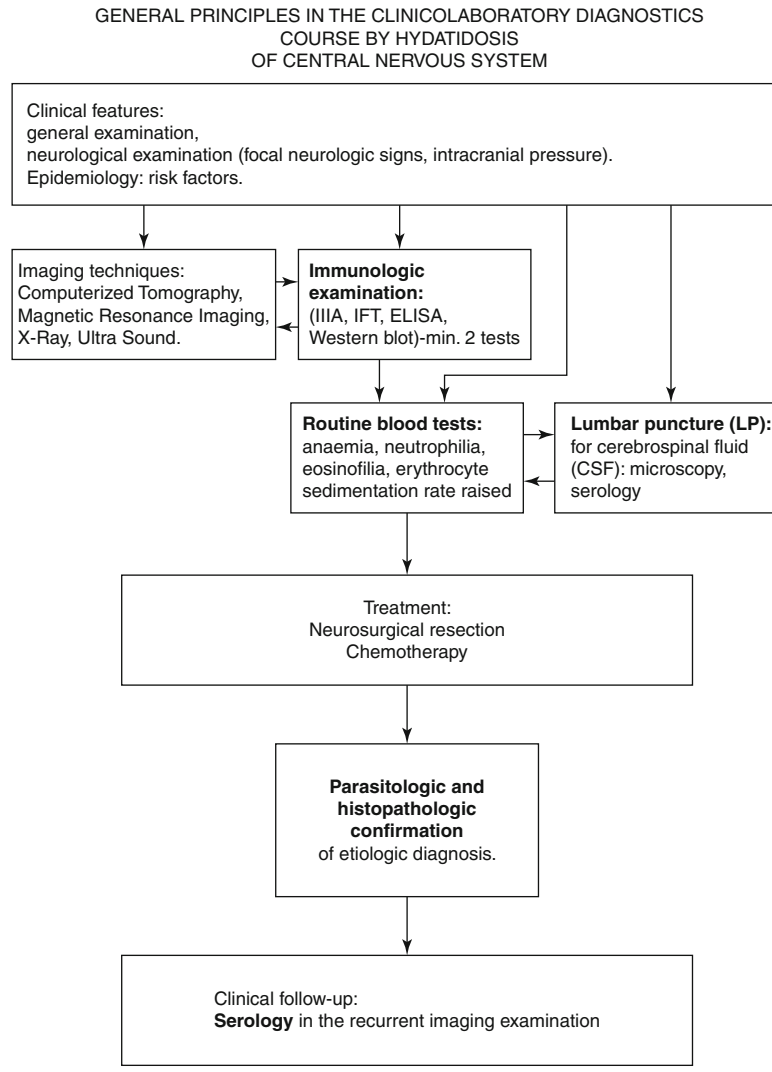

Fig. 10.1 General principles in the clinico-laboratory diagnosis course in hydatidosis of central nervous system (*Echinococcus granulosus* and *E. multilocularis*)

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Imaging of Cerebral Hydatid Disease

11

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Introduction

In humans, the two main types of hydatid disease are cystic echinococcus (CE) and alveolar echinococcosis (AE) that are caused by *Echinococcus granulosus* and *E. multilocularis*, respectively (da Rocha et al. 2005; Foerster et al. 2007; Aiken 2010).

Classification

There are different classifications of CE. It may be classified as simple, complex, or infected cysts or as unilocular or multilocular cysts (Abdel Razek et al. 2009; Brunetti et al. 2010). The World Health Organization Informal Working Group on Echinococcus of CE follows the natural history of the cyst and classifies CE according to its viability into active fertile (CE1 and CE2); transitional (CE3); and degenerated, inactive, and infertile cysts (CE4 and CE5). The use of such classifications facilitates the application of uniform standards and principles of treatment for each cyst type in different parts of the world. The presence of protoscoleces and scoleces at histopathological examination is helpful in the evaluation of viability of the CE and serves as a guide for radiologists working in a multidisciplinary committee with clinicians, surgeons, and pathologists (Abdel Razek et al. 2009; Brunetti et al. 2010).

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Methods of Examination

Routine pre- and post-contrast magnetic resonance imaging (MRI) is commonly used for diagnosis, localization, and classification of cerebral CE. Advanced MRI techniques such as magnetic resonance spectroscopy (MRS), diffusion-weighted MRI (DW-MRI), and perfusion-weighted MRI may help in the diagnosis of cerebral hydatid cyst. Multidetector computed tomography (CT) scan has also been used for the diagnosis of intracranial hydatid cysts, especially the calcified lesions (Demir et al. 1991; Topal et al. 1995; Tüzün and Hekimoglu 1998; El-Shamam et al. 2001; Sqahin-Akyar 2002; Bukte et al. 2004; Ravalji et al. 2006; Basraoui et al. 2010; Wani et al. 2010, 2011; Bartosch et al. 2011).

Imaging Appearance

The cystic lesion (CL) appears as a simple cyst without a discernible wall. This form must be considered in the differential diagnosis of cystic lesions of the brain. CL are active lesions, as they represent an early stage of cyst development (Abdel Razek et al. 2009, 2011).

The CE1 cyst: It is the most common type of CE and represents the active form of the disease. At CT scan, it appears as a large well-defined thin-walled hypodense cyst with marginal calcification along the wall in some cases (Bartosch et al. 2011; Basraoui et al. 2010; Bukte et al. 2004; Ravalji et al. 2006; Wani et al. 2010). On MRI, it appears as a spherical or oval and well-defined, smooth, thin-walled, homogeneous cerebrospinal fluid-isointense cystic lesion, which may reach up to 15 cm in size. Cerebral edema around the cyst is not a common finding, but may occur infrequently. The hypointense rim on T2-weighted MRIs represents the outer, host-derived pericyst, middle laminated membrane, and inner germinal layer (Sqahin-Akyar 2002; Bukte et al. 2004; Ravalji et al. 2006). A thin rim of contrast enhancement limited to the capsule may be detected. Contrast enhancement is not typical since the lesion is usually quiescent. Thin rim of CE, limited to the capsule region, may be detected (usually only one segment) due to focal meningeal adhesions and inflammatory reactions due to previous cyst leakage (Abdel Razek et al. 2009, 2011) (Fig. 11.1).

The CE2 cyst: It appears as a unilocular maternal cyst with peripherally arranged broad daughter vesicles. The presence of smaller daughter cysts within the primary maternal cyst is considered to be pathognomonic of a hydatid cyst. It signifies an attempt at survival by a damaged or dying cyst. Daughter vesicles (broad capsules) are small spheres that carry the protoscoleces. Daughter vesicles are formed from internal budding of the germinal layer. The wall of the daughter cysts appears as low signal intensity (Abdel Razek et al. 2009, 2011). A high-signal-intensity rim may be seen around the maternal cyst on T2-weighted images. This is explained by degenerating larvae releasing metabolic products that disrupt the blood-brain barrier with host inflammatory response (Fig. 11.2).

The CE3 type: It develops from rupture of the primary cyst with endocystic proliferation of the hydatid cyst, and the cyst contents are confined within the pericyst, resulting in maternal cyst with multiple large daughter cysts. The maternal and daughter cysts are isointense on both T1- and T2-weighted images. When the daughter cysts completely fill the maternal cyst, the cysts appear as multiseptated and may produce "grapelike," "wheel-like," "rosette-like," or "honeycomb-like" structures (Abdel Razek et al. 2009, 2011) (Fig. 11.3).

The CE4 type: It appears as a cystic lesion with serpentine bands or floating membranes representing the detached or ruptured membranes. When the viability of the parasite is lost, the intracystic pressure is lowered and the endocystic membranes are detached and float freely. Intracystic wavy or serpentine bands ("water-lily sign") may appear, representing the delaminated germinal layer and rupture of the membranes. The presence of detached membranes with a ball-of-wool appearance is a sign of severe degeneration. Degenerated cysts consist of a heterogeneous, solid-looking pseudotumor that may show a "ball-of-wool sign" as the cystic lesion gradually becomes smaller

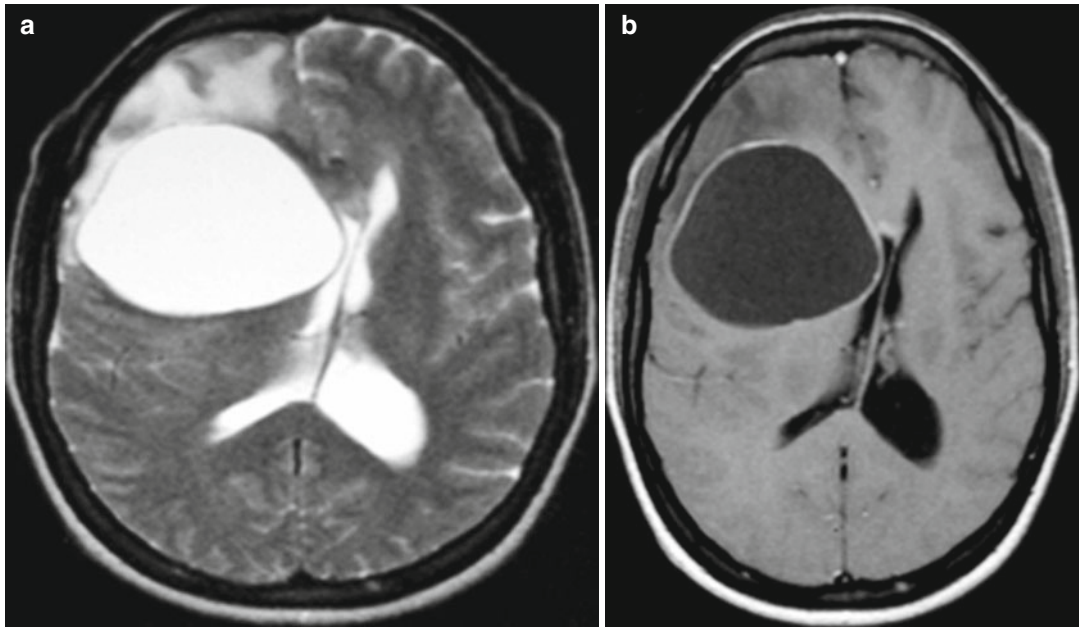

Fig. 11.1 CE1 type of hydatid cyst. (**a**) Axial T2-weighted MRI shows a large well-defined unilocular cystic lesion in the right parietal region with thick hypointense wall and mild marginal edema. (**b**) Post-contrast axial T1-weighted MRI shows homogenous low signal intensity of the cyst with mild marginal contrast enhancement

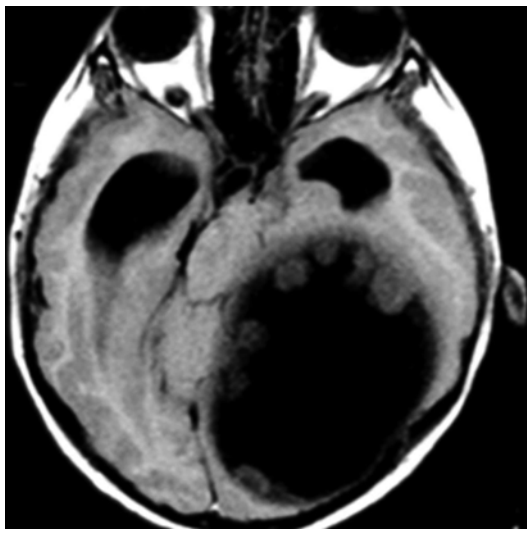

Fig. 11.2 CE2 type of hydatid cyst. Axial T1-weighted MRI shows a large maternal cyst with small peripherally arranged daughter vesicles

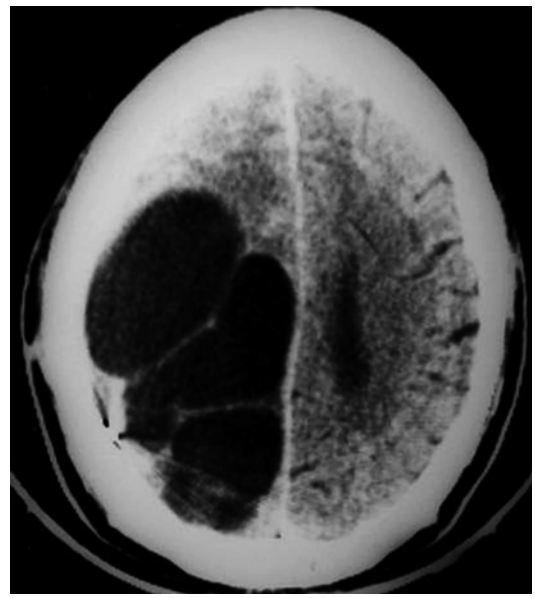

Fig. 11.3 CE3 type of hydatid cyst. Axial CT scan of the brain shows a large cyst with honeycomb appearance after surgery

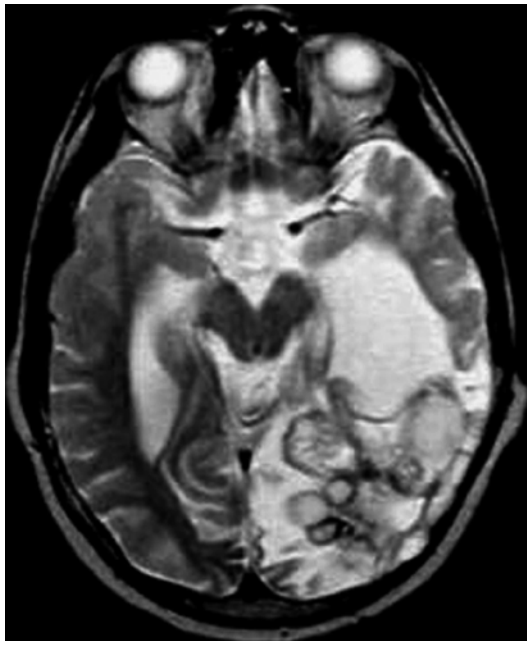

Fig. 11.4 CE4 type of hydatid cyst. Axial T2-weighted MRI shows a large cyst with ball-of-wool appearance in the left occipital region

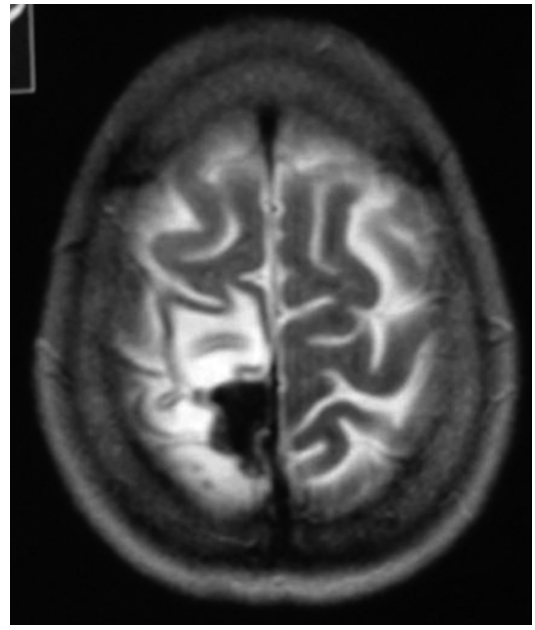

Fig. 11.5 CE5 type of hydatid cyst. Axial T2-weighted MRI shows a hypointense calcified dead cyst in the brain

and solidifies. Degenerating cysts show wavy or serpentine bands or floating membranes representing the detached or ruptured membranes (Abdel Razek et al. 2009, 2011) (Fig. 11.4).

The CE5 type: It is the infertile and dead form of CE. The dead cysts are characterized by a thick calcified wall in 50 % of patients. The degree of calcification varies from partial to complete calcification of the cyst. CT scan is best for detection of calcification. On MRI, the calcified lesion appears as signal void region (Abdel Razek et al. 2009; Basraoui et al. 2010; Bartosch et al. 2011) (Fig. 11.5).

Advanced Magnetic Resonance Imaging

Magnetic Resonance Spectroscopy

MRS may be added to the routine MRI protocol for a more accurate etiological diagnosis of a cystic lesion. MRS of cerebral CE shows dominant resonances of acetate (1.92 ppm), succinate (2.4 ppm), lactate (1.33 ppm), and glycine (3.56 ppm) and small contributions from alanine and isoleucine, leucine, and valine. The most specific metabolite of CE is a peak of succinate (2.4 ppm); however, a succinate peak has also been seen in pyogenic abscesses and neurocysticercosis. Other less-specific metabolites, such as lactate and acetate, are suggestive of infectious diseases. MRS studies ex vivo have found malate (4.3 ppm) and fumarate (6.5 ppm) in fertile cysts (Garg et al. 2002; Chawla et al. 2004; Hosch et al. 2008).

Diffusion Magnetic Resonance Imaging

CE is isointense with cerebrospinal fluid at diffusion-weighted MRI. The apparent diffusion coefficient (ADC) value of CE is $1.33 \pm 0.15 \quad 10^{-3}$ s/mm^2 (Kittis et al. 2004).

Special Types

Multiple Hydatid Cysts

Multiple cerebral hydatid cysts, secondary or primary, are rare. Secondary infertile cysts are due to the surgical, spontaneous, or traumatic

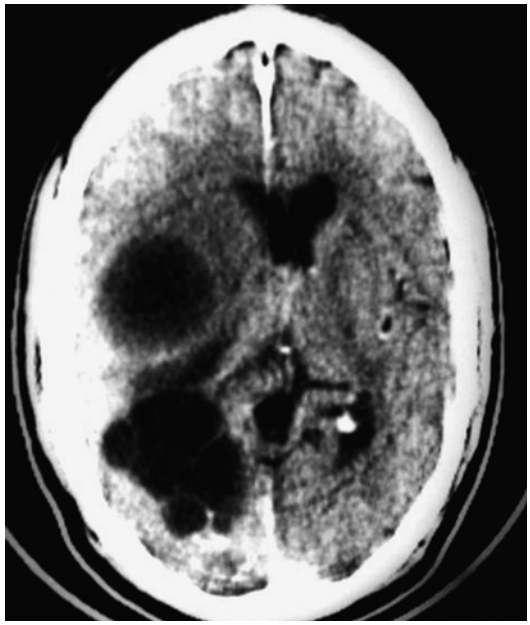

Fig. 11.6 Multiple hydatid cysts. Axial CT scan of the brain shows multiple hydatid cysts are seen in the right cerebral hemisphere

rupture of a viable primary lesion with spilling of the scolices inside the cerebral parenchyma, while multiple primary cysts result from embolization of a ruptured cardiac cyst (Al Zain et al. 2002; Lotfinia et al. 2007; Yurt et al. 2007) (Fig. 11.6).

Extraparenchymal Hydatid Cyst

The reported sites of extraparenchymal hydatid cyst include the subarachnoid space, cisterns, ventricles, pons, cerebellum, aqueduct of Sylvius, extradural space, and diploic space of skull bones (Diren et al. 1993; Tsitouridis et al. 1997; Lakhdar et al. 2010; Wani et al. 2010). Cranial extradural hydatid cyst is extremely rare because the physiologic flow of blood to the brain is mainly through the internal carotid system, so the likelihood of the larvae traveling through the external carotid system is very low (Cemil et al. 2009; Turgut 2010). Primary calvarial hydatid cysts arising from the dipole of the cranial bones with intracranial extension are extremely rare (Erman et al. 2001; Sharma et al. 2011). Different forms of extraparenchymal hydatidosis is discussed in detail in Chap. 21.

Infected Hydatid Cyst

When a secondary process occurs in the cyst, such as infection or rupture, the signal intensity tends to be slightly decreased on T2- and a little higher on T1-weighted images. When rupture, superinfection, or hemorrhage occurs in the cyst, the signal intensity may be slightly decreased on T2-weighted images and slightly increased on T1-weighted images (El-Shamam et al. 2001).

Stroke

Embolic stroke due to rupture of a hydatid cyst in cardiac cavity, a cause of ischemic infarction and multiple metastatic cyst formation, is an extremely rare entity (Martin et al. 1996; Turgut and Bayülkem 1998). Stroke as a complication of cardiac hydatidosis is discussed in detail in Chaps. 21 and 22.

Differential Diagnosis

CE on CT needs to be differentiated from porencephalic cyst, arachnoid cyst, brain abscess, and cystic tumor. Porencephalic and arachnoid cysts are not spherical and are not surrounded entirely by brain parenchyma. Porencephalic cyst shows signs of volume loss and gliosis in adjacent white matter. Arachnoid cyst is extra-axial in location, whereas intra-axial hydatid cyst is surrounded by brain parenchyma all around. Cystic tumor and brain abscess show definite contrast enhancement in the wall and/or mural nodule; perilesional edema is also present in case of abscess (Wani et al. 2010; Bartosch et al. 2011). The presence of multiple daughter cysts and hypointense ring in T2-weighted imaging is characteristic of CE (da Rocha et al. 2005).

Posttreatment

Methods

The treatment of cerebral CE is surgical and the aim of surgery is to excise the cyst completely without rupture to prevent anaphylactic reaction and local recurrence. The most commonly utilized surgical procedure designed to remove the intact cyst completely without rupture is by irrigating saline into the interface between the cyst wall and brain. However, medical treatment with albendazole has been reported with favorable results as an adjunct and, in certain circumstances, as the primary mode of treatment (Wani et al. 2010; Bartosch et al. 2011).

Surgical

The complications of hydatid cyst surgery are various and depend on the location, size, and multiplicity of the cysts. Intraoperative cyst rupture is the most common and serious complication which can lead to widespread dissemination followed by severe inflammatory or anaphylactic response. Subdural effusion occurs due to rapid drop of the intracranial pressure after the removal of the cyst with opening up the subdural space. Porencephalic cysts are abnormal brain cavities resulting from trauma and iatrogenic (postoperative) or perinatal vascular occlusion. These cavities are filled with cerebrospinal fluid and commonly connected with ventricles or subdural spaces (Fig. 11.7). Postoperative hemorrhage has been reported after surgery of hydatid cyst (Duishanbai et al. 2010; Tuzun et al. 2010).

Medical

Chemotherapy could be of great importance in patients with multiple cysts and in those unfit for surgery or suffering from recurrent disease. After medical treatment, the small cysts disappear, while large cysts are reduced in size and appear deformed or collapsed. Disappearance of daughter cysts has also been reported. Small foci of calcification have been seen on CT in the site of prior cysts, 12 ± 18 months after completion of treatment (Kalaitzoglou et al. 1998; Altas et al. 2010) (Fig. 11.7). Recently, MRS has been used for monitoring patient after medical treatment. The change in the levels of the alanine, succinate, acetate, and lactate in the cyst correlated well with the shrinkage and resolution of the cyst (Seckin et al. 2008).

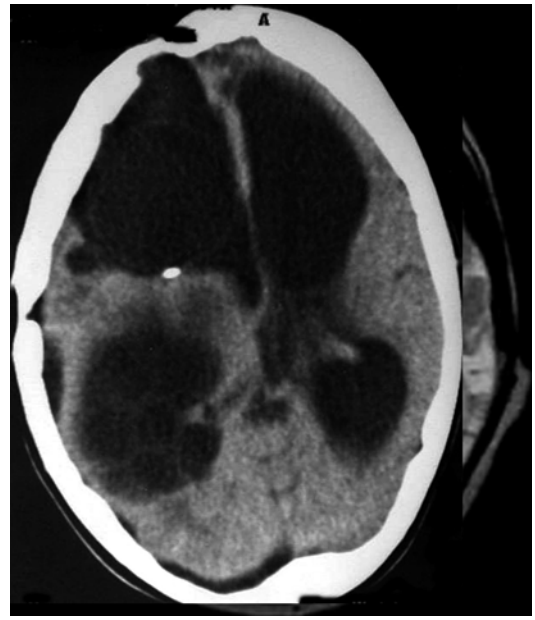

Fig. 11.7 Postoperative hydatid cyst. Axial CT scan shows a well-defined multilocular cyst which is seen in the right temporoparietal region associated with a thin-walled cyst in the right frontoparietal region of encephalomalacia. Note area of calcification is seen along the posterior wall of the cyst

Alveolar Echinococcosis

Alveolar echinococcosis (AE) is an uncommon form of hydatid disease caused by *E. multilocularis*. Cerebral infestation by AE and CE differ: AE occurs in adults who live in rural areas, whereas CE affects mostly children. CE infestation is usually self-limited, whereas AE infestation may appear as an infiltrative lesion in both the liver and brain, which makes total surgical removal difficult (Tunaci et al. 1999; Senturk et al. 2006; Ozdol et al. 2011).

AE features alveolar structures composed of numerous irregular cysts with a diameter between 1 and 20 mm that are not sharply demarcated from surrounding tissue. Central cystic cavities can result from necrosis of the inner part of the cyst. An irregularly thickened and partially calcified wall is present in most cases. This wall lies in the deep gray matter but may be in the posterior fossae. On CT and MRI, the lesions mainly appear as solid or multilocular cystic masses. Calcification and surrounding edema are common findings in these lesions. Peripheral ringlike, heterogeneous, nodular, and cauliflower-like enhancement patterns have all been reported. Perfusion-weighted MRI reveals low regional cerebral blood volume within the lesions because of gliosis and higher values in the periphery because of surrounding inflammation. This infection may mimic malignancy as a result of invasion of adjacent structures and destructive tissue growth (Bensaid et al. 1994; Piotin et al. 1997; Tunaci et al. 1999). On DW-MRI, the lesion is hypointense at b value 1,000 s/mm^2 with ADC value of $2.88 \pm 0.24 \quad 10^{-3}$ s/mm^2 (Kittis et al. 2004).

Conclusion

We concluded that imaging is essential to diagnose different forms of intracranial hydatid cyst that represent different developmental and degenerative stages of hydatid cyst. Also, imaging can detect exact location and multiplicity of the lesion. Furthermore, imaging can be used for monitoring patients after surgical or medical treatment. Finally, advanced MRI is helpful for differentiating hydatid cyst from simulating lesions.

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Imaging of Spinal Hydatid Disease

12

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Introduction

Hydatid disease (echinococcosis) is a parasitic infection caused more frequently by *Echinococcus granulosus* and less frequently by *E. multilocularis* (*E. alveolaris*), the liver and lungs being the most commonly involved organs (Turgut 1997). Involvement of the spine is rare but it is clinically challenging (Fig. 12.1). Alveolar echinococcosis of the spine is much rarer, and imaging findings, such as inhomogeneous osteolysis of vertebral bodies without loss of intervertebral disk height with an associating paravertebral mass, may be nonspecific (Toussaint et al. 2001).

Patients with hydatid disease usually present with symptoms caused by spinal cord or nerve root compression (Akhan et al. 1991; Pandey and Chaudhari 1997; Işlekel et al. 1998; Hilmani et al. 2004; Layadi et al. 2005; Adilay et al. 2007; Gopal et al. 2007; Kaen et al. 2009; Limaiem et al. 2010). Hydatid disease can be seen at any level of the spine (Bouras et al. 1984; Mathuriya et al. 1985; Göçer et al. 1994; von Sinner and Akhtar 1994; Pandey and Chaudhari 1997; Turgut 1997; Singh et al. 1998; Layadi et al. 2005; Adilay et al. 2007; Song et al. 2007; Arif and Zaheer 2009; Senoglu et al. 2009), but thoracic vertebrae are more commonly involved (Polat et al. 2003; Gopal et al. 2007), sometimes misleading to the diagnosis of Pott's disease (Bouras et al. 1984; Turgut 1997; Song et al. 2007) and mimicking tuberculous spondylodiscitis (Tabak et al. 2007). Intradural hydatid at the foramen magnum was reported with all features

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of spinomedullary compression including respiratory distress, so hydatid disease should be considered in the differential diagnosis of compressive lesions at the foramen magnum (Mathuriya et al. 1985).

Hydatid cysts were classified according to their relationship with the dura mater, spinal canal, and spinal cord (Pamir et al. 1984; Fahl et al. 1994; von Sinner and Akhtar 1994; Berk et al. 1998; Turgut 2002; Polat et al. 2003; Adilay et al. 2007; Gopal et al. 2007; Arif and Zaheer 2009; Güneş et al. 2009) as intramedullary hydatid cysts, intradural extramedullary hydatid cysts, extradural-intraspinal hydatid cysts (Fig. 12.2), hydatid cysts of the vertebrae (Figs. 12.3, 12.4, 12.5, 12.6, and 12.7), and paravertebral hydatid cysts (Figs. 12.4, 12.8 and 12.9) (Polat et al. 2003). Intradural hydatid cysts are rare (Pamir et al. 1984; Kahilogullari et al. 2005; Arif and Zaheer 2009; Güneş et al. 2009).

Lack of osteoporosis and sclerosis in involved bone, absence of damage to intervertebral disk spaces and vertebral bodies, paraspinal extension, and (in the thoracic spine) involvement of contiguous rib are the most common features of spinal hydatid disease (Polat et al. 2003). Hydatid disease of the spine usually begins in the vertebral body. The cysts show slow growth in the direction of least resistance (Polat et al. 2003; Phatak 2006). With time, the parasite replaces the osseous tissue and destroys the cortex. It then spreads from bone to surrounding tissue such as muscle and the spinal cord (Polat et al. 2003). Extension into the spinal canal results in spinal cord and neural compression (Gopal et al. 2007). Hydatid cysts that lack the typical radiographic appearance may be mistaken for arachnoid cysts (Secer et al. 2008).

Plain X-rays are routinely obtained as a part of initial imaging but radiographic findings of spinal hydatid disease are nonspecific (Fig. 12.3). Plain X-rays may show bone destruction (Fig. 12.4) and sometimes abnormal soft tissue masses in the paravertebral region (Phatak 2006). However, they may show no bony abnormalities (Gopal et al. 2007; Arif and Zaheer 2009). It should be remembered that, radiographically, no sclerosis or periosteal reaction is evident in the early stages of the disease (Farzan et al. 2006).

Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrate cystic cerebral hydatid disease effectively (Bükte et al. 2004) and they also serve for imaging of spinal hydatid disease (Figs. 12.1, 12.2, 12.3, 12.4, 12.5, 12.6, 12.7, and 12.9). After obtaining plain X-rays, CT and MRI should be used for further imaging as diagnostic tools of choice (Göçer et al. 1994; Turgut 1997; Gopal et al. 2007). CT and/or MRI techniques were found to be extremely useful, both for reaching the correct diagnosis and for proper surgical management of hydatid disease (Turgut 2002). CT and MRI have revolutionized neurosurgical practice for the diagnosis of hydatid cysts and allowed early diagnosis of the disease and provided localization of the lesions more accurately than we could do with plain X-ray, and also they could show multiple lesions (Turgut 1997); therefore, they are of value in preoperative planning of the surgical approach to hydatid lesions of the skeleton.

On CT and MRI, the appearance of the cystic fluid resembles that of cerebrospinal fluid (CSF) (Figs. 12.2, 12.3, 12.8, and 12.9) (Polat et al. 2003; Layadi et al. 2005; Gopal et al. 2007; Senoglu et al. 2009). In the past, myelography and CT myelography were used in the diagnosis of spinal hydatid disease (Işlekel et al. 1998), but now MRI has replaced the need for invasive myelography procedures.

Computed Tomography Scan

CT scan is effective in demonstrating the destructive hydatid lesions in vertebrae (Figs. 12.3, 12.4, 12.5, and 12.7), in determining their spread, and in establishing the presence of other hydatid cysts in adjacent soft tissues (Bouras et al. 1984; von Sinner and Akhtar 1994). CT could show multiple hydatid cysts in the ipsilateral psoas (Figs. 12.8) and quadratus lumborum muscles,

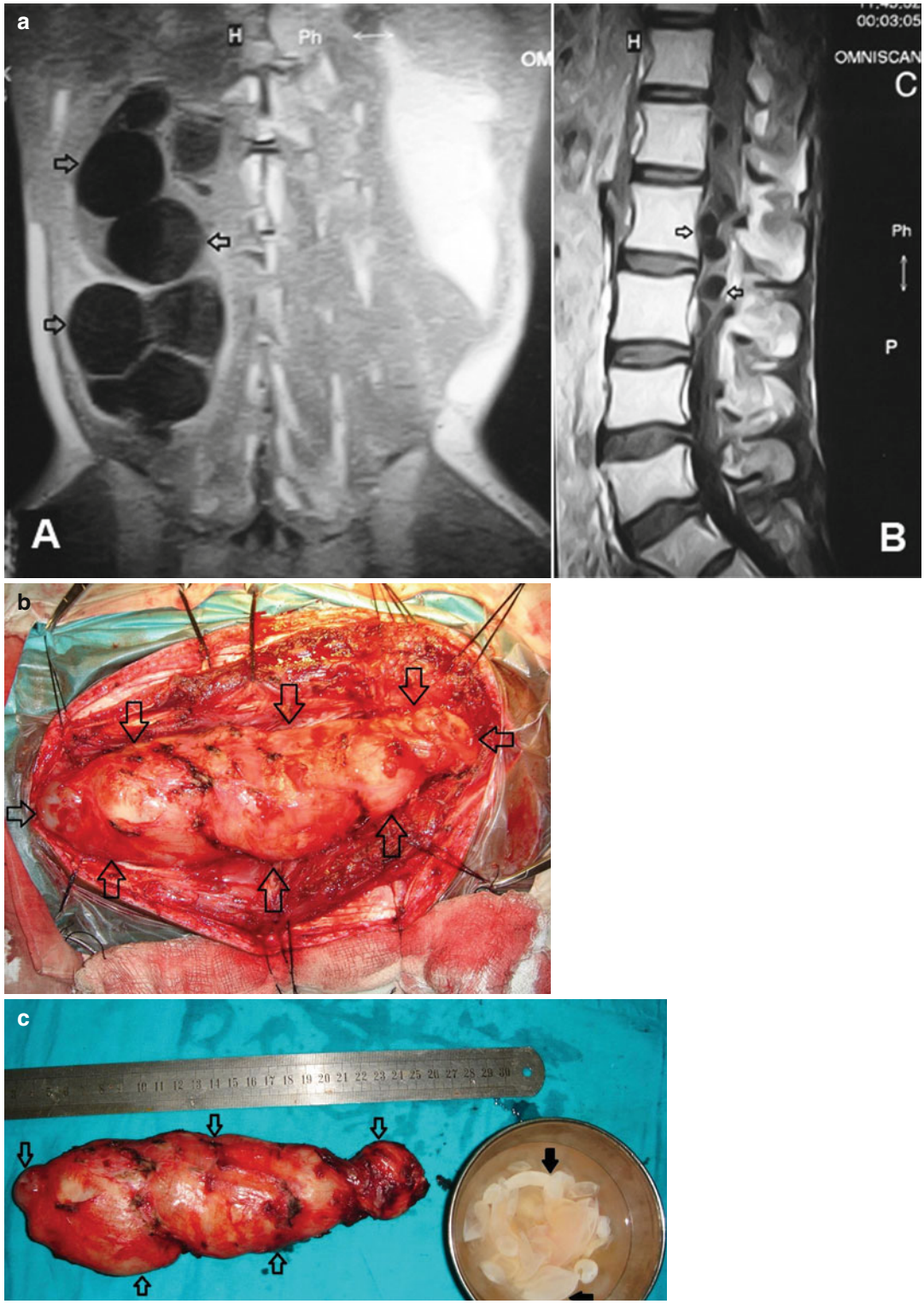

Fig. 12.1 (**a**) Spinal hydatid cysts (*arrows*). (**b**) Spinal hydatid preoperative view (*arrows*). (**c**) Spinal hydatid resected specimen (*arrows*) (Courtesy of D. Chowdhury, MD)

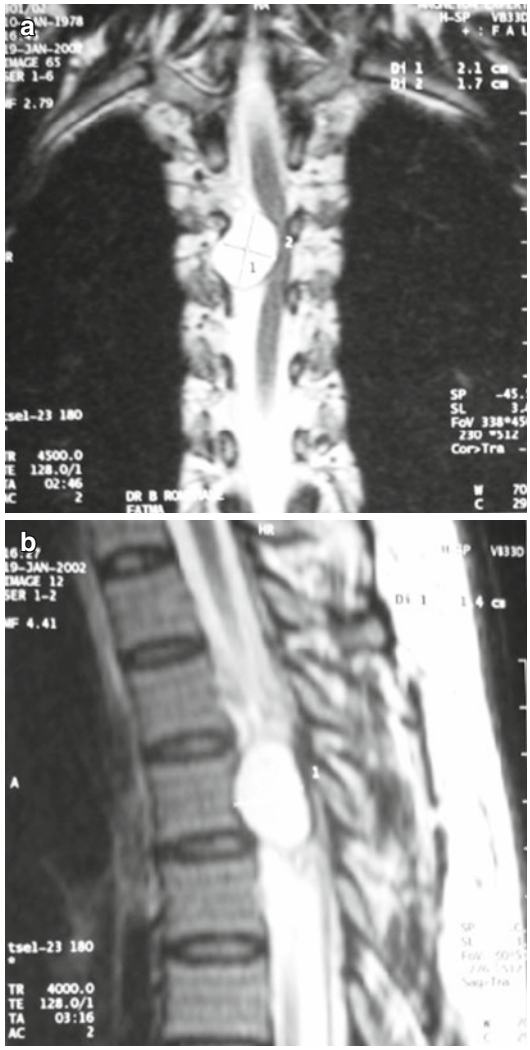

Fig. 12.2 (**a**, **b**) A 24-year-old male patient with extradural hydatid cyst at T4 vertebra corpus level (Courtesy of F. Limaiem, MD)

widening of the neural foramen, and extension of cyst into the neural canal compressing the spinal cord (Phatak 2006).

In a 73-year-old man with sacral/retroperitoneal hydatid disease, CT could demonstrate a large, multiloculated, lytic lesion that expanded anteriorly causing extensive destruction of the sacrum and extending into the sacral canal. CT shows the cystic nature of the lesions which are isodense to CSF (Senoglu et al. 2009), but it is not possible to differentiate an extramedullary hydatid cyst from an arachnoid cyst by using only the CT views (Tuncel 2008).

Usually no rim enhancement is evident after injection of contrast material, but there may be some exceptional cases. CT could show peripheral rim enhancement in a case with an infected intradural hydatid cyst at the foramen magnum (Mathuriya et al. 1985). In a 45-year-old woman with lumbar vertebral hydatid disease, axial contrast-enhanced CT could demonstrate increased contrast enhancement peripheral to the secondary lesions in the erector spinae muscles and spinal canal (Polat et al. 2003).

Contrast enhancement may be seen in alveolar echinococcosis. Contrast-enhanced CT images of an 80-year-old man with primary extrahepatic alveolar echinococcosis showed a multilobulated cystic mass in the right retroperitoneum originating from the psoas muscle, where the cystic components had fluidlike density and thickened septae with mild contrast enhancement. Besides, the lumbar spine presented lytic lesions of the first and second lumbar vertebra with partial cortical destruction (Nell et al. 2011).

Calcification is rare in spinal hydatid disease (Polat et al. 2003). However, on CT scan, the existence of calcification in the cyst wall, appearance of microvesicular polycystic vertebra, or the development of vertebral compression fracture can be observed in the last stage of involvement of the spine (Turgut et al. 2007).

CT was also used for the treatment where CT-guided needle aspiration and hypertonic saline irrigation of a multilocular extradural cervical spinal hydatid cyst causing severe spinal cord compression eliminated the need for emergency surgery and provided complete resolution of the patient's quadriplegia (Spektor et al. 1997).

Magnetic Resonance Imaging

More recently, MRI became the first imaging modality in patients with myelopathy and/or radiculopathy, with multiple daughter cysts within a parent cyst in spinal hydatidosis (Turgut

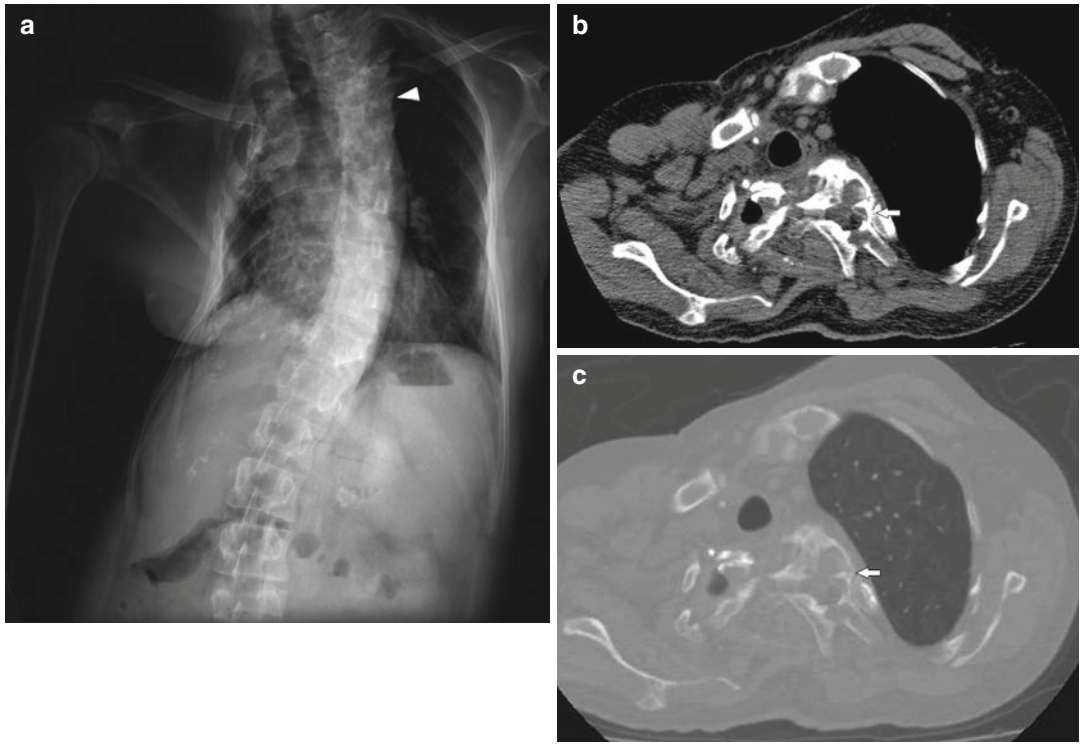

Fig. 12.3 Anteroposterior plain X-ray (**a**) of a 54-year-old male patient with thoracic spinal hydatid disease. There is marked kyphoscoliosis (*arrowhead*). Subtle radiolucent areas can be seen in the upper thoracic vertebrae. Unenhanced axial chest CT images with soft tissue window (**b**) and bone window (**c**) settings demonstrate hypodense cystic lesion in the vertebral corpus, which is isodense to cerebrospinal fluid, causing bone destruction and extending into the upper thoracic spinal canal (*arrow*). Chest deformities and subsequent tracheal deviation are prominent

et al. 2007). Although X-ray or CT images of spinal echinococcosis are similar to tuberculosis, metastases, giant cell tumors, or cysts of the bone, MRI was reported to show distinctive diagnostic features of spinal hydatid disease (Song et al. 2007).

MRI confirms the multicystic/multiloculated/multiseptated nature of the lesion (Figs. 12.1, 12.4, 12.8 and 12.9) (Gopal et al. 2007; Song et al. 2007; Güneş et al. 2009; Kaen et al. 2009; Senoglu et al. 2009; Turan Süslü et al. 2009) and is useful in the demonstration of complications such as spinal cord and/or nerve root compression (Gopal et al. 2007; Kaen et al. 2009).

MRI was stated to be the diagnostic procedure of choice in the face of neurological deficit (Turgut 1997). MRI characteristically shows a lesion resembling a bunch of grapes (Figs. 12.1, 12.8 and 12.9) which can help in distinguishing hydatid infestation from spinal tuberculosis. In spinal hydatid disease, cyst walls are thin and regular (Figs. 12.2 and 12.8); the presence of a markedly hypointense cyst wall on T1-weighted and T2-weighted images and the absence of wall enhancement with gadolinium are characteristic of hydatid disease (Limaiem et al. 2010).

On lumbar MRI of a 36-year-old man with extradural-intraspinal and paravertebral hydatid disease secondary to the spread of vertebral lesions, axial spin-echo T1-weighted image through the L3 vertebra showed multiple hypointense masses in the vertebral body and in the paravertebral and extradural-intraspinal areas, and corresponding axial fast spin-echo T2-weighted image showed multiple areas of increased signal intensity.

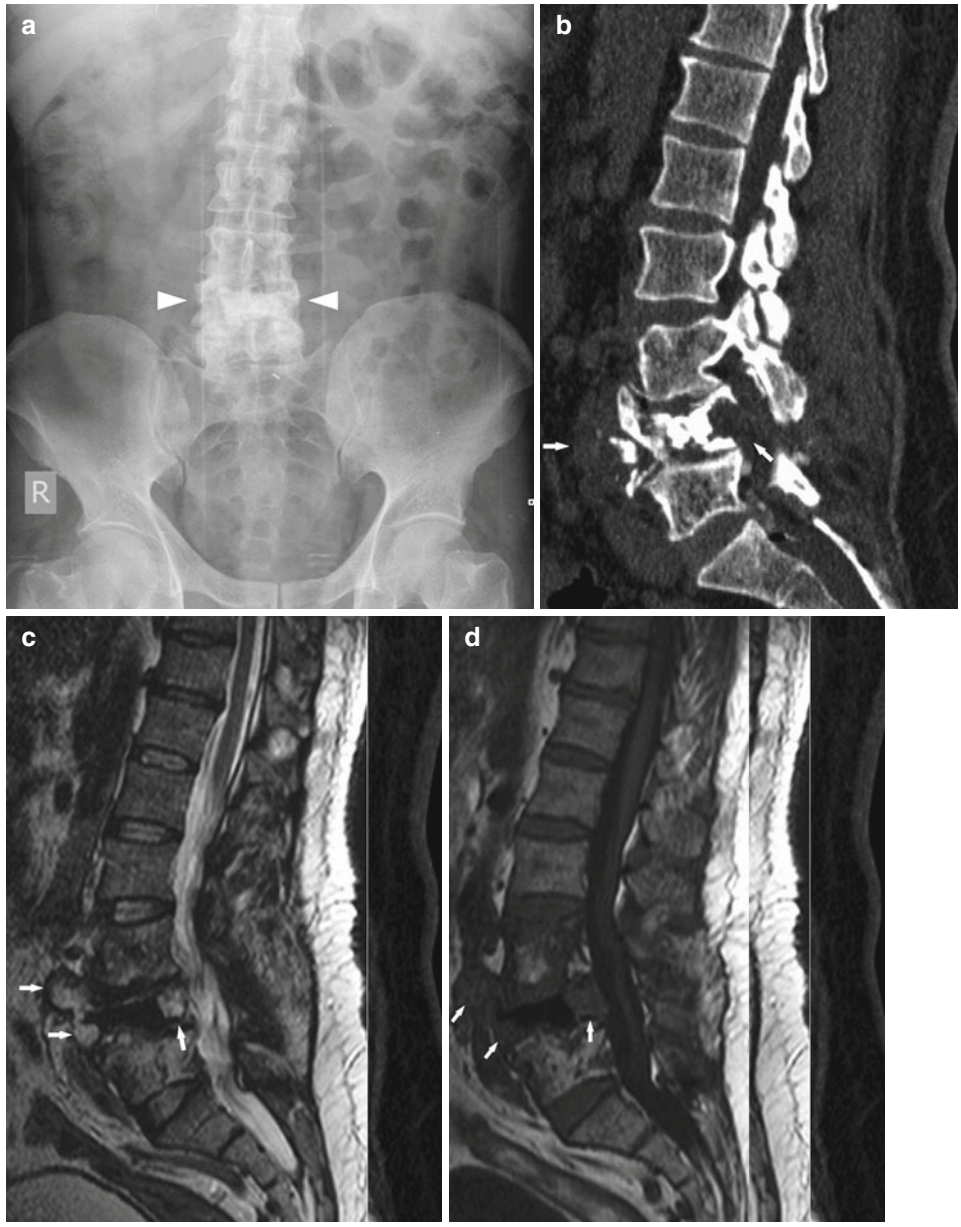

Fig. 12.4 Anteroposterior plain X-ray (**a**) of a 43-year-old male patient with lumbar spinal hydatid disease. Decreased vertebral height and diffuse sclerosis is noticed at L4 vertebra (*arrowheads*). Sagittal reformatted CT image with bone window settings (**b**) demonstrates expansion and destruction at L4 vertebra with both sclerotic and lytic areas (*arrows*). Anterior paravertebral lesions with soft tissue density can also be seen. Sagittal spinal MRI demonstrates loss of height and destructive appearance with associating cystic lesions, hyperintense on T2-weighted image (**c**) and hypointense on T1-weighted image (**d**) (*arrows*), some of which extend into anterior paravertebral areas

Extradural-intraspinal masses had low-signal-intensity rims, and there was also marked destruction of the right anterolateral portion of the vertebral body (Polat et al. 2003). On MRI of another patient, multiple hydatid cysts in ipsilateral psoas and quadratus lumborum

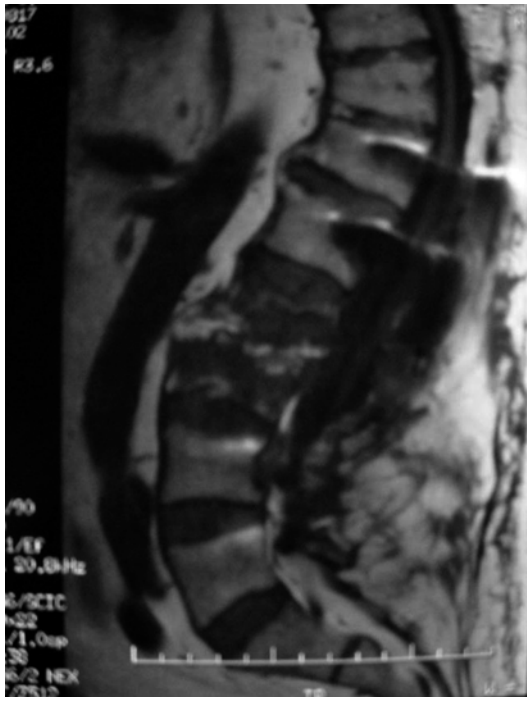

Fig. 12.5 A 59-year-old male patient who was operated 2 years ago had anterior debridement with partial corpectomy and grafting, posterior fusion. Despite the recurrence of disease, chemotherapy was not followed by the patient (Courtesy of A. Herrera, MD, PhD)

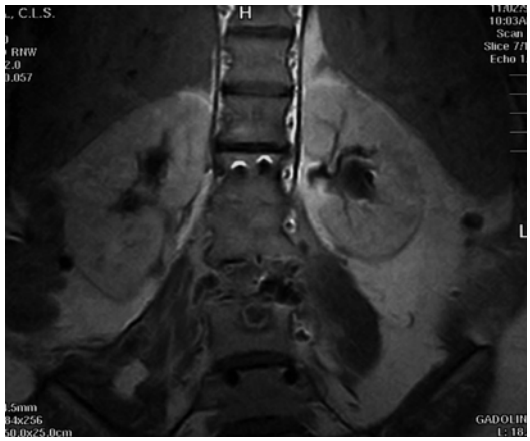

Fig. 12.6 A 46-year-old female patient. MRI lumbar spine hydatid lesions in L3 (Courtesy of A. Herrera, MD, PhD)

muscles were hypointense on T1-weighted images and hyperintense on T2-weighted images (Phatak 2006). In a 73-year-old man with sacral/retroperitoneal hydatid disease, MRI demonstrated a multilobular cystic lesion with thin and regular cyst walls, compressing the nerve roots. The cyst contents were hypointense on T1-weighted images and hyperintense on T2-weighted images, with an intensity similar to that of CSF (Senoglu et al. 2009). In a 25-year-old female, intradural lesions without vertebral involvement at lumbar level demonstrated low-intensity signal on T1-weighted images without enhancement after gadolinium injection and high-intensity signal on T2-weighted images (Hilmani et al. 2004).

In a pediatric case, an intradural, extramedullary cystic lesion which was seen to extend from L1 to L4 spine was hypointense on T1-weighted images and hyperintense on T2-weighted images (Arif and Zaheer 2009). In a 15-year-old male patient with a primary solitary hydatid cyst of the sacral spinal canal, plain X-rays and MRI revealed a widened sacral canal with pressure changes, and MRI confirmed the cystic nature of the lesion which had intensities that were similar to those of CSF (Pandey and Chaudhari 1997).

It should be kept in mind that MRI findings in alveolar echinococcosis of the spine may be nonspecific, unusual, or confusing. In an 80-year-old man with primary extrahepatic alveolar echinococcosis, T2-weighted axial images showed multiple small hyperintense lesions in the right psoas muscle, and corresponding fat-suppressed T1-weighted image after gadolinium administration confirmed the diagnosis of a multicystic mass and delineated the thickened, contrast-enhancing septations around the cystic components. T1-weighted image and T2-weighted STIR image of the lumbar spine in sagittal orientation showed the bone marrow replacement within the first, second, and third lumbar vertebrae (Nell et al. 2011).

MRI has been used postoperatively both to demonstrate recurrent cysts (Fig. 12.5) (Adilay et al. 2007; Arif and Zaheer 2009; Papakonstantinou et al. 2011) and to follow up the patient in order to show no recurrence of spinal cystic lesion (Fig. 12.10) (Arif and Zaheer 2009; Senoglu et al. 2009). On MRI, recurrent

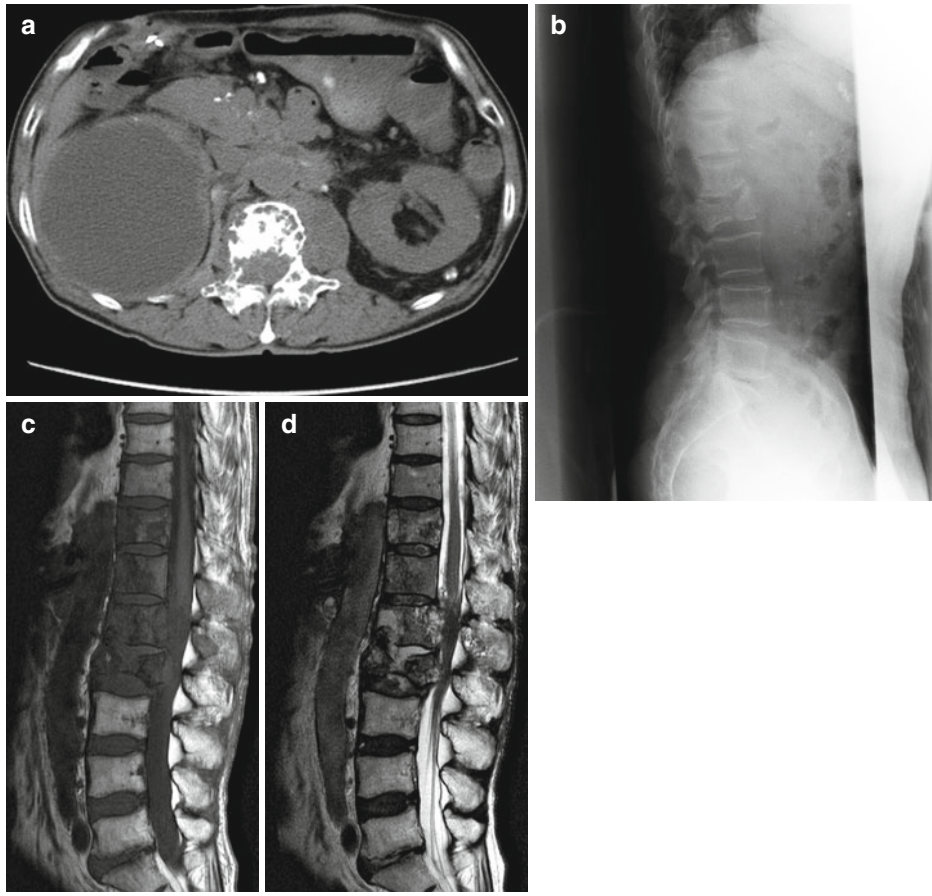

Fig. 12.7 (**a**–**d**) A 73-year-old male patient. He underwent palliative posterior decompression and instrumentation but died 2 years postoperatively (Courtesy of H. Sudo, MD)

hydatid disease is characterized by extensive involvement of the paravertebral soft tissues, soft tissues of the back at the site of previous laminectomies, and extradural space; extension into the intervertebral disk and iliopsoas muscles and skip lesions in the extradural space are not uncommon (Papakonstantinou et al. 2011).

Diffusion-weighted MRI (DW-MRI) can help differentiate complicated hydatidosis from other cystic lesions (Doganay and Kantarci 2009; Bhake and Agrawal 2010). Conventional MRI and DW-MRI were reported to be useful not only in the diagnosis of intradural extramedullary hydatid disease of the spine but also in determining a treatment protocol. Presence of restricted diffusion shows that the cystic lesions are complicated and infected, which require urgent surgery (Doganay and Kantarci 2009). In a 14-year-old boy, conventional MRI showed cystic multiloculated lesions in the lumbosacral spinal canal which were hypointense on T1 and hyperintense on T2-weighted images. DW-MRI of the boy showed hypointensity in the cystic lesions, and apparent diffusion-coefficient map images showed hyperintensity at the same level, without any evidence of restricted diffusion in the spinal canal (Doganay and Kantarci 2009).

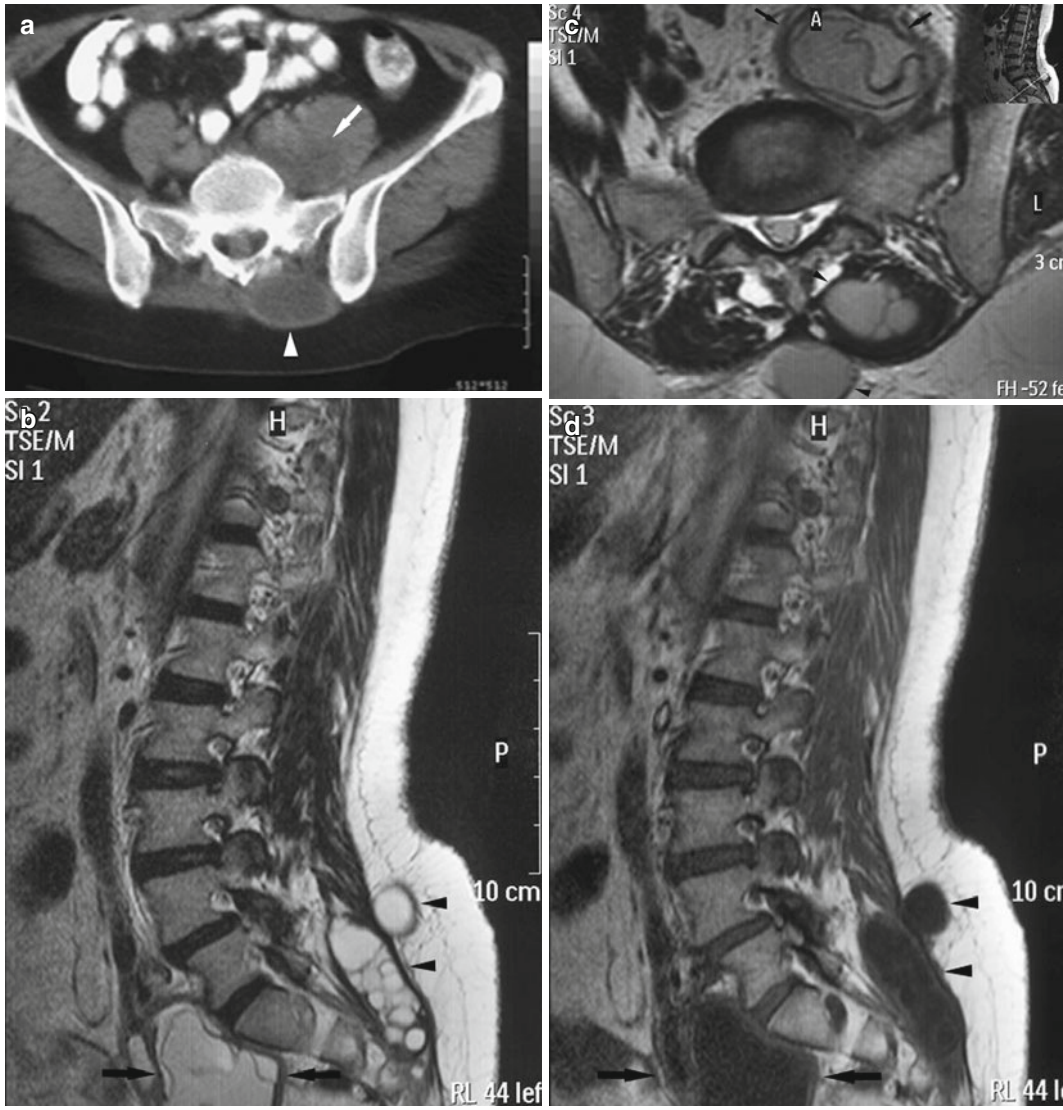

Fig. 12.8 In a 46-year-old female with multiple sacral paraspinal hydatid cysts on the left side, unenhanced axial pelvic CT image (**a**) demonstrates a hypodense hydatid cyst (*white arrow*) in the left psoas muscle which shows a close relation with left sacral neural foramina and nerves. Posterior to the sacrum, another hydatid lesion (*white arrowhead*) is located in the erector spinae muscle. MRI reveals multicystic-multiloculated sacral paraspinal hydatid lesions (*black arrows*: lesion anterior to the sacrum, *black arrowheads*: lesions posterior to the sacrum) as sharply demarcated hyperintense lesions on sagittal T2-weighted (**b**) and axial T2-weighted (**c**) images, which are hypointense on sagittal T1-weighted image (**d**). One of the posteriorly located cysts protrudes into subcutaneous fat (*black arrowhead*). On sagittal (**b**) and axial T2-weighted images (**c**), collapsed germinative membranes inside the cyst in the left psoas muscle were clearly demonstrated (*black arrows*). All the cysts are isointense to cerebrospinal fluid

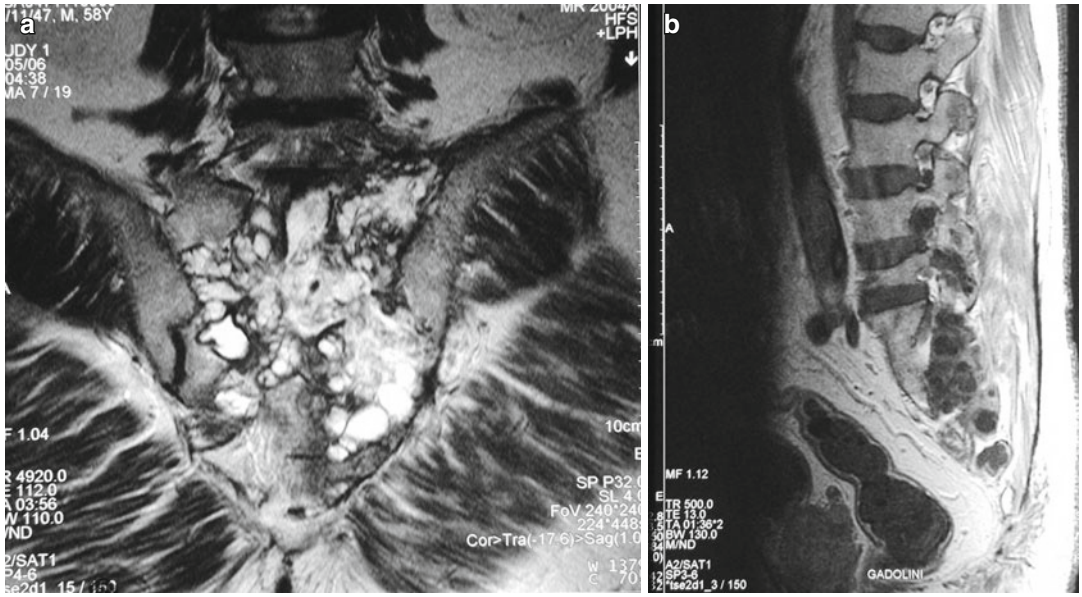

Fig. 12.9 (**a**, **b**) Sacral hydatidosis without accompanying neurological injury in a 61-year-old male patient. The patient with lung and liver hydatid cysts was not treated and transferred to his country of origin, Morocco (Courtesy of A. Herrera, MD, PhD)

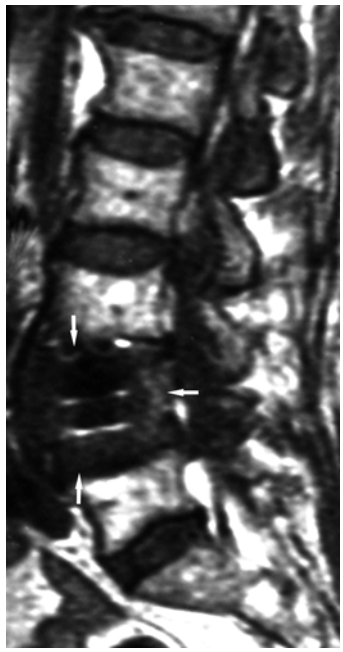

Fig. 12.10 Follow-up imaging of a 56-year-old male patient who was previously operated for lumbar spinal hydatid disease. Sagittal T2-weighted MRI demonstrates loss of height and decreased signal intensity in the operated lumbar vertebra (*arrows*). Neighboring disk spaces are fairly preserved. Despite the unfavorable effects of few metallic artifacts, there is no evidence of recurrent hydatid cyst

Conclusion

In the areas where the disease is endemic, hydatid disease should be considered in the differential diagnosis of a cystic lesion in the spine. In countries where tuberculosis is common, it should be known that spinal hydatidosis simulates tuberculosis spondylitis or chronic osteomyelitis (Turgut et al. 2007). There are ongoing MRI investigations to differentiate alive and fertile cysts from the inactive forms of hydatidosis and to monitor drug therapy (Turgut and Turgut 2010). It seems that MRI is the most efficient imaging modality in diagnosis of spinal hydatid disease and in demonstration of its complications.

Acknowledgments We thank Assistant Professor Ahmet Oguz Hasdemir, MD, Assistant Professor Halil Dönmez, MD, Mehmet Gümüş, MD, and Rukiye Dilli for their assistance.

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13 In Vivo Proton Magnetic Resonance Spectroscopy in Hydatidosis of the Central Nervous System

Avinash K. Kanodia

Contents

Introduction

Magnetic resonance spectroscopy (MRS) is a non-invasive technique that is used in clinical and research domains, for detecting various metabolites in normal and abnormal tissues and using them as an important adjunct in making a diagnosis. It has been available for several decades and established itself in a clinical role in various clinical conditions including brain tumours, dysplastic lesions, cystic lesions, epilepsy, etc. and is a powerful research tool in various other conditions (Castillo et al. 1998, 2001; Nelson et al. 2002; Ross et al. 2006). However, it is important to consider the results of MRS in context of the clinical problem and conventional magnetic resonance imaging (MRI), and the potential of being misled exists if the results are considered in isolation. There is also ample evidence in the literature, highlighting the limitations of MRS in certain conditions (Saindane et al. 2002; Szewczyk-Bieda et al. 2011). There is relatively limited literature about the applications of MRS in hydatid cyst and similar cystic lesions that highlights the usefulness and the potential limitations of MRS in the diagnosis of hydatid cyst and its differentiation from other cyst-like conditions of the brain.

Basics of Magnetic Resonance Spectroscopy

MRS utilizes nuclei with an odd number of protons and neutrons, such as ^{1}H, ^{31}P, ^{13}C, ^{19}F and ^{23}Na that have a magnetic moment, the most

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common in clinical use being ^{1}H. When an external magnetic field is applied, the nuclei resonate depending upon the gyromagnetic ratio and the external magnetic field applied (Cousins 1995; Matson et al. 1999). The nuclei in different metabolites resonate at a slightly different frequency compared to a standard, called the chemical shift. Signal acquisition follows a brief excitation of the tissue by the RF pulse, and it is the free induction decay (FID), which is transformed into spectrum by Fourier transformation. The horizontal axis represents the chemical shift, and plotted as parts per million (ppm) of the total resonance frequency, this remains constant for different metabolites. The signal intensity of a spectral peak is indicated by the area under the peak (i.e. the integral of the peak), rather than the height of the peak (Connelly 1996; Castillo et al. 1998). The ^{1}H MRS technique has the distinct advantage over others in that it can be more easily combined with MRI in the same setting, since it is performed with the same coil and ^{1}H is naturally more abundant than others.

To determine the volume of tissue from which magnetic resonance spectra are being obtained, two distinct approaches may be employed. First is the single-voxel spectroscopy (SVS) technique in which data is acquired from a single volume of interest (usually a cube of 8 ml or smaller), which can be repeated in other regions of interest. The second technique is chemical shift imaging (CSI) (also called magnetic resonance spectroscopic imaging or MRSI), in which a large region is excited before the signals are spatially encoded. With this technique, data from many voxels can be acquired simultaneously, and the increase in efficiency can be used to obtain smaller voxels (1–2 ml) than is feasible with SVS methods. It has the advantage that prior knowledge of the exact area of abnormality is not necessary (Duncan 1997). Thus maps can be obtained superimposed on the MRI image, where different colours or different shades of a single colour may be used to outline the area having increased concentration of a particular metabolite (Hetherington et al. 1995; Rudkin and Arnold 1999). Two-dimensional CSI is the most common approach; usually the study is done in a transverse plane although it can also be performed in other planes (Hunter and Wang 2001). Even larger volumes can be mapped using 3D CSI. However, the disadvantages over SVS technique are that magnetic field homogeneity is required over a larger area and that signals from individual voxels can contribute to their neighbours along with relatively lesser signal in each voxel (Connelly 1996).

The metabolites that are detectable using ^{1}H MRS depend on the acquisition conditions used. In SVS technique, the most commonly used localization techniques are point-resolved spectroscopy (PRESS) and stimulated echo method (STEAM). The PRESS technique is able to detect 100 % of all available signals, although only the metabolites with relatively longer or intermediate relaxation times may be seen. PRESS allows for sampling of relatively large volumes of interest (VOI) of tissue (3–27 cm^3). Moreover, to obtain higher signal to noise ratio (SNR), a relatively smaller number of signal averages or number of excitations (NEX) are required (Castillo et al. 1998; Hunter and Wang 2001). STEAM detects 50 % of all available signals, necessitating higher NEX to produce a good SNR. With STEAM, sampling of smaller VOI (1–3 cm^3) can be done, and this technique also allows for visualization of more metabolites with short relaxation times. In both techniques, a water suppression pulse is applied to the suppression of the water signal.

In the normal brain, three metabolites are usually present (Fig. 13.1). *N*-acetyl aspartate (NAA at 2 ppm) is detected mainly by its N-acetyl methyl group. It is a marker of neuronal density and viability, and its concentration decreases with many insults to the brain. In normal spectra, NAA is the largest peak. The choline peak (Cho at 3.2 ppm) contains contributions from glycerophosphocholine, phosphocholine and phosphatidylcholine and reflects total Cho stores. Cho is a constituent of the phospholipid metabolism of the cell membranes and reflects membrane turnover, and it is a precursor of acetylcholine and phosphatidylcholine (Miller 1991). The latter compound is used to build cell membranes, while the former is a critical neurotransmitter. Increased Cho reflects increased membrane synthesis or an increased number of cells (Castillo et al. 1998).

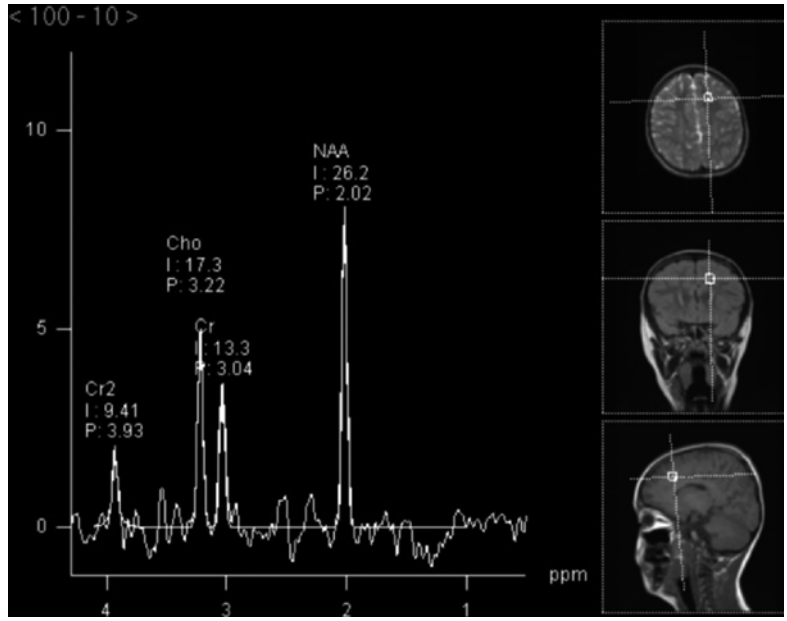

Fig. 13.1 In vivo ^{1}H MRS of the normal brain. Predominantly, three metabolites are seen at TE = 135 ms. These are NAA, Cho and Cr, NAA being the largest, seen at 2 ppm

The creatine peak (Cr at 3 ppm) contains contributions mainly from Cr and Cr phosphate. Cr probably plays a role in maintaining energy-dependent systems in brain cells by serving as a reserve for high-energy phosphates and as a buffer in ATP-ADP reservoir. The overall levels of Cr remain quite stable in most situations, and it is a good internal standard for comparison with other metabolites (Castillo et al. 1998).

Lactate (1.3 ppm) is a nonspecific marker often associated with anaerobic conditions in different situations. The configuration of lactate resonance consists of two distinct, resonant peaks (called a 'doublet') that are due to magnetic field interactions between adjacent protons (J-coupling) (Fig. 13.2). Lactate levels in the brain are normally very low or absent (Fig. 13.1). The presence of lactate indicates that the normal cellular oxidative respiratory mechanism is no longer in effect and that carbohydrate catabolism is taking place. At time to echo, TE = 272 ms, the lactate doublet projects above the baseline, whereas at TE = 136 ms, the lactate doublet is projected below the baseline (Castillo et al. 1998).

The results of MRS are compared and evaluated in various ways. The signal intensities of the metabolites are taken as a ratio against a standard metabolite, which is least likely to change (e.g. Cr in case of ^{1}H MRS). These ratios can be compared by taking the other side as control. Several quantitative methods are also used. The observed signal intensity is multiplied by the 90° pulse voltage, thereby compensating for differences in radiofrequency coil loading, and then comparing the signal intensities between different subjects. Using MRS, the concentration of metabolites can also be measured by determining the effects of T_1 and T_2 relaxation. Another method is that the signal intensity can be calibrated against a standard (phantom) (Gadian et al. 1994; Duncan 1997; Hunter and Wang 2001).

Cysts and Cyst-like Lesions of the Brain

A variety of cysts and cystic lesions can be seen, including arachnoid cysts, porencephalic cysts, neuroglial cysts, epidermoids, large perivascular spaces, cyst or necrosis associated with tumours, abscesses, parasitic cysts such as hydatid and neurocysticercosis (NCC), etc. (Osborn and Preece 2006). While history, clinical features, geographical factors and conventional CT and MRI appearances are often helpful in differentiating these lesions, the appearances are

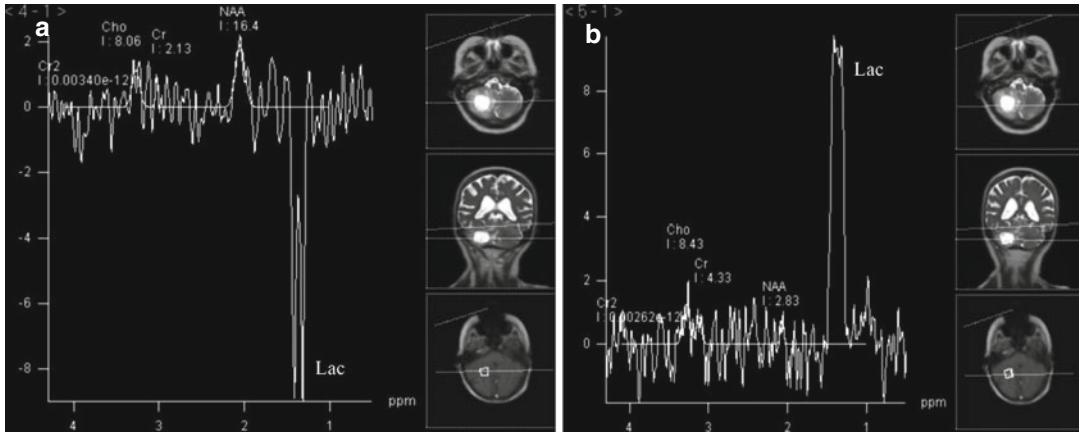

Fig. 13.2 In vivo ^{1}H MRS showing typical lactate peak in a necrotic mass (**a**) shows MRS with TE = 135 ms and (**b**) shows MRS with TE = 270 ms. The typical lactate peak is a doublet, projecting below baseline in (a) and above baseline in (b)

occasionally atypical and can present with diagnostic dilemmas. Since these represent vastly different pathologies requiring different treatment approaches, the importance of accurate diagnosis cannot be overemphasized. ^{1}H MRS utilizes a different, metabolite-based approach and provides a vital clue in several of these difficult situations.

Proton Magnetic Resonance Spectroscopy in Hydatid Cysts

Biochemical Basis of Magnetic Resonance Spectroscopy

In parasitic cysts, some anaerobic metabolism is usually present, even if the aerobic pathway is active to some extent (Garg et al. 2002). As a result, a variety of metabolites involved in anaerobic metabolism are usually found. Of the parasitic cysts, hydatid cyst is a typical example that shares many similarities and some differences with other parasitic cysts. The frequently described metabolites found in hydatid fluid in reasonable amounts are succinate, pyruvate, acetate, lactate and alanine, while a few others such as malate, fumarate, glycine, other amino acids, Cho (and Cho-containing compounds), propionate, etc. are found in smaller amounts or traces (McManus and Smyth 1978; Chang et al. 1998; Garg et al. 2002; Jayakumar et al. 2003). The frequency and success of detection of metabolites depend largely on the technique used.

Pyruvate is a product of glycolysis and reported to be found in abundance in hydatid fluid; investigators have confirmed its presence using mass spectroscopic measurements (Jayakumar et al. 2003). It is also thought to be an indicator of viability as it has not been detectable in cysts that show degeneration on histopathologic examination (Jayakumar et al. 2003). Pyruvate can be metabolized to acetate and lactate which are important and easily detectable metabolites in hydatid fluid, lactate being more prominently seen. Under anaerobic conditions, the partial tricarboxylic acid (TCA) cycle is active, in which phosphoenolpyruvate formed during glycolysis partially converts into oxaloacetate and then further into malate, using malate dehydrogenase (MDH). It further transforms into fumarate and succinate (McManus and Bryant 1995; Garg et al. 2002). In hydatid, the activity of MDH and other related enzymes has been reported as more favourable for succinate production by some of the investigators (Garg et al. 2002), who regard succinate as a very important metabolite present in significant amount in hydatid cysts and have confirmed its presence by specialized techniques (Garg et al. 2002). However, other investigators have given more importance to pyruvate, describing it as a marker of cestodial infestation and have downplayed the importance of succinate by

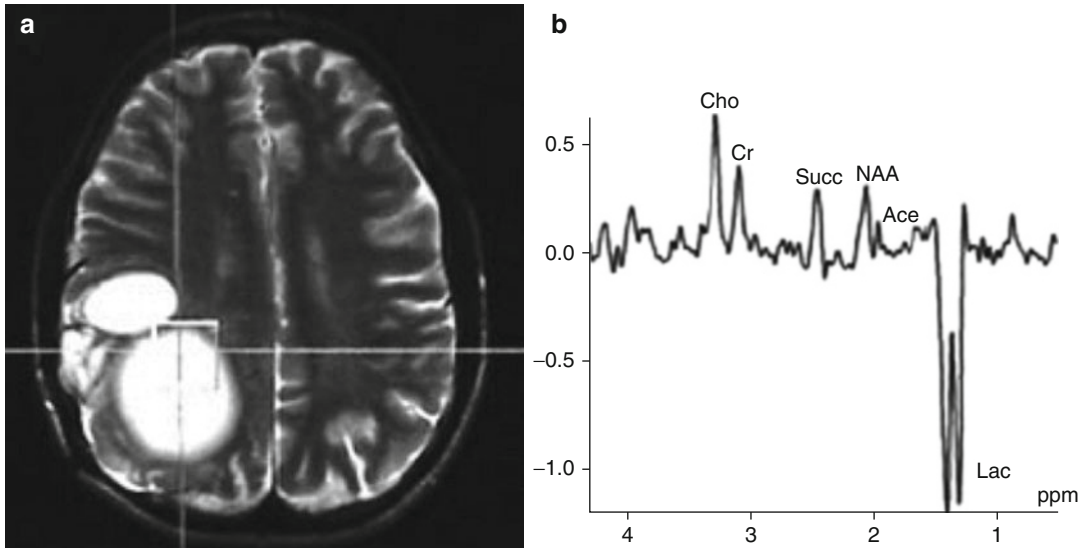

Fig. 13.3 In vivo ^{1}H MRS, showing the voxel over hydatid cyst (**a**) and the spectrum obtained using a TE of 135 ms (**b**). The MRS in (**b**) shows a large inverted lactate peak (*Lac*), a prominent succinate (*Succ*) peak and a smaller acetate peak (*Ace*). Further choline (*Cho*), creatine (*Cr*) and NAA peaks are present due to contamination from the surrounding tissue (From Chand et al. (2005) with permission)

citing low biochemical activity of succinate dehydrogenase (Jayakumar et al. 2003). Therefore, in the literature, there is no consensus on the relative importance of succinate and pyruvate, and as discussed below, it has important ramifications for ^{1}H MRS.

The only significant amino acid found is alanine, which is derived from pyruvate (Kohli et al. 1995; Jayakumar et al. 2003), while others such as leucine, valine and isoleucine are found in small amounts. Fumarate and malate are only detectable in traces but are considered as important metabolites that indicate fertility and can also be useful for differentiation from NCC cysts (Garg et al. 2002).

Technical Factors of In Vivo Proton Magnetic Resonance Spectroscopy

While both PRESS and STEAM techniques have been used, PRESS is more commonly performed. Both SVS and CSI techniques have been successfully used. At 1.5 T, different researchers use (time to repeat) TR of 1,500–3,000 ms with satisfactory results. Usually, a (time to echo) TE of 135–144 ms is used, as the metabolites usually found in hydatids are reasonably detected at these TE values, although some researchers have also used shorter TEs in addition (Chang et al. 1998). A variable NEX can be performed, depending on several factors. It is preferable to obtain the spectrum from the cystic part, avoiding the solid tissue/wall/host tissue as it can result in further metabolites (Fig. 13.3).

Typical Spectrum of In Vivo Proton Magnetic Resonance Spectroscopy in Hydatid Cysts

Of the several metabolites described, only a few are routinely picked up reliably on in vivo ^{1}H MRS due to sensitivity issues. In particular the peak at 2.4 ppm is important as both pyruvate and succinate are detected at 2.4 ppm. These are difficult to differentiate on in vivo ^{1}H MRS, and as discussed above, there is no consensus in the literature as to which of these metabolites are predominantly represented at 2.4 ppm, although their presence has been confirmed in separate studies using different techniques (Garg et al.

2002; Jayakumar et al. 2003, 2004). While this issue is pending, awaiting further investigation, still, a prominent peak at 2.4 ppm (pyruvate/succinate) is one of the most important features in in vivo ^{1}H MRS.

Other important metabolites detected by in vivo technique are lactate (1.3 ppm, seen as a doublet), acetate (1.9 ppm) and alanine (1.5 ppm) (Chang et al. 1998; Garg et al. 2002; Jayakumar et al. 2003). While these could be variable, lactate is usually seen as a significant peak. Acetate is detectable although it is a smaller peak relative to the succinate/pyruvate. As a result, the ratio of succinate/acetate is generally quite high in hydatid cysts and is an important differentiating feature with pyogenic abscesses, where acetate/succinate ratio is high (Poptani et al. 1995; Martinez-Perez et al. 1997; Dev et al. 1998; Chand et al. 2005). It has been further suggested that various metabolites described in hydatid cysts may not be seen in all spectra, due to changes in internal milieu during evolution of the cyst (Jayakumar et al. 2003). Also, various forms of echinococcus may have different consumptions of oxygen and glycogen, thereby producing different concentration of metabolites (Jayakumar et al. 2003). Thus, despite having some uniformity in basic spectra, variations are possible.

Ex vivo ^{1}H MRS detects a larger number of metabolites from hydatid fluid. These include amino acids leucine, valine and isoleucine (0.9–1.2 ppm), glycine (3.56 ppm), Cho (3.2 ppm), malate (4.3 ppm), fumarate (6.5 ppm), glucose and some of the aromatic amino acids (Garg et al. 2002).

In Vivo Proton Magnetic Resonance Spectroscopy in Other Cystic Conditions

Neurocysticercosis

The size and appearance of NCC are usually fairly different from hydatid cysts and rarely present a diagnostic dilemma; however, large and racemose lesions can create difficulty in diagnosis on routine MRI (Jayakumar et al. 2003). The issue becomes important due to the different management of these conditions (medical in NCC versus surgical in hydatid).

Being a parasitic infection, NCC and hydatid have similar metabolic pathways, and ^{1}H MRS in NCC follows closely that of hydatid with minimal differences (Jayakumar et al. 2004). The same metabolites are usually found in vivo, including succinate/pyruvate (2.4 ppm), acetate (1.9 ppm), lactate (1.3 ppm) and alanine (1.5 ppm), although these are generally lower in concentration than hydatid, attributable to a difference in enzyme activity that determines the concentration of these metabolites (Garg et al. 2002; Jayakumar et al. 2004). However, another unidentified peak at 3.3 ppm has been described by Chang et al. 1998, thought to be representing Cho (and Cho-containing compounds) by other authors (Jayakumar et al. 2004), which has not been confirmed but may potentially serve as a differentiating feature.

Ex vivo ^{1}H MRS has additional features helpful in differentiation (Garg et al. 2002). These include the absence of malate and fumarate, which are described in fertile hydatids. Creatine (3 ppm) can also be seen, attributable mainly to diffusion from host tissues (Garg et al. 2002).

Pyogenic Abscess

The in vivo ^{1}H MRS spectrum of pyogenic abscesses is significantly different from hydatid cysts. The presence of an amino acid (AA) peak at 0.9 ppm is usually considered as a sensitive marker, attributed to the presence of proteolytic enzymes, released by neutrophil breakdown (Mishra et al. 2004; Pal et al. 2010). These could sometimes be absent, notably in treated abscesses (Pal et al. 2010). AA peak is not usually encountered as a significant peak in in vivo ^{1}H MRS in hydatid. Lactate (1.3 ppm) is also an important metabolite, sometimes the only metabolite seen such as in treated abscesses (Pal et al. 2010).

Acetate (1.9 ppm) is another very important peak in abscesses caused by anaerobes. It is thought to be a result of enhanced glycolysis, resulting in

pyruvate formation that converts into acetate and succinate. Biochemical reactions leading to acetate formation are thought to be more favourable than those leading to succinate formation, leading to prominent acetate peak (Pal et al. 2010). Succinate (2.4 ppm), while usually presenting small amounts, may or may not be detectable by in vivo ^{1}H MRS (Pal et al. 2010). As a result, the ratio of acetate/succinate is quite high as compared to hydatid cysts (Poptani et al. 1995; Martinez-Perez et al. 1997; Dev et al. 1998). Acetate and succinate are not observed in abscesses by aerobic organisms as the pyruvate is metabolized in TCA cycle in the usual manner (Pal et al. 2010).

Cysts/Necrosis Associated with Tumours

A variety of tumours can have cysts, such as pilocytic astrocytomas, or even associated with benign tumours such as meningiomas. High-grade gliomas are more usually associated with necrosis. The ^{1}H MRS spectra limited to the cysts or necrotic parts of tumours usually show a prominent lactate or lactate/lipid peak (1.3 ppm) (Fig. 13.2). Other metabolites are generally absent, unless there is contamination from surrounding solid tissue (Chang et al. 1998).

Epidermoids

Epidermoids usually have typical imaging features on MRI and rarely present a diagnostic difficulty, in relating to hydatid cysts. The in vivo ^{1}H MRS is significantly different from hydatid and shows a relatively small or medium lactate peak (1.3 ppm), while no further metabolites are usually described (Chang et al. 1998).

Other Cysts

A variety of developmental and incidental cysts and cyst-like lesions are encountered, including arachnoid cysts, porencephalic cysts, neuroglial cysts, large perivascular spaces, etc. On in vivo ^{1}H MRS, these are generally devoid of any peaks (Chang et al. 1998), although there is some literature about the presence of excitatory amino acids such as glutamate and aspartate in some of the arachnoid cysts (Hajek et al. 1997). However these are usually seen at much shorter TE values and not at the usual intermediate values used for hydatid cysts.

Conclusion

In vivo ^{1}H MRS can be a useful tool in differentiating cystic lesions of the brain including hydatid cysts especially when used as an adjunct to MRI rather than in isolation. There are significant overlapping features with NCC which are rarely large enough in isolation to present a diagnostic dilemma, while there are sufficient important differentiating features from other cysts lesions. The in vivo ^{1}H MRS features of various cystic conditions have been summarized in Table 13.1.

Table 13.1 Relative importance of different metabolites in cysts/cystic conditions of brain on in vivo ^{1}H MRS

		Succinate/pyruvate (2.4 ppm)	Acetate (1.9 ppm)	Lactate (1.3 ppm)	Alanine (1.5 ppm)	AA peak (0.9 ppm)	Choline[a] (3.3 ppm)
Hydatid cyst		+++	+	+++	+	–	–
Neurocysticercosis		++	+	++	+	–	+
Anaerobic pyogenic abscess	Untreated	+	+++	+++	–	+++	–
	Treated	–	–	++	–	–	–
Tumour cyst and necrosis		–	–	+++	–	–	–
Epidermoids		–	–	+/++	–	–	–
Other cysts		–	–	–	–	–	–

[a]Choline, unconfirmed peak at 3.3 ppm (Chang et al. 1998)

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Surgical Treatment of Spinal Hydatidosis

14

Erdal Kalkan, Fatih Keskin, and Fatih Erdi

Contents

Introduction

Spinal hydatid cyst is an important and serious form of hydatid disease which is caused by a cyclophyllid cestode, the echinococcus. *Echinococcus* has four subgroups: *Echinococcus granulosus, E. multilocularis, E. oligoarthus* and *E. vogeli (Pamir et al. 2002). E. granulosus* and *E. multilocularis a*re clinically important in humans, and hydatid disease is most commonly caused by the larval stage of *E. granulosus. E. multilocularis* or *E. oligoarthus* are much less important in humans (Pamir et al. 2002; Sengul et al. 2008). The species of *Echinococcus* are discussed in Chap. 3.

Echinococcus has definitive and intermediate hosts. The definitive host is mainly a domestic dog and occasionally other carnivores such as hyenas and jackals. The exact habitat of the adult worm is the jejunum of the definitive host. The parasite has three proglottids: one immature, one mature and one gravid. The gravid proglottid is shed in the excreta of the definitive host and ruptures to release 500–800 ova (Pamir et al. 2002). The intermediate hosts including humans are most commonly sheep, cattle and goats, camel and other herbivores such as deer, kangaroos and wallabies. The intermediate hosts digest the ova in the infected food or water. After digestion of the chitin, outer layer embryos (oncospheres) develop in the intestine to penetrate the duodenal mucosa and disseminate through the portal circulation. The oncospheres which rescue from the immune system of the host develop into cysts in tissues. The cysts consist of an outer fibrous layer

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and a cestode-derived inner germinal membrane containing scolices (Pamir et al. 2002).

The hydatid cysts generally occurs (up to 70 %) in the liver and lungs (12–30 %). Bone involvement in hydatid disease has been reported to be only 0.5–4 %, and spinal involvement is found in 50 % of these cases (Ouma 2006). Spinal cyst hydatid can occur by direct extension from pulmonary or pelvic infestation or less commonly begin in the vertebral body (Kalkan et al. 2007; Senoglu et al. 2009). The vertebral body infestation usually begins in the centre of the vertebral corpus and subsequently extends outward into the epidural and paravertebral area (Senoglu et al. 2009).

Vertebral hydatid disease was classified into five groups in 1928 by Dew: intramedullary, intradural extramedullary, extradural, vertebral and paravertebral extending to the spine (Dew 1928). Fiennes and Thomas (1982) reported isolated extradural spinal infestation. Secondary extension from paravertebral tissues or cysts involving the muscles or even the lungs is occasionally seen. In 90 % of cases the disease is confined to the bone and epidural space (Senoglu et al. 2009). Intradural extramedullary involvement is found in only 9 % of the all spinal cases (Figs. 14.1, 14.2, and 14.3); this can be primary (Kalkan et al. 2007) or secondary as a complication of surgery with dural opening or tear (Pamir et al. 2002). Primary intramedullary hydatid cyst is rarely seen (Ley and Marti 1970).

The most common symptoms and signs in vertebral involvement are paraparesis (62 %), increasing back or radicular pain (55 %), sensory loss (36 %), sphincter disturbance (30 %) and paraplegia (26 %). The time period between the onset of the symptoms and medical consultation varies between 6 and 15 months (Thaler et al. 2010).

A full discussion of the clinical findings of spinal hydatidosis is given in Chap. 8.

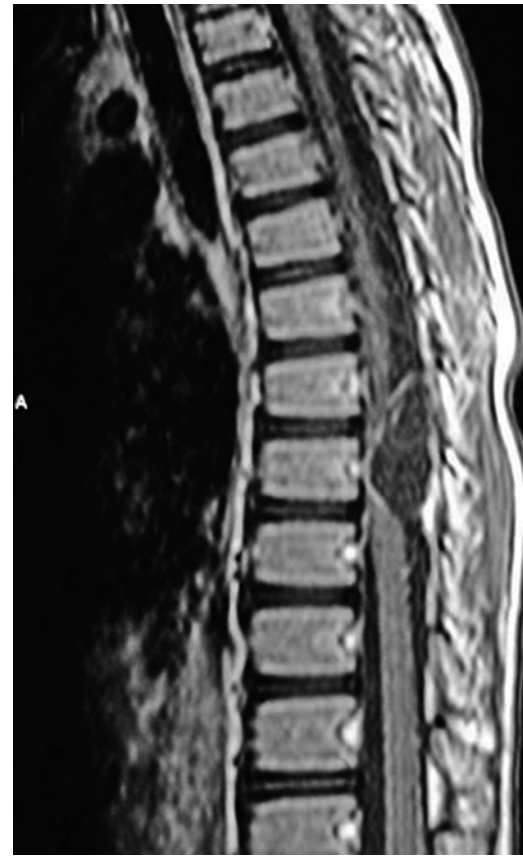

Fig. 14.1 Posteriorly located intradural extramedullary hydatid cyst can be seen on sagittal T1-weighted MRI. The cyst was compressing the spinal cord from the posterior aspect at the T7–8 level

Pathology

Portovertebral shunts play an important role in most of the genesis of spinal lesions in hydatid cysts. The vertebral body is generally the first target. When echinococcal larvae are carried to a vertebral body, the parasite grows multilocularly along the bony intratrabecular space and infiltrates and destroys the bone like a tumour, because of a lack of defensive reaction of the bony tissue (Işlekel et al. 1998). Pathological fractures occur due to compression or avascular necrosis of the cortical bone. Subsequently the disease usually spreads to the pedicles, laminae or the ribs. The intervertebral discs are spared in the early stages of the disease. Finally the infestation may extend beyond the vertebral body and periosteum with the development of a cyst with space-occupying symptomatology. It was observed that hydrophilic degeneration of the *Echinococcus* embryo without reactive osteitis could develop over a number of years, with damage and erosion

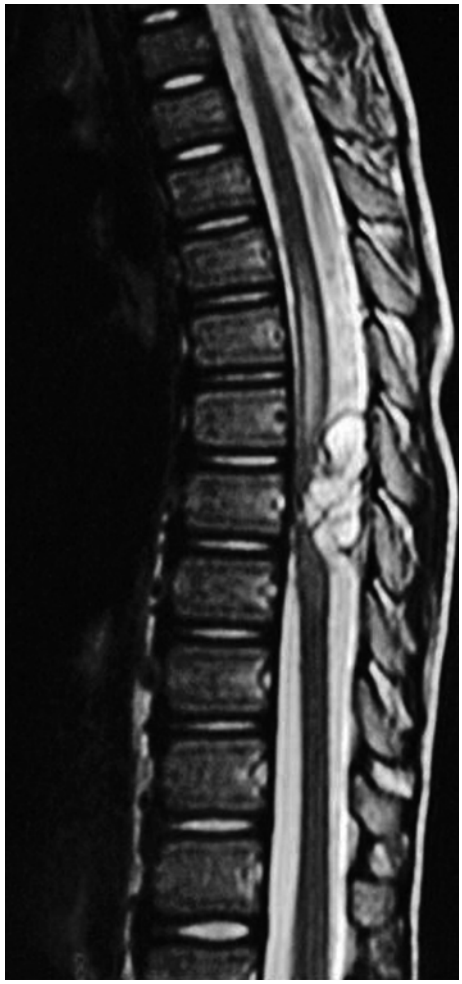

Fig. 14.2 Intradural extramedullary hydatid cyst on T2-weighted sagittal MRI. There was cord oedema

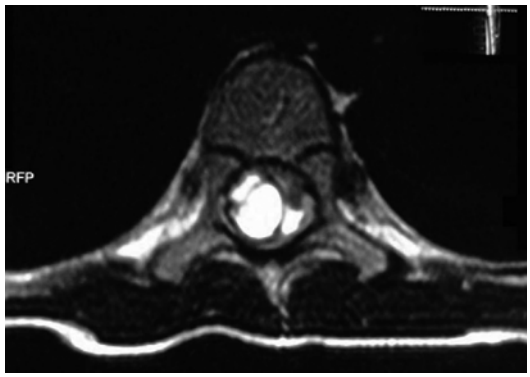

Fig. 14.3 T2-weighted axial MRI shows intradural extramedullary multilocular hydatid cyst. Right-sided lesion was compressing the spinal cord transversely

of the trabecular composition of the bone by the expanding vesicles, with subsequent cystic progression and invasion of all vertebral structures (Tsitouridis and Dimitriadis 1997). When the cyst perforates the cortex, it extends to the paravertebral structures and into the spinal canal or neural foramina (Kalkan et al. 2008). Bone destruction and puslike fluid may be encountered during operation, leading to the name 'ossifluent abscess' (Pamir et al. 2002). Papanikolaou (2008) described three mechanisms for the intraosseous invasion as mechanical, ischaemic and cellular process. The mechanical process affects the surrounding tissues by expansion, compression, dislocation and repression which cause bone and nerve tissue atrophy and osteitis. The ischaemic process affects the nutrient vessels by obstruction and compression which cause bone necrosis and sequestra formation. The cellular process affects the bone tissue by osteoclast proliferation and causes destruction.

The pathology of spinal hydatidosis has been discussed in detail in Chap. 9.

Surgical Treatment of Spinal Hydatidosis

Surgery is currently the mainstay treatment modality for spinal hydatidosis. The first surgical intervention in spinal hydatidosis was reported in 1819 by (Reydellet 1819; Rayport et al. 1964). Most of the cases admitted to surgeons with spinal cord compression syndrome symptomatology are urgent surgeries (Pamir et al. 2002). Patients with spinal hydatid disease usually present with a long history of back pain or other non-specific symptoms of spinal cord compression. Weakness of the limbs occurs in the later stages. Paraplegia or radicular compression is said to occur in 25–84 % of patients (Baysefer et al. 1996). Preoperative diagnosis and the real extent of the disease are very important for operative planning. Preoperative diagnosis of the lesion guides the surgical preference. The correct diagnosis, natural history and serological and radiological studies are essential (Kalkan et al. 2008). Generally,

routine laboratory tests do not show specific values. Eosinophilia is mostly limited (15 %) or absent. An intradermal Casoni test result is positive in 95 %, but there are up to 40 % false-positive results. Indirect haemagglutination test and enzyme-linked immunosorbent assay are established methods for the detection of anti-Echinococcus antibodies (immunoglobulin G). Serological tests are 80–100 % sensitive and 88–96 % specific for liver hydatid disease. They have 50–56 % sensitivity for lung disease and only 25–56 % for other organs like spinal cyst hydatid (El-On et al. 2003; Thaler et al. 2010).

Successful treatment of the spinal hydatidosis is challenging because of its invasiveness and its potentially severe complications. Surgical excision is the first and most effective option. The total eradication of the cyst without rupture should be the primary goal of the surgery (Thaler et al. 2010). In clinical practice, however, this is not possible in the spine because there is no one cyst but a multitude of small cysts. Either anterior or posterior approaches can be preferred for the surgical treatment. Pure intradurally or epidurally located lesions at all spinal levels are approached posteriorly. In these cases surgical excision without intraoperative rupture results in cure (Pamir et al. 2002). Bone involvement is very important for defining the recurrence rates. Surgical planning should be made according to this.

Spinal disease most frequently involves the thoracic segments (46–50 %). Lumbar segments (20–29 %) and sacral segments (20–23 %) are also involved frequently. Cervical spine is the least common affected segment (Pamir et al. 2002). Twenty-eight reports of spinal hydatid disease, published during the past five decades, from Turkey, were reviewed, and 71 patients with spinal hydatid disease were collected (Turgut 1997). According to this study, spinal echinococcus involved the thoracic segment of the spine in 35 patients (49 %), the lumbar segment in 28 patients (39 %), the cervical segment in three patients (4 %), the thoracolumbar segment in three patients (4 %) and the sacral segment in one patient (2 %) (Turgut 1997). One patient had non-contagious lesions in the cervical and lumbar segments (Turgut 1997).

Surgical Treatment of Cervical Spinal Hydatidosis

Hydatid disease in the vertebral column is rare in cervical spine. Several procedures can be useful for the spinal hydatid cyst in the cervical region. Cervical laminectomy is the favourite approach for spinal hydatidosis affecting the cervical aspect of the spinal canal. Intradural lesions are also approached posteriorly. The posterior approach to the cervical spine is relatively straightforward and is well known by all neurosurgeons. Avoidance of risk to the anterior vascular and visceral structures is an advantage of this approach. Potentially greater discomfort and longer hospital stays and increased incidence of spinal deformity are the major disadvantages of this surgery. Postlaminectomy kyphosis is common if the laminectomy is performed in an immature spine. Resection of 50 % or more of one facet or its capsule results in a significant risk of subsequent instability (Tandon and Vollmer 2006). The use of lateral mass plating is a significant improvement for the treatment of cervical spine instability. Keller et al. (1997) reported a case of postoperative kyphosis after an anterior corpectomy with simple bony fusion in a spinal hydatid patient. Progressive myelopathy occurred, in this reported patient, and it was successfully treated with a posterior lateral mass plating.

The anterior approach may be utilised for decompression and stabilisation of the cervical spine in a variety of conditions. Anterior approaches including corpectomy with simple bony fusion and corpectomy with anterior plating have been reported for the treatment of cervical spinal hydatidosis (Keller et al. 1997). Anterior instrumentation, in addition to bone grafting, has been generally successful in the cervical spine when treating infection and may obviate the need for posterior instrumentation.

Surgical Treatment of Thoracic Spinal Hydatidosis

Spinal hydatidosis most commonly affects thoracic spinal segment (Figs. 14.4, 14.5, and

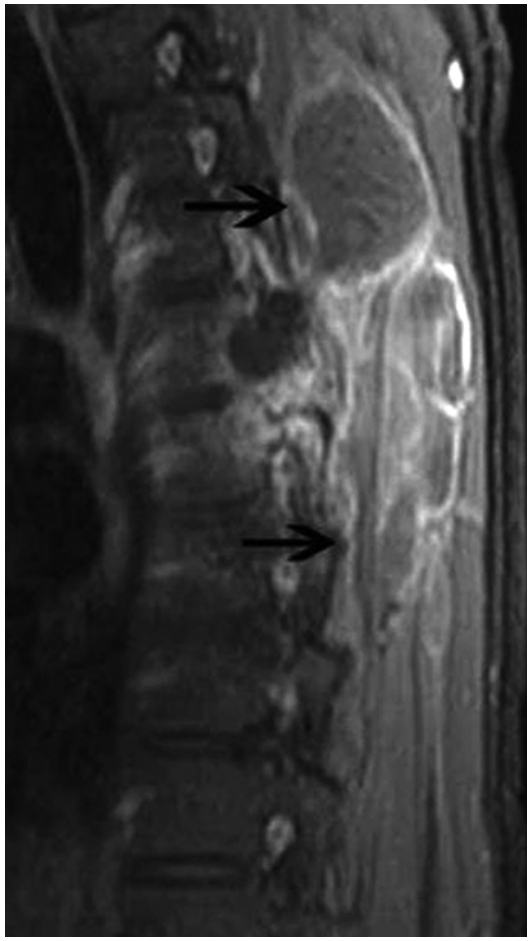

Fig. 14.4 T1-weighted sagittal MRI obtained after contrast administration shows multiloculated cystic lesion at the T4 level. *Black arrows* indicate rim enhancement of the cystic lesion

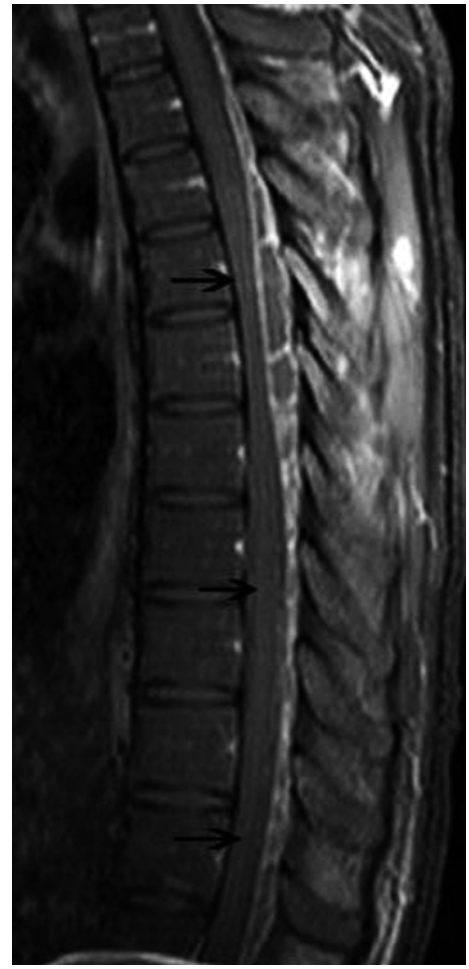

Fig. 14.5 T1-weighted sagittal fat-saturated MRI obtained after administration of intravenous contrast material reveals rim-enhancing loculated cystic lesions through posterior epidural space (*black arrows*)

14.6). The reported approaches in thoracic cases were mainly posterior. The posterior approach via laminectomy is the main choice of treatment (Pamir et al. 2002). Complete surgical removal and most extensive removal of the infected bone must be the goal of the surgery. Decompression of the cord, resection of the cysts, infected bone resection and deformity correction can be done in one approach under direct vision of the cord through a posterior approach (Figs. 14.7 and 14.8). Extradural multiple cysts and cysts located in the bone or in the paravertebral region are the most commonly seen scenario (Figs. 14.9 and 14.10). Daughter cysts may form within the main cyst (Işlekel et al. 1998). Surgical excision without intraoperative cyst rupture results in a cure in pure intradural or pure epidural lesions. In most cases the cysts are multiple and extensive. It is nearly impossible to remove these cysts without rupture. During laminectomy, cysts are almost always ruptured (Işlekel et al. 1998). More extensive lesions with vertebral body involvement can be also approached posteriorly via a transpedicular route (Pamir et al. 2002).

Simple decompression with laminectomy is performed most frequently due to its low morbidity and mortality, but it is not free from risks. Access to the vertebral body through a laminectomy is

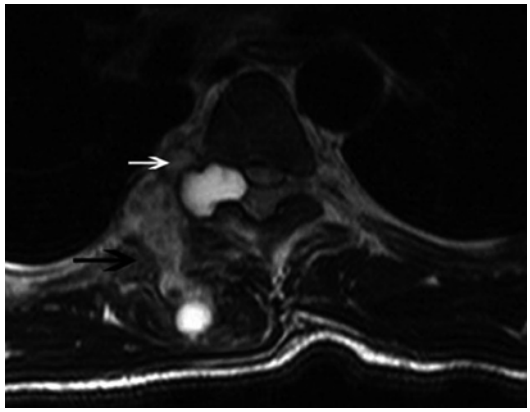

Fig. 14.6 T2-weighted axial MRI reveals heterogeneously hyperintense multiloculated cyst infiltrating paravertebral muscles (*black arrow*) as well as epidural space through neural foramen (*white arrow*)

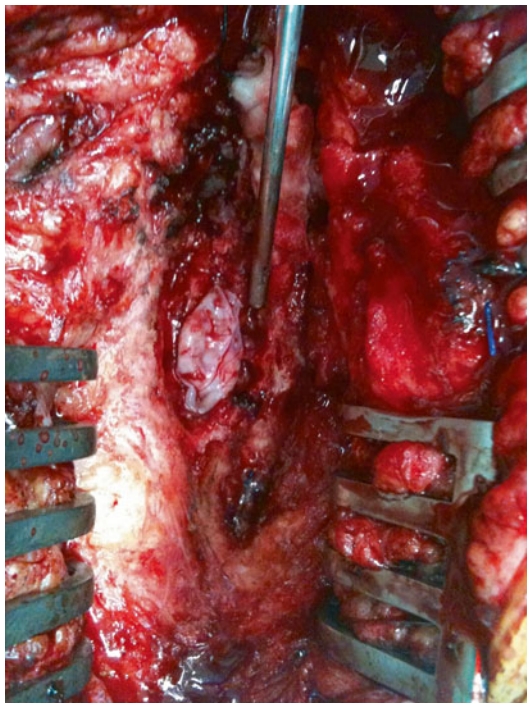

Fig. 14.7 Intraoperative view of a posterior laminectomy site. Extradurally located hydatid cyst can be seen

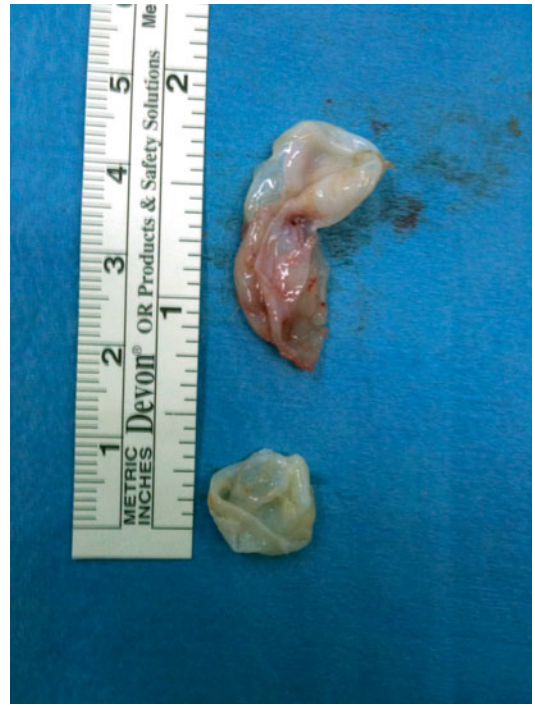

Fig. 14.8 Some of the cysts which were retrieved during surgery

limited, resulting in poor outcomes, especially in recurrent disease. Despite treatment, the disease frequently relapses with progressive destruction of the vertebral column and neurological deterioration (Senoglu et al. 2009). Kaoutzanis et al. (1989) suggested that routine laminectomy for spinal hydatid did not significantly affect the outcome. Turtas et al. (1980) reported a 50 % recurrence rate after posterior decompression alone. Thaler et al. (2010) indicated that partial hydatid cyst resection, inappropriate stabilisation and posterior multilevel laminectomies without posterior stabilisation have led to progressive deformities of the thoracic spine. They concluded that no cases of reoperations due to spinal deformity were found when cyst resection and posterior laminectomy were combined with anterior or posterior stabilisation.

Khazim et al. (2003) reported seven cases of spinal hydatid disease treated with posterior decompression and were followed up for an average of 20 years. They concluded that the long-term results were very poor, with high rates of mortality, localised and extra-vertebral recurrence, significant neurological deficits, spino-cutaneous fistulae, spinal instability and pain. Spinal column deformity often occurs in children after multilevel laminectomies for spinal tumours, and its incidence, in these

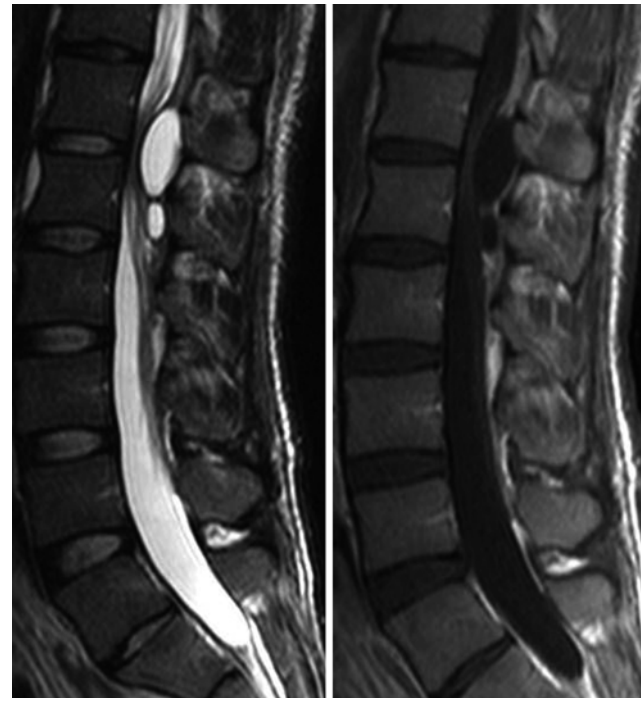

Fig. 14.9 T2- and T1-weighted sagittal contrast-enhanced MRI shows multiloculated hydatid cyst with rim enhancement. The lesion was located in posterior epidural space at the level of T12–L1

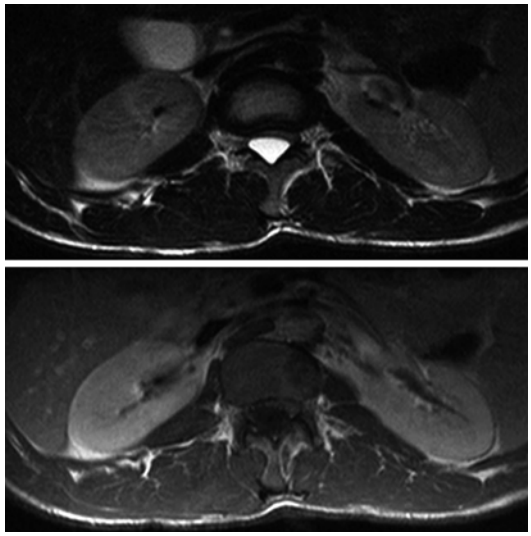

Fig. 14.10 T2- and T1-weighted axial MRI shows cystic lesion which was compressing the dural sac anteriorly

patients, has been reported to be 24–100 % (Papagelopoulos et al. 1997).

Herrera et al. (2005) presented a large series which consisted of 20 spinal hydatid cases. In this series seven thoracic region cases were reported: they exposed the spine posteriorly in all except two patients, and they recommended posterior decompression alone only in cases with isolated neural arch and in extraosseous extradural presentations (Herrera et al. 2005). For the lesions situated in the vertebral body, they recommended an anterior approach to remove the infested bone (Herrera et al. 2005). They also recommended a posterior approach to remove the involved posterior elements and to add a posterior fixation (Herrera et al. 2005). Technically, they used Harrington or Luque spinal instrumentation and pedicle screws for posterior fixation (Herrera et al. 2005).

Khazim (2006) suggested that if stabilisation with pedicle screws is performed, the disease might be iatrogenically seeded into the vertebral body if viable scolices are present at the surgical site. Fusion or stabilisation is not recommended if only partial or complete laminectomy without excessive facet joint excision is performed (Khazim 2006). In our clinical practice we decide to add instrumented fusion depending on whether instability is already present or is created by surgery.

Anterior approach to the thoracic lesions is another alternative for the treatment of thoracic

spinal hydatidosis. Transthoracic corpectomy with anterior fusion and anterior approaches with costotransversectomy can also be performed according to the bony involvement of the disease. For lesions situated in the vertebral body, an anterior approach can be used to remove the infected bone (Herrera et al. 2005). Thaler et al. (2010) suggested that anterior compression was falsely treated with posterior laminectomies further destabilising the spine and accelerating the kyphotic deformity. The bony apex due to the kyphotic deformity was continuously causing anterior pressure on the cord causing neurological deterioration with episodes of paraplegia. In a kyphotic deformity, the posterior approach with costotransversectomy gives a perfect view of the operative field especially for the resection of the posterior wall of the bony apex. An anterior approach via thoracotomy would provide a better vessel control in cases of vascular injury; however, it is inappropriate in terms of apical resection and cord control.

Successful anterior approaches, with symptom-free period of 2 or 3 years after surgery, have been reported by some authors (Pamir et al. 2002; Akesen et al. 2011). The cysts which extended into the thoracic cavity via neural foramina can be removed with an anterior approach. Anterior approaches have also been used for complementary treatment strategies for thoracic spinal hydatidosis. Prabhakar et al. (2005) presented a series of four spinal hydatidosis in which they presented two thoracic ones which were treated with combined posterior and anterior approaches. Firstly laminectomy and posterior decompression were performed, and subsequently this surgery was complemented with anterior decompression and fusion. Akesen et al. (2011) presented a case of multilevel thoracic spinal hydatidosis which was treated by a three-level anterior corpectomy after posterior decompression and fusion. They suggested that multilevel spinal involvement should not be a reason to avoid surgical treatment if the lesion can be excised with a three-level corpectomy. Stability of the anterior column must be ascertained to prevent postoperative kyphosis. An extensive resection with stabilisation and grafting is shown to prolong survival in selected cases (Turtas et al. 1980).

After corpectomy a tricortical iliac strut graft or a lyophilised iliac crest allograft or an autologous costal graft can be placed for anterior support. Also a titanium cage packed with autogenous bone graft can be placed in the bone defect formed. Sapkas et al. (1998) reported his concerns about the possible infestation of graft material and advocated the use of acrylic cement for osteosynthesis. Bhojraj and Shetty (1999) have a contrary idea. They suggested that an anterior approach should be avoided to prevent the spread of the disease to the chest and abdominal cavities (Sapkas et al. 1998).

In brief, appropriate surgical treatment would include complete cyst resection without violation of the wall, appropriate decompression of the cord, correction of the deformity and appropriate anterior and posterior instrumented stabilisation techniques (Thaler et al. 2010).

Surgical Treatment of Lumbosacral Spinal Hydatidosis

The lumbar segment is the second most common disease location in spinal hydatidosis (Turgut 1997; Pamir et al. 2002). Simple laminectomy is the most common procedure for surgical treatment (Pamir et al. 2002). This approach allows simple and easy decompression with low morbidity and mortality. But in cases of bone involvement, access to the vertebral body is limited with a laminectomy (Figs. 14.11 and 14.12). In addition spillage of scolices is unavoidable in cases of bone involvement. Laminectomy only may result in rupture of cysts and scolex spillage (Senoglu et al. 2009).

Abdominal retroperitoneal corpectomy with posterior fusion and subsequent surgery for vertebral body was reported in lumbar hydatidosis (Lam et al. 1997). Baysefer et al. (1996) presented a case of L4 vertebral hydatid cyst which was operated through an anterior approach. Anterior spinal decompression by a retroperitoneal abdominal approach was performed. The vertebra was excised and an autologous iliac bone graft was inserted into the defect. Later they performed a posterior fusion for stabilisation.

We have previously reported a case of spinal hydatidosis which eroded the 2nd lumbar vertebral body and pedicle and extended to the paravertebral and abdominal region and neural foramina (Fig. 14.13). The patient was operated through an anterolateral approach, the lesion was removed and L2 partial corpectomy was performed. Interbody fusion was accomplished using an L1–L3 distractable cage, and stabilisation was performed using an L1–L3 bicortical screw-plate system (Fig. 14.14). The patient was symptom-free at his 6-month follow-up, and

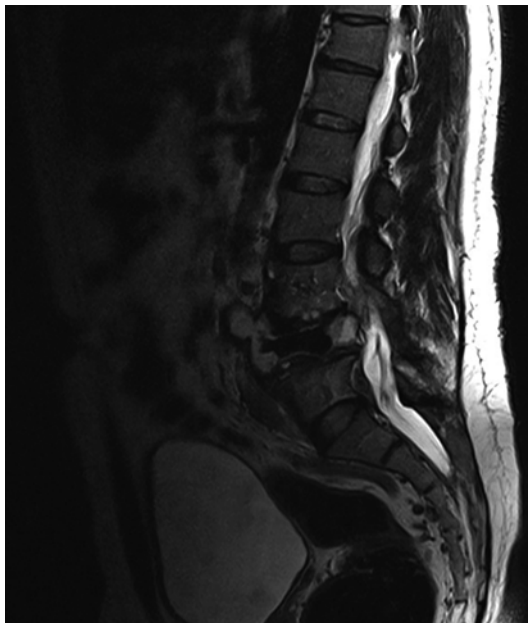

Fig. 14.11 T1-weighted sagittal MRI shows spinal hydatid cyst with L4 corpus involvement. There is bone destruction, partial collapse and retroperitoneal extension

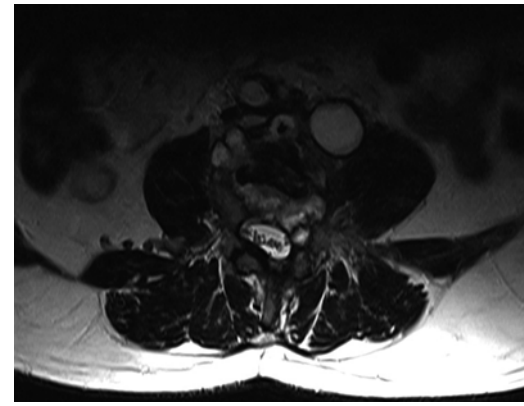

Fig. 14.12 T2-weighted axial MRI sequence through L4 vertebral body. The corpus was almost completely destroyed

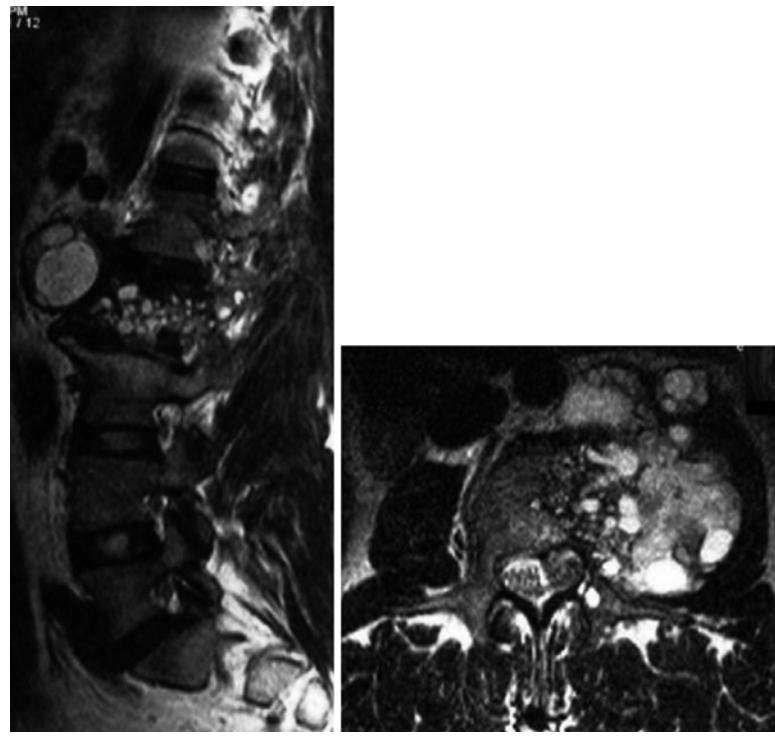

Fig. 14.13 Sagittal T2-weighted (*right*) and axial (*left*) MRI sequences show L2 vertebral body destruction with left psoas expansion. The lesion was extending through the left neural foramen and compressing the root

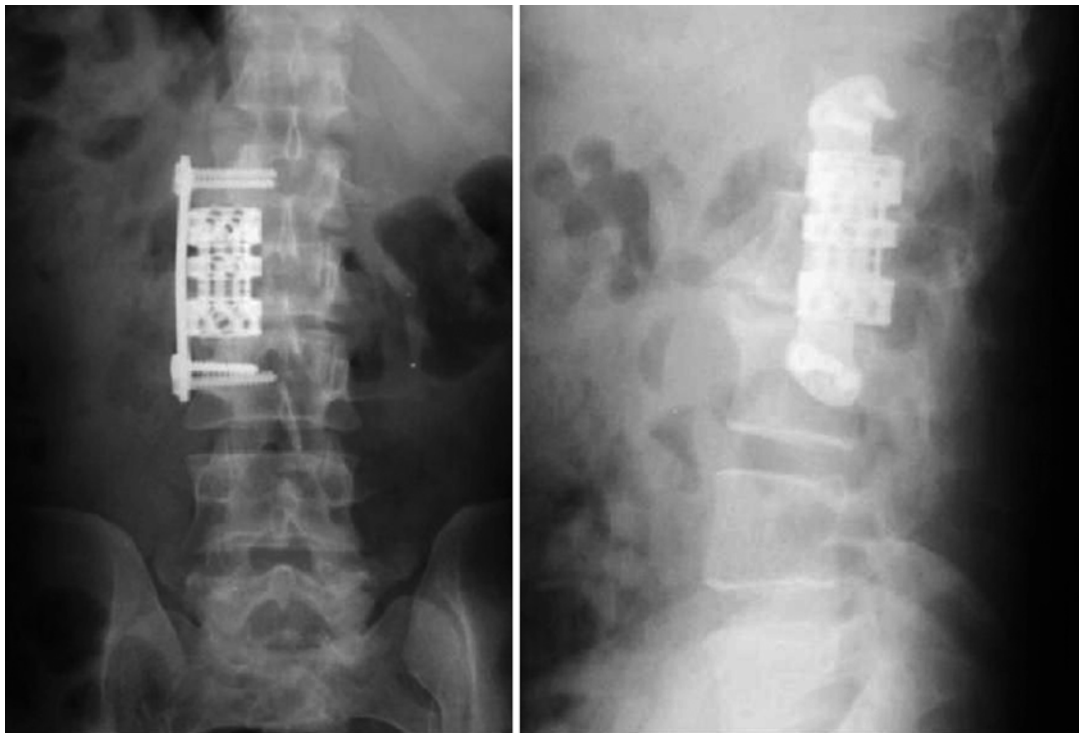

Fig. 14.14 Postoperative plain radiographs of the case shown in Fig. 14.13 show L1–3 distractable cage and L1–3 screw-plate system

magnetic resonance imaging (MRI) revealed total removal of the disease (Kalkan et al. 2008). Senoglu et al. (2009) presented a case of sacral spinal hydatidosis which was treated with combined anterior and posterior approach. Firstly an anterior extraperitoneal approach was performed, and then a posterior approach with bilateral S1 hemilaminectomy was done.

Scolicidal Agents

Although the effectivity is not proven, most surgeons advocate intraoperative scolicidal agents as well as adjuvant pharmacotherapy (Pamir et al. 2002). Scolicidal agents like 3 % hypertonic saline, cetrimide, chlorhexidine, 80 % alcohol, 0.5 % silver nitrate, 10 % formalin, sodium hypochlorite and glycerine phenol are used in abdominal hydatid cyst disease (Pamir et al. 2002; Khazim et al. 2003). The use of povidone iodine as a scolicidal agent is reported in spinal cases, but long-term results are lacking (Pandey and Cahudhari 1997). Hypertonic saline is the most frequently used agent in spinal hydatidosis. Hypertonic saline is a scolicidal agent due to the difference of osmolality between the hypertonic saline and the interior of the cyst. It causes the sclerosis of the cyst (Herrera et al. 2005). Işlekel et al. (1998) reported an operative mortality due to toxic myelitis caused by formalin after a dural tear. Formalin irrigation is also reported to add to the morbidity by increasing tissue necrosis and should be avoided in spinal cases (Pamir et al. 2002).

Chemotherapy for spinal hydatidosis is discussed in detail in Chap. 16.

Minimally Invasive Techniques

Diagnostic or therapeutic fine needle aspiration of hydatid cysts is frequently used in abdominal hydatid disease. Puncture-aspiration-injection-reaspiration (PAIR) refers to an ultrasound-

guided technique consisting of puncture and evacuation of the contents of the hydatid cyst, injection of scolicidal agents such as 95 % ethanol and reaspiration of the contents of the cyst. This technique was first developed by Mueller et al. (1985) as an alternative treatment method against surgical excision of the liver hydatid cysts. Spektor et al. (1997) described the successful decompression of an extradural cervical spinal hydatid cyst by computed tomography (CT)-guided fine needle aspiration with complete resolution of quadriplegia. Bilgic et al. (2009) reported a case of primary hydatid cyst of the erector spinae muscle which was treated successfully with PAIR technique. At the final follow-up 26 months after the aspiration, the patient was free of symptoms and ultrasonography revealed solidification of the cyst content and thickening and irregularity of the cyst wall, all of which were considered as signs of cure.

Other minimally invasive techniques such as endoscopic evacuation of cyst material are reported in the literature (Acikgoz et al. 1996). Pamir et al. (2002) suggested that minimally invasive methods may be of value in selected patients with localised spinal disease, in whom surgical therapy is contraindicated. They suggested that these minimally invasive techniques are still experimental and the efficacy and safety has not been established. Potential complications of this technique are anaphylaxis and the risk of iatrogenic spreading (Thaler et al. 2010). In addition, simple drainage of the infested cystic area is reported to result in pyogenic osteomyelitis and is strongly discouraged (Rao et al. 1991). Spector et al. (1997) suggested that with adequate prophylaxis against anaphylaxis and dissemination, CT-guided aspiration of spinal hydatid cysts with hypertonic saline irrigation and subsequent chemotherapy may be an alternative to surgical therapy in selected cases.

Complications

The surgical treatment has some specific and non-specific complications. Cyst rupture is an important complication especially in the pure intradurally or epidurally located hydatid cyst cases without bone involvement. Extreme caution should be taken not to rupture intradural or epidural solitary cysts, as complete removal might potentially result in a cure. If any cyst ruptures into the intradural space, the surgical area should be irrigated with hypertonic saline, but this seems relatively ineffective, and recurrence is unavoidable in these cases (Braithwaite and Lees 1981).

Cyst rupture during surgery has a potentially fatal but rare complication: anaphylactic shock. Turgut (2001) reported 3 deaths from 'anaphylactic shock' out of the 268 reviewed intracranial hydatid cases in the Turkish literature. There is no reported case of anaphylactic shock in spinal hydatid cyst. Recurrence is a major complication of the surgical treatment. The recurrence rate has ranged from 30 to 100 %. The average number of procedures per patient has been reported as 2.6–4.6 (Khazim et al. 2003).

Infection, deep venous thrombosis, pulmonary embolism, cerebrospinal fluid leakage, postoperative mortality and increased neurological deficit are some important non-specific complications of surgical treatment. A mortality rate of 0–3 % is reported which progressively increases to 15 % in reoperations (Pamir et al. 2002). Işlekel et al. (1998) reported on the death of a case due to formalin irrigation, the formalin having seeped into the CSF through an intraoperative tear of the dura.

Complications of spinal hydatidosis are discussed in detail in Chap. 18.

Surgical Results

The prognosis of vertebral hydatidosis is very poor, especially if neurological deficits are present. Even with extensive surgery results are far from being curative and recurrences are almost universal (Pamir et al. 2002). Up to 40 % of patients are reported to have recurrent symptomatology within 2 years from the initial operation. In recurrent lesions the major goal is restoration of neurological status and preservation of spinal stability. The presence of disease involving the paravertebral tissues further warrants the use of adjuvant therapy. Nevertheless, most patients experience a downhill course with worsening

neurological status and progressive destruction of the vertebral column with multiple recurrences. The incidence of paraplegia in recurrent disease is reported to be as high as 45 %. Recurrence is considered a bad prognostic factor in spinal hydatid disease. Operative mortalities up to 14.4 % were reported in recurrent cases. Most patients having such treatment have had several operations for recurrence.

Keller et al. (1997) reported a cervical case operated on six times with preservation of spinal stability and neurological status. They concluded that despite multiple recurrences, spinal stability could be achieved and should be the goal. Recurrences occur 2–28 months (mean, 25.2 months) after the initial operation. The recurrence rate for intradural extramedullary disease is reported to be low. The high recurrence rate is primarily responsible for the poor survival rate in only 5 years after the onset of symptoms. Lam et al. (1997) reported that the average age at death is 41 years. Operative mortality rates up to 15 % are reported in the literature and are known to increase with subsequent operations. Paraplegia due to recurrent disease is reported to be as high as 45 % (Pamir et al. 2002). Overall mortality rates were reported as 14–58 % for groups of patients with or without paraplegia (Khazim et al. 2003).

Khazim et al. (2003) suggested that the poor results of surgical treatment can be partially explained by the fact that the diagnosis was not suspected until the lesion was encountered intraoperatively. They concluded that a high level of suspicion is paramount in making the diagnosis. This is more important in countries where the disease is not endemic.

Işlekel et al. (1998) reported a case which was operated in a western country where the hydatid disease is not endemic. The pre- and postoperative diagnoses were a dermoid cyst. Opening of the dura during the first operation presumably led to the intradural invasion and recurrences. This patient was operated upon eight times and died of renal complications.

Conclusion

Spinal hydatidosis should be considered as a locally aggressive tumour, the treatment of which ideally should be radical excision of all affected tissues with a margin of healthy tissue. Technically, this is very unlikely to be achieved because of the absence of distinct anatomic planes, containment within small spaces having bony boundaries and the existence of neural structures in close vicinity. Nevertheless, marginal or intralesional excision of the hydatid lesions is possible through combined anterior and posterior approaches.

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Surgical Treatment of Cerebral Hydatidosis

15

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Contents

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Surgical Indications

There are no clear-cut surgical indications for intracranial hydatid cysts in the existing medical literature. Unlike other intracranial lesions, an intracranial hydatid cyst has its own characteristic, biological behavior, and clinical manifestations, such as benign growth, relatively mild neurological deficit, and large size at presentation (Turgut 1997; Duishanbai et al. 2011). Owing to such distinct characteristics, almost all patients with intracranial hydatid cysts need to undergo one or more surgical interventions for the rapid relief of intracranial pressure or decompression of surrounding neural, vascular, and parenchymal brain tissues. Increased intracranial pressure and progressive neurological deficit are the main surgical indications. Surgical treatment is mandatory for all patients once the correct diagnosis is made, except for patients with multiple organ involvement in poor general conditions and deep-located cysts in which surgery may produce additional neurological deficit or even death. Recurrent hydatid cysts, multiple hydatid cysts, and hydatid cysts which are resistant to chemotherapy still need surgical treatment (Yurt et al. 2007).

Preoperative Care

Preoperative chemotherapy, albendazole, is not indicated for primary intracranial solitary hydatid cysts, while intracranial hydatid cyst with

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extraneuronal involvement still needs preoperative chemotherapy (Turgut 2001; Duishanbai et al. 2010). Epilepsy is one of the common symptoms of supratentorial intraparenchymal hydatid cyst; thus, antiepileptic drugs are recommended for such a subgroup of patients. Intermittent usage of dehydrating agents such as 20 % mannitol is recommended for patients with increased intracranial pressure who are at risk of developing brain herniation or impending loss of vision. Good nutritional status and absence of other associated infections are important for a successful surgical treatment. Intraoperative antibiotics are also recommended for all surgical cases. Usually, blood preparation is not mandatory except for infants or children with big cyst which needs large craniotomies.

Surgery

Anesthesia

Patients with an intracranial hydatid cyst receive general anesthesia. General anesthesia should be deep enough to prevent brain bulging and inadvertent movement of the patient.

Positioning

The positioning of the patient depends on the location of the given cyst. Supine and lateral positions are used for supratentorial hydatid cysts, and prone and sitting positions are used for infratentorial ones. To facilitate the delivery process of a hydatid cyst by gravity, head positioning is very important. At the time of delivery, the surgeon should be able to rotate or lower the head at will to facilitate the delivery. So, the patient's head should not be securely fastened to the operating table (Turgut 2001, 2002; Duishanbai et al. 2011).

Craniotomy

Craniotomies for the removal of cerebral hydatid cysts are always larger in size than the standard neurosurgical craniotomies for other space-occupying lesions, as well as large skin flaps (Duishanbai et al. 2010). Commonly used approaches may include temporo-frontal, temporo-fronto-parietal, and temporo-parieto-occipital approaches. On rare occasions, cysts are found in the orbit, pons, intra- or parasellar regions, cerebellopontine angle, thalamus and petroclivus, aqueduct of Sylvius, and jugular foramen; and those may need more sophisticated surgical approaches (Gökalp and Erdoğan 1988; Kayaoglu 2008; Kamath et al. 2009). Multiple cerebral hydatid cysts may need multiple craniotomies (Akdemir et al. 2007; Yurt et al. 2007).

Surgical Procedures

Surgery is the method of choice for the treatment of cerebral hydatid cysts whenever possible, but alone it may not cure hydatid cyst in some conditions such as multiple hydatid cysts in deep locations and multiple organ involvement (Turgut 2001). Although the Dowling-Orlando technique has long been used as a golden surgical technique for the treatment of cerebral hydatid cysts, it is not always applicable to the hydatid cyst in extraneural spaces and atypical areas such as the orbit, epidural spaces, brain stem, periventricular regions, cavernous sinus, and basal cisterns (Rivierez et al. 1992; Yüceer and Gökalp 1998; Yilmazlar and Aksoy 1999; Khaldi et al. 2000; Rumboldt et al. 2003; Beskonakli et al. 2005; Boudawara et al. 1975). Although the removal of a solitary cerebral hydatid cyst can easily and safely be achieved by a modified Dowling's technique in uncomplicated cases, complete removal of multiple cysts or those located in atypical areas is usually difficult, and radical extirpation of the cyst is not possible without rupture. In these cases, techniques other than Dowling's technique, such as puncture-aspiration-injection-reaspiration (PAIR) of the cyst, may be used. The materials used in irrigation are devitalizing solutions like 0.1–1 % cetrimide, chlorhexidine, 80 % alcohol, 0.5 % silver nitrate, 10 % formalin, sodium hypochlorite, glycerin-phenol, and hypertonic saline. Up until now, the main surgical choice for the removal of intracranial hydatid cysts may include (a) the modified Dowling-Orlando technique, (b) the percutaneous

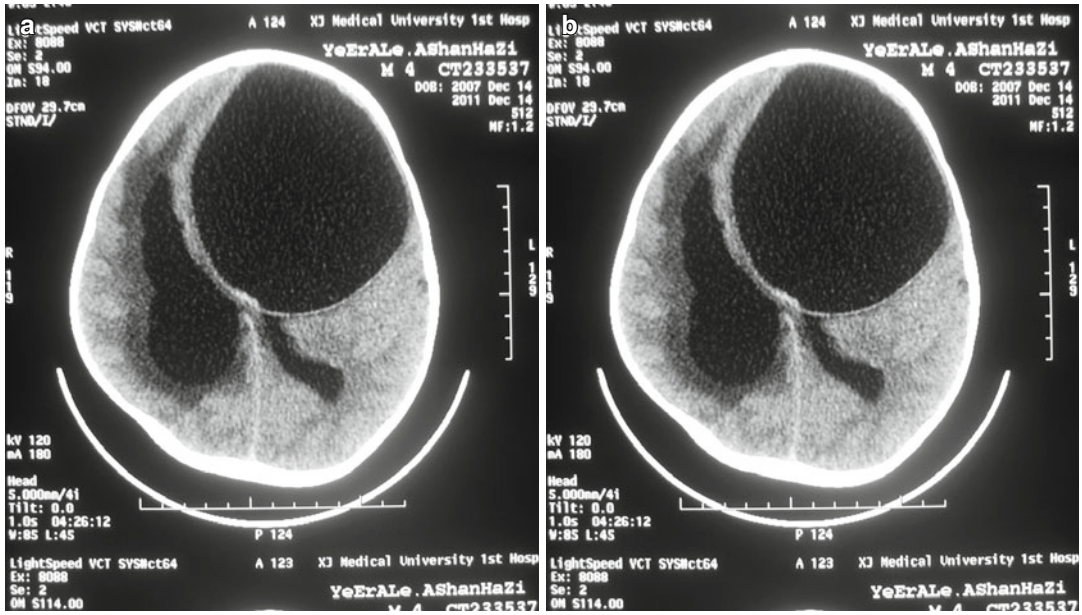


Fig. 15.1 A plain CT showing a giant frontal hydatid cyst in a 4-year-old Kazakh boy (**a**) and an intubated patient and a large skin incision marked in supine position with the head turned a little toward the opposite side of the lesion (**b**)

or intraoperative PAIR method, (c) microsurgery, or (d) a combination of the above three methods. Surgical strategy should be tailored according to the type of cyst for a favorable outcome with minimal mortality and morbidity (Turgut 2001). Hydatid cysts which are located in extradural spaces and in the orbit can be removed with microsurgical techniques (Gazzaz et al. 2000; Erman et al. 2001; Turgut 2001). Akdemir et al. (2007) and Cemil et al. (2009) reported that hydatid cysts of the internal acoustic canal and jugular foramen have been removed via retrosigmoid suboccipital craniotomy.

Modified Dowling-Orlando Technique

After the correct diagnosis, patients with cerebral hydatid cyst may be treated on an emergency basis or as elective surgery according to the neurological symptoms and signs (Fig. 15.1a). Herniated cases or cases that are at risk of herniation should be treated urgently. The timing of surgery is based on the neurological and neuroimaging findings. Early cyst extirpation (within 3 days) is reserved for giant hydatid cysts that cause severe neurological deficits, and late extirpation (more than 3 days) is performed in patients who have relatively small cysts and those which need to undergo further evaluation for the differential diagnosis or to improve their general condition (Turgut 2001, 2002).

Positioning

The patient should be positioned in the correct operating position according to the location and size of the given cyst, and the head should not be fastened securely to the operating table for the possible changes in its position intraoperatively (Haddad and Haddad 2003) (Fig. 15.1b).

Craniotomy

The craniotomy should be planned to be larger than craniotomies utilized in usual space-occupying lesions, and the excess should be planed toward the inferior edge of the cyst (Fig. 15.2). It is preferable to use clamps rather than Raney scalp clips to secure hemostasis of the scalp. The sharp edges of the Raney scalp clips may injure the falling cyst. It is preferable to use a manual burr hole handle and a Gigli saw than an electric or air-powered drill because the vibrations of the later may rupture

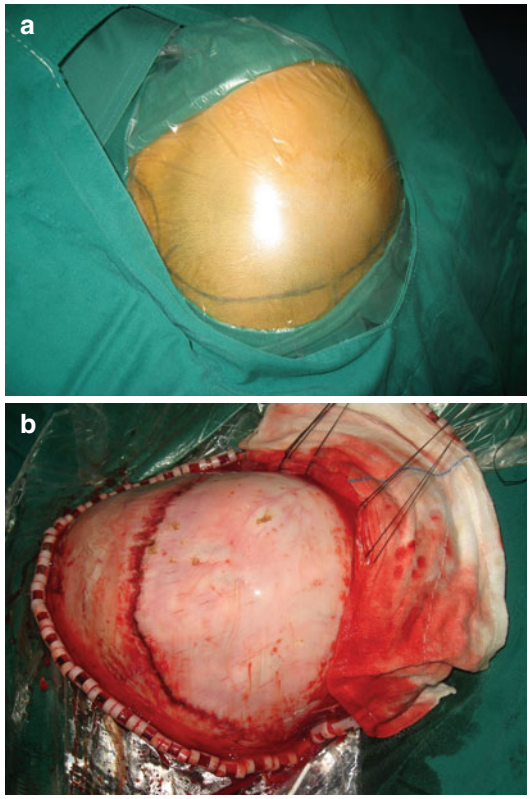


Fig. 15.2 A plain CT showing the operating filed sterilized and draped (**a**) and a large skin flap reflected (**b**)

a cyst in its proximity. The bone flap is then carefully lifted and separated from the underlying dura matter and removed as a free flap (Fig. 15.3a). One must be sure not to leave sharp bony edges in the field. These should be carefully trimmed and smoothened to prevent and inadvertent rupture of the cyst (Haddad and Haddad 2003).

The dura is carefully opened starting away from the expected position of the cyst, and any adhesions to the underlying brain or ectocyst should be released carefully (Fig. 15.3b). Tucking of the dura is strongly recommended after the opening of the dura, not before, to prevent possible injury of superficially lying cysts. On illumination, through the thinned dura, cyst fluid may be observed in some patients once the cranium has been opened (Fig. 15.3c). Usually there is a very thin cortical tissue, if any, under the dura mater (Fig. 15.3c).

Operative Field Draping

This is of paramount importance. It may prevent cyst rupture, and in case of such inadvertent rupture, this draping will minimize the damage. Fine gauze imbibed with 0.1 % Cetrimide is placed around the bone edges of the craniotomy, as well as over the normal brain tissue. The same type of gauze covers all clamps and/or Raney scalp clips and fishhooks if in use. Rolls of wet gauze are tucked between the edges of the dura and the cortex to prevent the seepage of fluid into the base of the brain, in case of rupture.

The Delivery

Usually a small surface of the cyst appears through the cortex. This area is not large enough to permit the safe delivery of the cyst. The arachnoid is carefully opened. As seen in Fig. 15.3d, "episiotomies" are performed in silent areas. While carrying these episiotomies, no cautery, uni- or bipolar, should be used. Any significant blood vessel should be clipped and not coagulated. These vascular clips could be removed at the end of surgery and the blood vessels coagulated then. The episiotomies are carried though the depth of the cortex until the cyst wall is seen (Fig. 15.3e). At this stage the "membranes" should be ruptured to allow a normal delivery. The membrane in these cases is the pericyst. In the brain, there is a very fine pericyst which at times may rupture spontaneously. If it remains intact, it will hamper delivery. One can tear it with a blunt instrument. Once the apparent portion of the pericyst is resected, the head of the patient is readjusted in a way to have the cyst in the most dependent position (Fig. 15.3f). A band of soft gauze, soaked in cetrimide, is laid on the cortex from the interphase between the cyst and cortex, in its most dependent position and extending to the receptacle which will receive the specimen. This receptacle should contain some cetrimide to prevent the direct fall of the cyst against the container's solid bottom. A fine pliable rubber tube is inserted in the space between the pericyst and ectocyst, and a 0.1 % Cetrimide solution is gently injected to break the adhesive effect between the peri- and ectocyst and to float the cyst (Fig. 15.3g). At this moment Credé's maneuver by pressing on the cortex

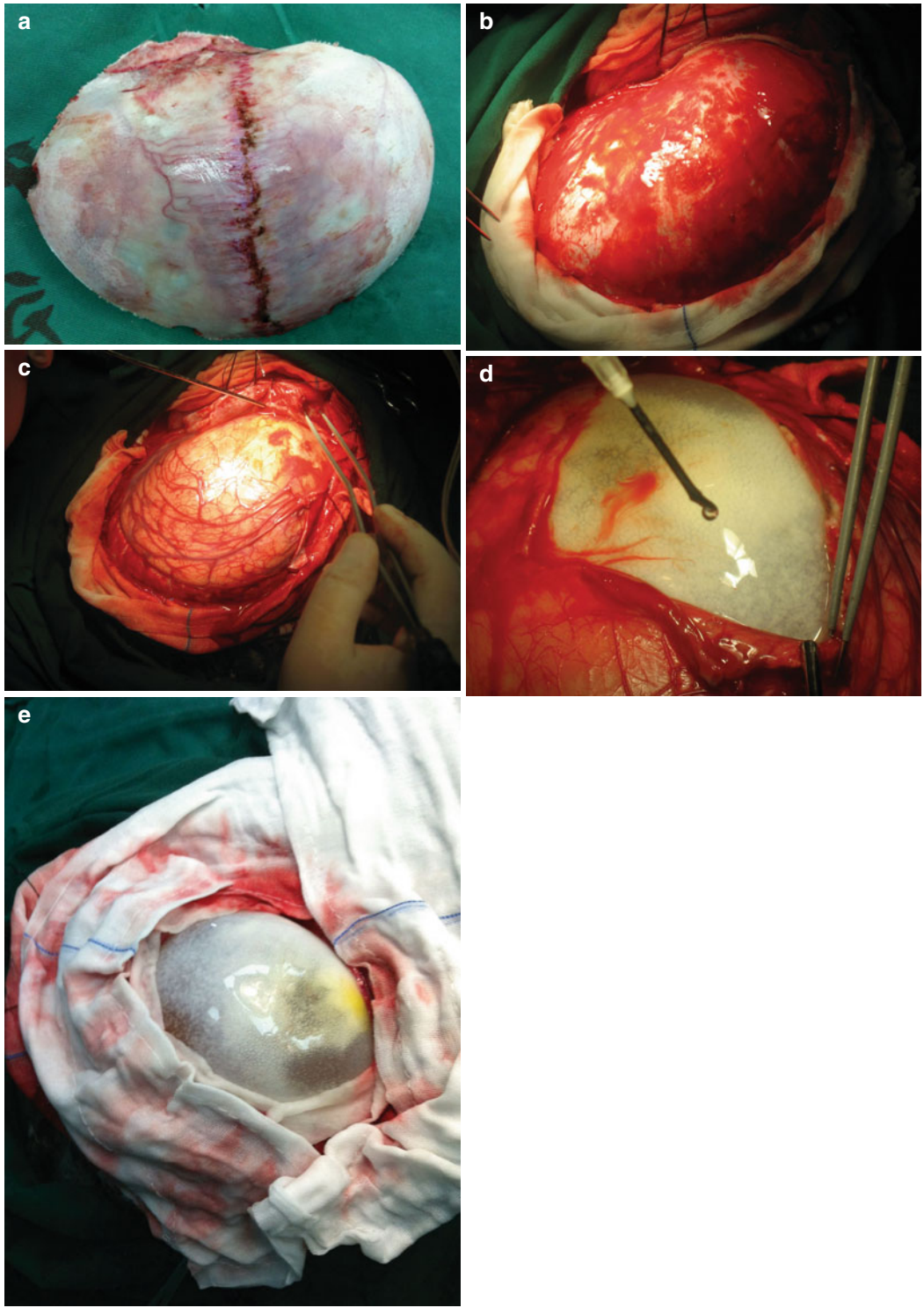
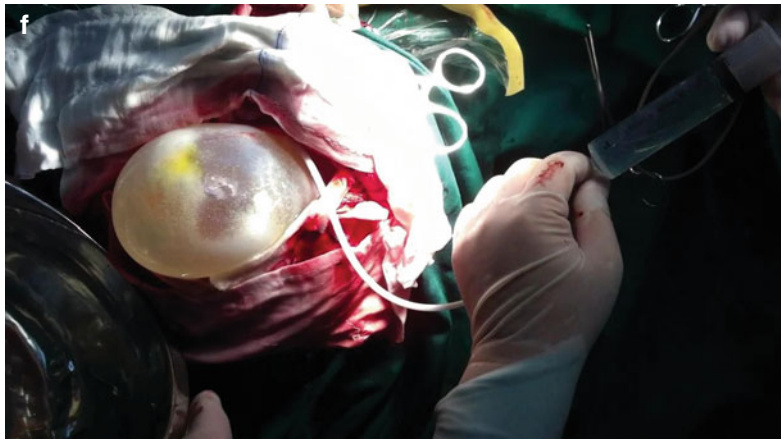
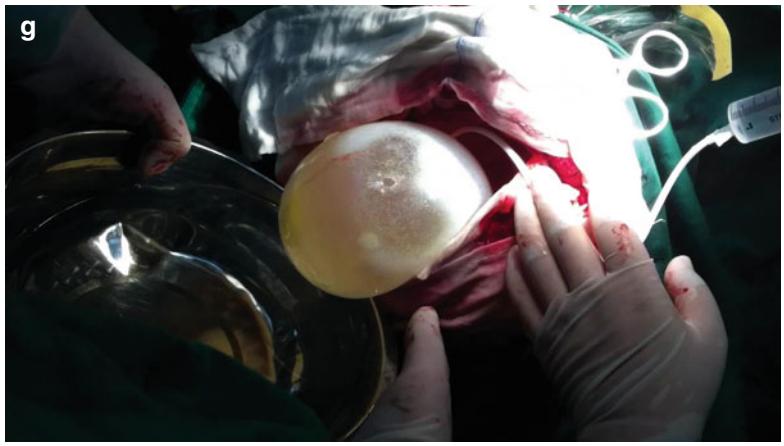
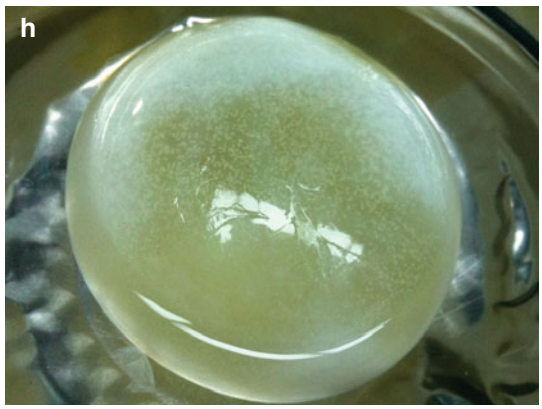


Fig. 15.3 A plain CT showing a large free bone flap removed (**a**), a tense dura (**b**), a thin layer of cortical tissue overlying the hydatid cyst (**c**), a meticulous cortical dissection performed to expose the cystic wall (**d**), the entire cystic wall exposed (**e**), the operating table tilted toward the lesion side and the head of the patients lowered and a fine plastic tube inserted between the cystic wall and brain tissue (**f**), floating of hydatid cyst after injecting saline with the syringe (**g**), intactly removed hydatid cyst in a bowel with water (**h**), and the irrigation procedure after the removal of the hydatid cyst (**i**)







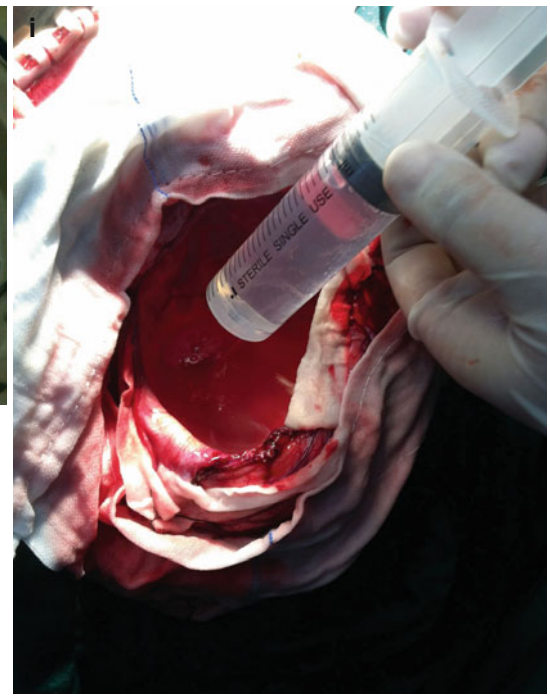


Fig. 15.3 (continued)

superior to the cyst and asking the anesthesiologist to compress both jugular veins in the neck in an effort to increase the intracranial pressure and gradually expulsing the cyst. In case the cyst does not come out, the head is further lowered until the cyst flows out of its cavity in the brain into the prepared receptacle (Fig. 15.3h). It is extremely important to maintain a blunt wide brain retractor in the upper portion of the cavity to prevent the brain from collapsing, which may tear crossing the veins, and to simultaneously fill the cavity with cetrimide while the cyst is being delivered (Fig. 15.3i). Once the cyst is delivered, hemostasis is completed and all the gauze is retrieved. The closure of the craniotomy is then performed in the usual manner (Turgut 2001; Haddad and Haddad 2003; Izci et al. 2008; Duishanbai et al. 2011).

Delivery of Deep Lesions

In case the cyst does not present on the surface of the cortex, the latter should be cut with a fine blunted tip pair of scissors in a silent area overlying the cyst. The opening is enlarged and deepened, with blunt dissection, until the pericyst appears. This procedure, which was called by one of the authors a "cesarean section," should be performed with extreme care lest the cyst rupture. We have used the cortical ultrasound to detect the remaining distance between the cyst and our instrument. In case the cyst is large, its delivery is similar to the cortical cyst. However, more frequently, one is dealing with small cyst, and we found that an appropriate size kitchen spoon is very helpful in raising the cyst into the receptacle.

Puncture-Aspiration-Injection-Reaspiration (PAIR) Technique

This technique should only be used in case the previously described delivery technique is impossible to use. This, as its name indicates, involves the puncture of the cyst with a fine needle and aspirating its content and partially and carefully injecting a scolicidal solution which should be left in place for a minimum of 10 min. Then the remaining fluid is reaspirated, and the collapsed chitinous membrane is removed with a forceps. The problem in this procedure is that there is always spillage around the needle puncture, and if the cyst is rapidly and completely emptied, it collapses and cannot be refilled properly. Although the area of spillage is irrigated with a scolicidal solution to prevent anaphylactic complications and recurrences, each puncture invariably leads to some spillage of the contents into the operative field, and cyst recurrences are frequent. For example, total removal of a pontine hydatid cyst is practically impossible with Dowling's technique, which requires forcing saline beneath the cyst in order to displace it outward.

The PAIR technique was introduced in the mid-1980s for treating liver hydatid cyst (Filice and Brunetti 1997). It is usually used for cerebral hydatid cyst in deep location or eloquent areas where removal of the hydatid cyst without rupturing is impossible or may cause additional neurological deficit (Muthusubramanian et al. 2009). Non-intentional burr hole draining was reported, but it is a very risky procedure (Anvari et al. 2009). The PAIR technique should always be performed by skilled and experienced physicians well prepared to deal with complications. According to expert recommendations, the PAIR should be accompanied by chemotherapeutic coverage to minimize the potential risk of secondary echinococcosis. In this indication, albendazole is given in daily oral doses of 10 mg/kg of body weight 24–4 h before and 15–30 days after the intervention (World Health Organization Informal Working Group of Echinococcosis 2001). There are several case reports which speak of a successful outcome in removing pontine, basal ganglion and in the interpeduncular cistern hydatid cysts (Boudawara et al. 1999; Erşahin et al. 1995; Yilmazlar and Aksoy 1999; Beskonakli et al. 2005).

Microsurgery

Hemispheric hydatid cysts usually do not need a surgical microscope, but hydatid cysts in deep locations, eloquent areas, and around vital structures need good illumination and magnification for fine dissections on the approach to the cyst or around the cyst wall. We recommend that microsurgery be applied in deep-seated lesions. The use of the magnification during the early part of the surgery of a hydatid cyst is extremely helpful because, at a crucial stage of the procedure, it

prevents inadvertent damage to the very thin cyst wall and allows development of the critical surgical plane (Kurtsoy et al. 1999; Balak et al. 2006). Gamma knife treatment has been tested in only a limited number of cases (Schnider 1999).

Postoperative Care

It is recommended that the patients should stay in a neurosurgical intensive care unit overnight until the anesthesia wears off. Antiepileptic drugs may be administered and patients' activities restricted to limit fluctuations in intracranial pressure during the early postoperative period. Albendazole is administered at a dose of 10 mg/kg for 3 months in case of cyst rupture (Duishanbai et al. 2010). Postoperative neuroimaging, computed tomography (CT) or magnetic resonance imaging (MRI), is recommended in the first postoperative day to excluding complications.

Surgical Results and Complications

The results of surgical treatment depend on several factors, including the location, size, and multiplicity of the cysts (Uzun et al. 2010). Giant cysts with a thick wall are no more difficult to remove than smaller ones, which are prone to rupture (Turgut 2001, 2002). Furthermore, it is considered that patients with multiple cysts have high morbidity and mortality rates owing to the number of surgical interventions needed to remove them all, but these patients frequently tolerate multiple surgical procedures. The ratio of cysts to patients was 2.2, and the recurrence and mortality rates for intracranial hydatid cysts were 14 and 10 %, respectively (Turgut 2002). Although it is rarely possible to expel a cyst intact from an extradural localization in the central nervous system without rupturing it, its rupture into this space, fortunately, does not inevitably lead to a severe anaphylactic response, in contrast to widespread subarachnoid dissemination. Cysts in deep locations have posed surgical problems, and some cysts have inadvertently ruptured during surgery. In the postoperative period, subdural effusions and porencephalic cysts can occur as a complication in children and adolescents (Sandhu et al. 2000; Tuzun et al. 2010).

Brain abscess has also been reported to be a rare complication (Kabatas et al. 2009). The shunting procedure is a technique used when postoperative CT/MRI shows ventricular dilatation, subdural effusion, and/or porencephalic cyst. Complications of surgical intervention depend on several factors including the location, size, and multiplicity of the cysts, as well as the presence of contamination (Ozek 1994). Recently, Ciurea et al. (2006) reported that the dimensions of the lesions had a strong influence on the possibility of total removal and on the rates of recurrence and postoperative complications. The most common complication is a rupture of the cyst into the subarachnoid space, which leads to widespread dissemination into the subarachnoid space, followed by severe anaphylactic reaction. If the cyst membrane is torn intraoperatively, the area of spillage is irrigated with hypertonic saline solution or cetrimide to prevent recurrences. However, while doing PAIR, each puncture invariably leads to some spillage of the contents into the operative field, and cyst recurrences are extremely dangerous. Advances in diagnostic and surgical techniques have greatly improved the prognosis of patients with intracranial hydatidosis. Unfortunately, however, delivery of the cyst with extradural localization is rarely possible without rupture, in contrast to parenchymal cystic lesions. Disseminated, multiple intracranial cystic lesions, development of systemic implantations, and failure to remove the primary focus are the main causes of poor outcome.

These complications are discussed in Chap. 17.

Long-Term Surgical Outcome

The treatment of choice for the intracranial hydatid cyst is surgical, but the long-term results of the surgical treatment differ according to the location, size, and multiplicity or extraneuronal involvement. In general, primary solitary cerebral hydatid cyst which has been removed

unruptured will have excellent outcome with or without postoperative albendazole treatment, while intraoperative ruptured hydatid cysts, multiple hydatid cysts, and hydatid cysts with extraneuronal involvement have a poor outcome and would need postoperative long-term albendazole treatment (Altinörs et al. 2000; Onal et al. 2001; Turgut 2001, 2002; Tuzun et al. 2004; Ciurea et al. 2006). Disseminated, multiple intracranial cystic lesions, development of systemic implantations, and failure to remove the primary focus are the main causes of poor outcome.

Conclusion

Intact surgical removal of the cyst with its contents is the method of choice of treatment in the majority of intracranial hydatid cyst using the modified Dowling's technique whenever feasible. Hydatid cysts in deep and critical areas of the brain, multiple intracranial hydatid cysts, hydatid cysts with multiple organ involvement, and ruptured cysts at surgery would need chemotherapy, albendazole. Based on the literature review, optimal management strategy for a patient with intracranial hydatidosis is given in Fig. 15.4 (Turgut 2001, 2002).

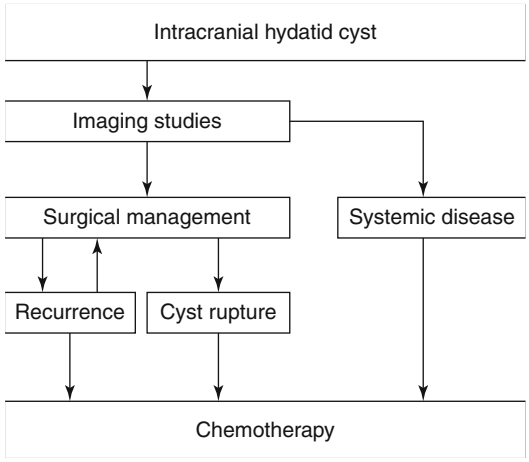


Fig. 15.4 Algorithm depicting the imaging and treatment management pathways for central nervous system hydatidosis in pediatric and adolescent patient groups (Adapted from Turgut (2001) p. 296)

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Chemotherapy for Central Nervous System Hydatidosis

16

Sipho K. Dlamini and Ntobeko B.A. Ntusi

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Introduction

A larval form of the parasite *Echinococcus* (family Taeniidae) causes hydatidosis, of which four species result in human disease: *Echinococcus granulosus* (cystic hydatid disease), *E. multilocularis* (alveolar hydatid disease), *E. vogeli* (polycystic type), and *E. oligarthus*. Consequent to the ubiquitous nature of *E. granulosus*, cystic echinococcosis is an important public health concern, with a global disease burden of 1,009,662 people and 3.6 million disability-adjusted life years (DALYs) (Budke et al. 2006). The species of *Echinococcus* is discussed in Chap. 3.

Central nervous system (CNS) hydatidosis is uncommon, occurring only in 2–3 % of cases of hydatidosis (Altinörs et al. 2000; McManus et al. 2003), and is usually caused by cystic echinococcosis and very rarely by alveolar echinococcosis (Turgut 2001; McManus et al. 2003). CNS hydatidosis may be classified into two forms according to the location of a given cyst, (a) intracranial and (b) spinal hydatid disease, which have different clinical manifestations and management approaches. CNS hydatid disease is diagnosed with neuroimaging such as computed tomography (CT) and magnetic resonance imaging (MRI) complemented by immunodiagnostic techniques (Figs. 16.1, 16.2, and 16.3).

The historical management of patients with CNS hydatidosis has been surgery, as it was the only modality of treatment available. Current treatment options include surgery, percutaneous

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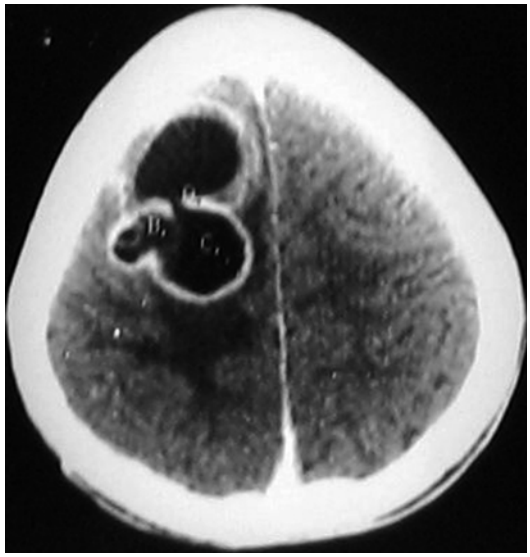

Fig. 16.1 CT scan of a 10-year-old male patient showing a hydatid cyst in the frontoparietal region (Courtesy of F. Limaiem, MD)

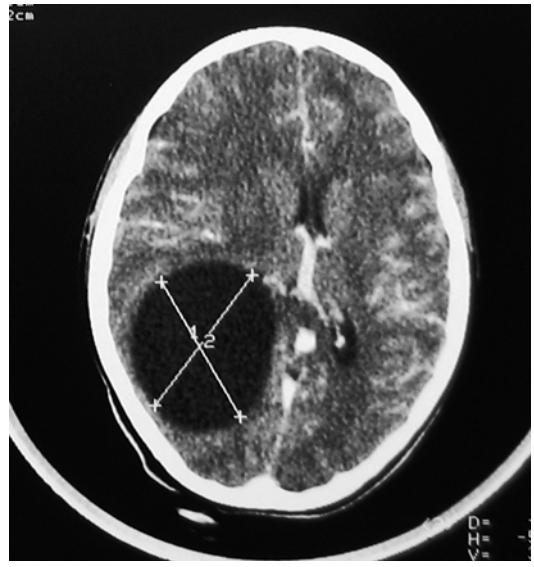

Fig. 16.3 CT scan of a 15-year-old female patient showing hydatid cyst in the right occipital region (Courtesy of F. Limaiem, MD)

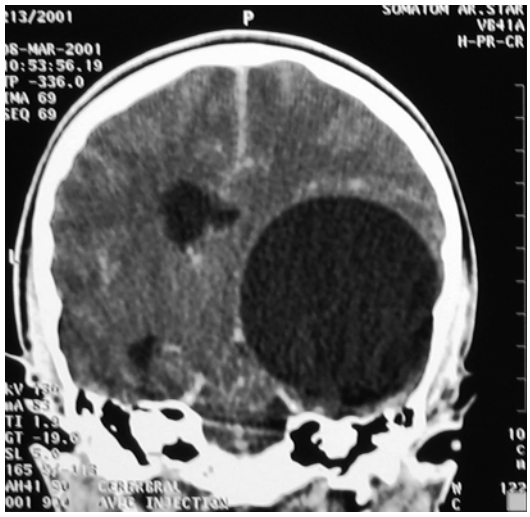

Fig. 16.2 CT scan of a 12-year-old male patient showing hydatid cyst in the right temporoparietal region (Courtesy of F. Limaiem, MD)

evacuation, chemotherapy with benzimidazoles, and the watch and wait approach. The decision on which the treatment strategy is approached must be individualized for each patient, and combination therapy is often employed. Indications for treatment are complex and based on the characteristics of the cyst and other factors such as available medical/surgical expertise, equipment, and the ability of the patient to adhere to long-term monitoring (Brunetti et al. 2010). Spinal hydatid disease and alveolar CNS echinococcosis are treated primarily surgically and often with adjuvant chemotherapy.

Cystic Central Nervous System Hydatidosis

Cystic CNS hydatidosis is managed with surgery as the initial mode of therapy. Either surgery is combined with chemotherapy or, in some instances, chemotherapy is used singularly. Surgical therapy results in the complete resolution of lesions in the majority of cases. The response to albendazole (ABZ) is reported to be 64–100 % (Todorov et al. 1992a, b; Kalaitzoglou et al. 1998), and there have been a few case reports that have reported complete resolution of lesions following ABZ therapy. Both surgery and chemotherapy, alone or in combination, may result in complete eradication of cystic CNS hydatidosis.

Alveolar Central Nervous System Hydatidosis

Alveolar CNS hydatidosis is managed primarily with surgery where complete resection of the lesion is mandatory. This should be followed by chemotherapy for a limited period thereafter (2 years is recommended). Where surgery is not feasible, then chemotherapy, ABZ, or mebendazole (MBZ) as the only mode of therapy is acceptable, and this is usually administered long term or even lifelong. Since the introduction of chemotherapy after 1976, the 10-year survival has increased from less than 10 to 85–90 % in the chemotherapy era (Ammann and Eckert 1996).

Indications for Chemotherapy for Hydatidosis of the Central Nervous System

Surgery remains the first line of therapy for CNS hydatidosis and is the most effective form of therapy. Chemotherapy for CNS hydatidosis became a reality with the introduction of the two benzimidazoles, MBZ and ABZ, respectively, in 1976 and in 1982. Flubendazole (FBZ) was also shown to be effective for treatment of cystic echinococcosis (Ceballos et al. 2011) but is less efficacious than ABZ and is not used for the management of CNS hydatidosis. ABZ is most widely utilized, owing to its higher absorption in the gut and better gastrointestinal tolerability. Over the last 30 years, the use of chemotherapy in hydatidosis has evolved with a consensus now established on the indications, dosage, and follow-up of patients following initiation of therapy with benzimidazoles (World Health Organization [WHO] Informal Working Group on Echinococcosis 1996).

Traditional indications for chemotherapy for CNS hydatidosis include multiple or multiseptate cysts, large cysts (>10 cm), and cysts that are difficult to reach surgically or where the surgery would be clearly hazardous (El-On 2003; Ntusi and Horsfall 2008) (Table 16.1). Furthermore, patients with recurrence of CNS hydatid cysts are treated medically (Stojkovic et al. 2009), as

Table 16.1 Indications for chemotherapy for central nervous system hydatidosis

1. Multiple/multiseptate cysts
2. Large cysts (>10 cm)
3. Cysts difficult to reach via surgery
4. Recurrent CNS hydatid cysts
5. Surgery is contraindicated
6. Cases where surgery is clearly hazardous

are those for whom surgery would be contraindicated. There have been few case reports of the use of ABZ as the sole treatment of CNS hydatidosis with complete resolution of lesions on imaging (Kalaitzoglou et al. 1998; Ntusi and Horsfall 2008) in instances in which surgery was not feasible. However, there is no clinical trial evidence for the superiority of ABZ versus surgery for CNS hydatidosis.

The adjunctive use of benzimidazoles before or after invasive procedures is now commonly practiced. The rationale for this indication is that perioperative administration may be important for cyst volume reduction and in minimizing the risk of rupture during the procedure (Morris 1987; Horton 1989).

In alveolar CNS hydatidosis, adjunctive chemotherapy with ABZ or MBZ following surgery is always indicated. In this instance, chemotherapy must be administered for a minimum of 2 years, and patients should be monitored for 10 years thereafter (Hemphill and Müller 2009). In instances where surgery is not feasible for alveolar hydatidosis, it is recommended that chemotherapy be used long term or lifelong. Currently, no evidence or guidelines are available for the perioperative use of benzimidazoles for alveolar CNS echinococcosis.

Indications for Surgical Treatment of Hydatidosis of the Central Nervous System

Surgery remains the cornerstone of management for uncomplicated cysts in CNS hydatidosis. The aim of surgical therapy is radical removal of the cyst without spillage of its content. Single lesions

are more amenable to surgical removal compared to multiple lesions. All forms of spinal hydatid disease and alveolar CNS echinococcosis are treated surgically (Turgut 1997; Bresson-Hadni et al. 2000; Turgut 2001), as are lesions with bone involvement. Furthermore, patients who remain refractory to medical therapy or show progressive neurological decline despite chemotherapy should be considered for surgical treatment (Stojkovic et al. 2009).

Medical Chemotherapy for Hydatidosis

Benzimidazoles

Mechanism of Action

The action of benzimidazoles is their inhibitory effect on the uptake of glucose by the parasite, thus leading to the depletion of glycogen stores (Sheth 1975). The drug inhibits glucose uptake by the cestode, but does not affect serum glucose concentration in humans (Fierlafijn 1971). The benzimidazoles also result in degenerative alterations in the germinal layer of the cyst, leading to cellular autolysis (Schantz et al. 1982). In vitro studies have demonstrated disruption of microtubule structure and function in metacestodes treated with ABZ (Lacey 1988). Furthermore, benzimidazoles have been shown to have a higher affinity for parasite tubulin compared to that of the human host (Friedman and Platzer 1980; Gottschall et al. 1990), explaining their selective capacity for parasite immobilization and death.

Evidence of Efficacy

Benzimidazoles form the mainstay of medical chemotherapy for CNS hydatidosis. The efficacy of MBZ has been reported variably, with no consensus regarding the effective dose or optimal duration of therapy (El-On 2003). ABZ is more effective in the treatment of hydatidosis, most likely related to its superior intestinal absorption and particularly the higher penetration of its metabolite, ABZ sulfoxide, into the cyst cavity (Davis et al. 1989; Casado et al. 1996). ABZ is most efficacious in young cysts and in cysts less than 8 cm in size (Todorov et al. 1992a, b; Teggi et al. 1993).

There are limited data from randomized clinical trials, demonstrating efficacy of the benzimidazoles in the management of hydatidosis. FBZ has been shown to be inferior to ABZ and MBZ (Davis et al. 1986). Several trials have demonstrated the superiority of ABZ to MBZ, with a response rate of 75–85 % versus 50–60 %, respectively (Saimot et al. 1983; Todorov et al. 1992a, b; Teggi et al. 1993; Liu and Weller 1996; Luchi et al. 1997). The results of chemotherapy are affected by cyst characteristics such as size, age, and location, as well as by host characteristics (El-On 2003). ABZ is associated with evidence of radiological improvement in hydatid cysts in 68–82 % of patients (Falagas and Bliziotis 2007; Stojkovic et al. 2009). Prolonged courses of ABZ have been shown to be effective in the management of CNS hydatidosis (Teggi et al. 1993; Ntusi and Horsfall 2008).

Administration and Dosing

MBZ is given orally. About 2–10 % of the drug is absorbed intestinally and converted to its active metabolites, ABZ sulfoxide and ABZ sulfone, by the liver (El-On 2003). MBZ is excreted in the bile as glucuronide or a sulfate conjugate (Gottschall 1993). The usual dose in adults is 40–50 mg/kg/day, given in three equally divided doses after meals. Treatment is usually given for 3–6 months (Table 16.2).

ABZ is also given orally. Its absorption in the gastrointestinal tract is better than for MBZ. It is metabolized by the liver to ABZ sulfoxide. The standard dose is 10–15 mg/kg/day, usually 800 mg/day, given in two equally divided doses. Absorption is improved by a fatty meal. Therapy is given for 3–6 months. Previously, ABZ was given for 4 week courses, followed by two drug-free intervals, due to safety concerns. Nevertheless, continuous therapy does not increase side effects (Teggi et al. 1993).

Pharmacokinetics

MBZ is minimally absorbed in the gut, with 95 % of the drug being bound to proteins. Metabolism

Table 16.2 Administration and dosing of chemotherapy for central nervous system hydatidosis

Chemotherapy	Mechanism of action	Dose	Duration	Side effects
Mebendazole	Inhibition of glucose uptake by parasite Disruption of microtubules by inhibition of the polymerization of tubulin into microtubules	40–50 mg/kg/day in three divided doses	3–6 months	Nausea, vomiting, diarrhea, and abdominal pain
Albendazole	Inhibition of glucose uptake by parasite Disruption of microtubules by inhibition of the polymerization of tubulin into microtubules	10–15 mg/kg/day in two divided doses	3–6 months	Gastrointestinal disturbances, abnormalities in liver function, leukopenia, and hematuria
Praziquantel	Increases the cell permeability to calcium in cestodes	25 mg/kg/day (in combination with albendazole)	No clear data	Dizziness, headache, malaise, abdominal pain, and nausea

is extensively hepatic. The time from ingestion to peak serum concentration is 2–4 h, with a half-life of elimination of 1–12 h. Excretion is primarily in feces, with very little in the urine.

ABZ has a good volume of distribution within the hydatid cysts and the cerebrospinal fluid, with protein-binding capacity of 70 %. Metabolism primarily takes place in the liver mainly through sulfoxidation (and less through hydrolysis and oxidation), with extensive first-pass effect. The time from ingestion to peak serum concentration is 2–5 h. The half-life of elimination is 8–12 h. The drug is excreted in the urine and feces (de Silva et al. 1997).

Adverse Effects

The adverse effects of the benzimidazoles may be related to the drug itself or its metabolites, but, for the most part, both drugs are well tolerated. Because of its poor absorption, MBZ has a better side effect profile than ABZ. Common adverse reactions include abdominal pain, diarrhea, and vomiting. CNS reactions include dizziness, drowsiness, headaches, and seizures. Reversible hepatotoxicity is well documented, with increase in liver enzymes. Dermatologic reactions may include angioedema, exanthema, itching, urticaria, toxic epidermal necrolysis, and Steven-Johnson syndrome. Less commonly, the benzimidazoles may be associated with hypersensitivity, hematuria, or bone marrow suppression (neutropenia or agranulocytosis).

Contraindications

Benzimidazoles should not be used in patients with liver disease or bone marrow suppression. ABZ and MBZ are relative contraindications in pregnancy, as they have been shown to induce embryotoxicity and teratogenicity in rats. However, they have been shown not to cause harm in human pregnancy (Bradley and Horton 2001).

Praziquantel

Mechanism of Action

Praziquantel (PZQ) is a heterocyclic pyrazinoisoquinoline that is effective against protoscoleces and therefore active against early cysts having no activity against mature cysts. PZQ increases the cell permeability to calcium in cestodes, causing contractions, increased motility, and paralysis of the worm musculature leading to detachment of their suckers. The in vivo consequence of PZQ is dislocation of the worm in the intestines and loss of sensitivity of the skin to proteolytic enzyme activity (Doenhoff et al. 2008).

Evidence of Efficacy

PZQ, in combination with ABZ, has been shown to be better than ABZ alone (Cobo et al. 1998; Mohamed et al. 1998). However, the role of PZQ as single therapy for CNS hydatidosis has not been defined (Wen et al. 1993). Furthermore, there is evidence for improved outcomes when

PZQ is combined with ABZ for management of cyst spillage pre- and post-intervention (Cobo et al. 1998) compared to either drug alone.

Administration and Dosing

PZQ is administered orally and given at a dose of 25 mg/kg/day alone or in combination with ABZ.

Pharmacokinetics

Over 80 % of the orally administered PZQ is absorbed via the intestines. Metabolism is hepatic, with extensive first-pass effect and 80 % protein-binding capacity. PZQ increases the serum concentration of ABZ fourfold. The time from ingestion to peak serum concentration is 1–3 h. The half-life of elimination is 0.8–1.5 h for the drug and 4.5 h for the metabolites. Excretion is mostly in the urine.

Adverse Effects

PZQ is usually well tolerated. It may cause abdominal discomfort and nausea. Dizziness, fever, headache, seizures, and malaise have been described. Less commonly, the drug may cause hepatotoxicity, ventricular fibrillation, atrioventricular block, ventricular ectopy, and hypersensitivity.

Contraindications

PZQ should be used with caution in patients with cardiovascular disease, hepatic impairment, and history of seizures. There are no adequate studies in human pregnancy.

Monitoring Response to Treatment

Monitoring of patients treated for CNS hydatidosis, known as pharmacovigilance, is important for evaluating the success of chemotherapy and presence of adverse reactions and complications. Cysts can grow at a rate of 1–50 mm per year, persist for years without change, rupture or collapse, or disappear completely following treatment. The optimal approach to monitoring must be individualized for each patient.

The ideal monitoring strategy involves repeat imaging at 3–6-month intervals until the CNS findings are stable and thereafter followed by monitoring every 12–24 months. In the first 3 months of treatment, evaluation every 2–4 weeks of leukocytes and liver enzymes is recommended. The use of serological markers to assess response or relapse of hydatid disease is currently not recommended as serological tests may be elevated despite complete removal of cysts with surgery.

Watch and Wait Approach

The "watch and wait" approach is one of the recognized strategies which have evolved over the decades in the management of hydatidosis, even though there is still no clear-cut data evaluating its role as a treatment strategy. In cases where patients have inactive or degenerating cysts, it may be appropriate to observe these without any medical therapy (Junghanss et al. 2008; Brunetti and Junghanss 2009). CNS hydatid disease requires close follow-up with neuroimaging.

Prevention of Hydatidosis

Prevention of cystic hydatid disease can be achieved by avoidance of dogs, in particular stray dogs. Prohibiting home slaughter of domestic animals (e.g., sheep) will avoid dogs consuming infected viscera. Careful rinsing of vegetables and contaminated fresh produce may reduce infection. Prevention of alveolar echinococcosis requires avoidance of foxes and other infected canid hosts.

In theory it is possible to prevent echinococcosis through vaccination of the intermediate host (sheep) and the definitive host (dog). However, at present there is no vaccine against cystic echinococcosis available for dogs. Important strategies in prevention of human hydatidosis and elimination of the parasite in the hosts include regular deworming of dogs and the controlled slaughtering of infected sheep. Such efforts have led to disease eradication in the first world, and it is estimated that in places where the disease is endemic, it could take 20 years to

achieve this (WHO Informal Working Group on Echinococcosis 1996).

Conclusion

CNS hydatidosis remains an uncommon complication of human echinococcal infestation. Surgery is the first line and most effective form of therapy for cystic and alveolar CNS disease. Chemotherapy is usually administered in combination with surgical management. Chemotherapy with ABZ (with or without PZQ) is effective in the management of patients not amenable to surgery or in those with pre- and post-intervention cyst spillage.

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Complications of Cerebral Hydatidosis

17

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Introduction

The frequency and the seriousness of the complications in hydatid disease brought us to compare its course to a malignant condition as early as 1963 (Haddad FS et al. 1963). These complications of cerebral hydatidosis are studied in three time frames, the preoperative, operative, and postoperative periods. In the preoperative period, these complications are blindness, calcification of the cyst, infected and complicated cysts, caseation, formation of "chitinoma," hydrocephalus, leakage of cyst fluid in the surrounding brain, spontaneous intracranial rupture of the cyst, bulging and thinning of the skull in the vicinity of the cyst, perforation of the skull and or dura by the intact cyst, cerebral stroke and hydatid embolization from disease in the heart, infertility due to cyst pressure on the hypothalamo-pituitary axis, and nephrotic syndrome. In the treatment period, these complications are inadvertent rupture or intentional cyst puncture, cystoperitoneal shunt, cysto-atrial shunt, anaphylactic shock, and complications of medicinal treatment. During the posttreatment period, these complications are recurrences; porencephalic cyst; subdural effusion; pneumo- or hydrocephalus; bleeding in the epidural, subdural, or intraparenchymal spaces; wound infection; meningitis and abscess formation; cerebrospinal fluid leaks; pulmonary embolism; calcifications; glioma; choreiform movements; mental retardation; seizures; and death.

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Complications During the Pretreatment Period

Blindness

It is one of the worst complications. It is due to the delay in the institution of treatment in a patient who suffers from marked increase in intracranial pressure accompanied by papilledema. In hydatid of the brain, the patient is often a child, and the separation of the sutures as well as the slow progression of increased intracranial pressure is not accompanied by the usual drowsiness, nausea, and vomiting seen in other brain expanding lesions. Thus, severe papilledema is often seen in conjunction with a relatively well-conserved physical and mental condition and may be overlooked. Blindness usually affects both eyes simultaneously and is irreversible. Decreased visual acuity, which may be the only symptom, sets in gradually and might not be of the same intensity in both eyes. This decreased acuity is an important warning and if taken seriously should lead to an early intervention which might reverse the process either partially or totally.

Calcification

This is a very rare condition (Legrè and Massad 1957; Alvarez et al. 1982). Robinson (1961) evaluated it at 1 % and Abderrahmen et al. (2007) at less than 1 % of all cerebral hydatid cysts. Ouboukhlik et al. (1994) report 4 calcified cysts out of 48 cases. The author of this chapter has seen only one such case out of 39 operated cases. Kooy (1940) was the first to describe a linear calcification in the wall of a cerebral hydatid cyst, and Roger (1944) was the first to describe a circular and globular calcification. Since then a number of cases have been reported (Legrè and Massad 1957; Samiy and Zadey 1965; Gomori et al. 1988; Rudwan and Khaffaji 1988; Nurchi et al. 1992; Peter et al. 1994; Choukri et al. 2001; Bouaziz 2005; Turgut et al. 2007). These calcifications were observed in different time frames. They have been noticed as early as 6 months after the onset of symptoms (Samiy and Zadey 1965) and as late as 20 years (Choukri et al. 2001). On plain x-ray, the calcification appears as a linear (Kooy 1940), curvilinear (Roger 1944), or nonhomogeneous mass (Abderrahmen et al. 2007). It involves the pericyst and may rarely extend into the ectocyst (Acquaviva et al. 1966; Alvarez et al. 1982). Intracystic calcifications are rare and may represent calcifications in the wall of the enclosed daughter cysts (Aksungur et al. 1994). Rudwan and Khaffaji (1988) believed this intracystic calcification "most likely represented a calcified collapsed cyst membrane."

These calcifications are best demonstrated on computed tomography (CT) scans. In calcified cysts, the pericyst may enhance on gadopentate magnetic resonance imaging (MRI) (Aksungur et al. 1994). On histopathologic examination, the surrounding brain reveals the presence of gliosis and macrophages (Alvarez et al. 1982). It is usually assumed that calcified cysts are dead cysts (Aksungur et al. 1994). However, it has been shown that some of these calcified cysts contain viable brood capsules and are still fertile (Samiy and Zadey 1965; Choukri et al. 2001).

The pathogenesis of such calcifications is not well known but is attributed by Radwan and Khaffaji (1988) to "degeneration" of the cyst. Robinson (1961) sees it as a sign of healing. Often the calcified pericyst is adherent to the ectocyst either by strands of tissue or over a variable surface area. These adhesions are more severe when the cyst is in contact with the dura or the falx. It is important to realize, prior to surgery, that the cyst is calcified, as it might change the plan of the intervention. In this case, surgery is usually difficult and may result in further complications (Rudwan and Khaffaji 1988; Peter et al. 1994). Some have removed the calcified pericyst with the cyst as it is sometimes impossible to separate them from each other. What follows is a personal case which illustrates the previous two subdivisions on blindness and calcification.

Case 1

NM, a 13-year-old girl, was admitted to hospital on November 28, 1965, complaining of bouts of headache of 4-year duration, worse on the right side, and accompanied by vomiting. In the past

2 years, her vision had gradually decreased until she became completely blind. In the past 6 months, she complained of weakness on the left side, especially in the upper extremity. Examination revealed a fully conscious, well-oriented, totally blind patient with bilateral optic atrophy. There was loss of position sense and astereognosia in the left hand with a bilateral Babinski sign. The patient brought with her plain x-rays showing separation of the sutures and a thin rim of calcification in the right posterior parietal region. A right carotid arteriogram revealed an anterosuperior shift of the terminal branches of the anterior cerebral as well as those of the middle cerebral arteries by an avascular mass within the rim of calcification. At operation, the dura was adherent to the underlying brain by multiple thin strands of fibrous tissue. These were released. In the occipital region, where the bone was extremely thin, the brain had been spliced open by the calcified shell which was partially adherent to the dura. The entire area was freed, and the shell of calcium was carefully removed over an area of 3.5 cm in diameter to uncover the ectocyst. Clearly the calcium lay in a thickened pericyst and did not involve the ectocyst. Attempts at delivering the cyst were not successful because of adhesions between the ectocyst and the calcified pericyst. The opening was enlarged by carrying three episiotomies in the brain, especially toward the occipital lobe which, in the present case, was safe in view of the blindness, and the ectocyst was further uncovered over an area 5 cm in diameter. In two areas, the cyst wall was very thin, and great care was taken not to rupture it. The head of the patient was tilted, and the jugular veins were compressed in an attempt at raising the intracranial pressure and expulsing the cyst. Fluid was injected in the bed of the cyst. What we have called the Credé maneuver – pressure on the brain to help deliver the cyst (Haddad and Haddad 2000; Haddad and Haddad 2003) – was possible in this case in spite of the calcified shell surrounding the cyst. The cyst was beginning to deliver (Fig. 17.1a). As it was dropping into the basin, it tore because of some unnoticed adhesions of the ectocyst to the calcified pericyst in its medial region. A most interesting finding was observed. No fluid was present in the mother cyst which, in turn, was filled with daughter

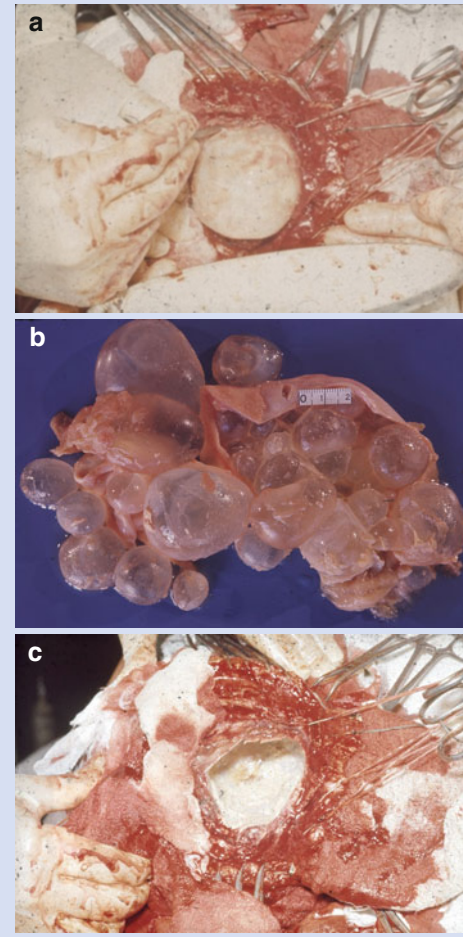

Fig. 17.1 (**a**) Delivering the cyst by applying the Credé maneuver. (**b**) Opened cyst showing the multitude of daughter cysts. (**c**) The cavity left by the cyst, note the uncollapsed cyst bed because of the calcification

cysts, some of which were attached to the endocyst (Fig. 17.1b). The cavity, left by the cyst, did not collapse due to the calcification of the pericyst (Fig. 17.1c). This cavity was thoroughly irrigated with saline, and the wound was closed. Seen 13 months later, on December 28, 1966, the patient was perfectly normal except for blindness.

Infected or Complicated Cysts

Although most authors use the term "infected," some use the term "infected or complicated" cyst (El-Shamam et al. 2001). The term complicated is more appropriate as, in spite of an extensive search in the literature, nothing has been found concerning the pathogenesis nor the pathogens in these cases. The cultures of the pus in the cases of Ersahin et al. (1993) and Turgut et al. (1997) did not yield any growth. In these cases, rim enhancement and paracystic edema are seen on computed tomography (CT) scan (Krawjewski and Stelmasiak 1991). The best method of diagnosis is by magnetic resonance imaging (MRI) which reveals "varying degrees of perifocal edema and contrast enhancement" (El-Shamam et al. 2001), and Nourbakh et al. (2010) report on T2 imaging a "hyperintense area of perifocal edema, complete and incomplete (segment) rim of contrast enhancement." These cysts become so adherent to the surrounding brain that their delivery intact becomes next to impossible (Rudwan and Khaffaji 1988). Mathuriya et al. (1985) described a case of infected intradural extramedullary hydatid cyst at the foramen magnum.

In 1948 Obrador and Urquiza reported a 9-year-old girl who harbored a "large" infected cyst in the left frontoparietal region. This was excised, and the culture of the pus did not yield any growth. This case is interesting because the abscess had formed around a shrunken hydatid vesicle measuring 7 cm in length. It is not clear whether the abscess was primarily pericystic or intracystic, and, with the rupture of the cyst in situ (see section "Spontaneous intracerebral rupture of the cyst"), the pus poured to the outside. Zahed et al. (2010) reported a case of infected hydatid cyst occurring prior to surgical intervention in a 20-year-old female suffering from a tender cystic swelling over the right temporal region associated with proptosis of the eye on the same side. The histopathology of the excised specimen was reported as an infected hydatid. The frequency of these infected cysts is extremely low, yet El-Shamam et al. (2001) found 4 out of 16 cases, and Kocaman et al. (1999) reported it in 3 out of 23 cases. An interesting case is that of Erongun et al. (1994) where an infected cyst was removed from the left occipital lobe of a 12-year-old boy with multiple adjacent cysts which were not infected. Twenty days after surgery, a cyst was found on CT scan in the left temporoparietal region. The family refused surgery. Fifty days later the child went into deep coma and died in spite of a rapid decompression by needle aspiration. The author does not mention the consistency of the fluid obtained.

Could it be possible that the cyst, which was found in the left temporoparietal region, had been missed at the time of surgery and, relieved from the surrounding pressure, rapidly expanded, in a matter of 70 days? This lapse of time is too short for a new cyst to produce symptoms.

Another interesting case is that of Goinard and Descuns (1952) where a thin blade of sterile pus was localized in the space between the ectocyst and a markedly thickened pericyst.

Other single cases have been reported in the literature (Obrador and Urquiza 1948; Arana-Iniguez and San Julian 1955; Boixados 1973; Mathuriya et al. 1985; Turgut et al. 1997; Turgut and Turgut 2002; Polat et al. 2003).

Although the content of these complicated cysts were considered as sterile, from the point of view of hydatid recurrence, the case of Yuceer et al. (1998), proved the opposite. They reported on a case 12-year-old child. A year earlier, the patient harbored "a large hydatid cyst with rim enhancement and calcification of the cyst wall." At operation the cyst ruptured and "purulent material" was drained. The patient presented a year later with multiple recurrent cysts in the bed

of the previously removed infected and calcified cyst. This is why these cysts have to be as carefully delivered as are regular hydatid cysts.

Caseation

Caseation of the cyst content was described by Kooy (1940) in two cases. Both cases had peripheral calcifications. In one of these cases, the caseous material contained hooklets, and in the second there was a conglomeration of daughter cysts. It is not known whether these hydatid particles were active or dead. Radwan and Khaffaji (1988) reports on a patient whose cyst was filled with "mucoid gelatinous material," and there were adhesions between the dura, arachnoid, and overlying cortex. This case too showed, on plain skull films, a "fairly round, calcified lesion. When the cyst capsule was incised, mucoid gelatinous material was evacuated." No other reference related to caseation was found in the literature.

Chitinoma

Nanassis et al. (1999) resected from the frontal lobe of a 35-year-old woman a solid, partially cystic tumor, with focal calcifications, which on pathologic examination revealed an "acellular eosinophilic material with focal necrosis that surrounded typical protoscolices of Echinococcus granulosus." This acellular material was identified as chitin, hence the nomination of this mass "chitinoma." This term has been refuted by Turgut and Turgut (2002). It is interesting to note that there is a great deal of resemblance between this present case and those reported under "caseation," which leads one to believe that this might be a more advanced case of caseation.

Hydrocephalus

Although hydrocephalus is not expected to be associated with such large cerebral supratentorial cysts, it does occur. El-Shamam et al. (2001) detected, on MRI, 4 preoperative hydrocephalics out of 16 patients and in only one was the cyst in the posterior fossa. Abbassioun et al. (1978) described two cases of hydrocephalus out of two posterior fossa cysts discovered on CT scan. Villarejo et al. (1983) reported such a case that required a ventriculoperitoneal shunt preoperatively later removed together with the cyst.

Leakage

Leakage of hydatid fluid in the surrounding tissues was reported to occur through a "thick porous" cyst wall (Griponissiotis 1957). This leakage produces a chronic type of inflammation with adhesions of the cyst wall to the surrounding tissues and its invasion with leucocytes. On CT scan and MRI, edema is observed in the surrounding brain. The description of the case of Gonzalez-Ruiz et al. (1990) is reminiscent of such a condition, although the authors believed it was an intracerebral rupture of the cyst. There was a hyperdense cyst wall visible on CT scan; the cyst was tightly adherent to the dura "producing inflammation and subsequent gliosis of the surrounding brain." Could this leakage be the precipitating factor for the calcification in the pericyst? Nothing is found in the literature to refute or confirm this presumption. This condition makes the "delivery" of the cyst much more hazardous.

Spontaneous Intracerebral Rupture of the Cyst

This is an exceptionally rare condition and is accompanied by severe pericystic edema (Ozek 1994). It is usually ushered by an abrupt and important deterioration in the clinical status of the patient and may lead to dissemination of the disease. No reason for the spontaneous rupture of such cysts has been advanced except for that given by Griponissiotis (1957). He suggested that head injury may cause a cyst, adherent to the parietal dura, to rupture in the extradural space giving rise to numerous extradural cysts. He gave

such an example. One of the causes of multiplicity of hydatid cysts in the brain may be due to the advent of a single cyst rupturing spontaneously in situ, as suggested by Nurchi et al. (1992). These authors removed approximately 30 cysts, measuring between few millimeters and 8 cm, from a single location (the right occipital lobe).

Bulging and Thinning of the Skull

The continued pressure and constant pulsations of those cysts lying adjacent to the peripheral dura, against the skull, produce, with time, bulging of the skull which may be extreme (Samiy and Zadey 1965). The skull in this area may become excessively thin. This thinning of the skull, described as early as 1888 by Vergo in the right frontal region in a 10-year-old child (quoted by Simpson and Verco 1976), may render the bone paper thin, a finding called "the parchment skull sign." Dew described this aspect of hydatid disease as early as 1934. Phillips (1948) describes a case where "the bone was so thin that the flap could be cut with a strong scissors" (see Case 8).

Cysts Perforating the Skull and/or Dura

Phillips (1948) states that the "cyst had eroded the calvarium and was presenting beneath the scalp." The skull is more at risk than the dura because the latter is more elastic. Should the pressure persist, the already thinned and necrotic skull disintegrates. This perforation was very well shown on a lateral MRI view in the article of Polat et al. (2003), where the brain, containing a cyst, passed through the skull to rest under the galea. Tizniti et al. (2000) describe a similar case. Goinard and Descuns (1952) made note of a case where the cyst had perforated the dura. It has also been described in intracranial extradural cysts (Samiy and Zadey 1965; Sharma et al. 2010; Zahed et al. 2010). Griponissiotis (1957) believed the pathogenesis of such a condition is due to an injury to the skull in the presence of an intracranial hydatid cyst attached to the dura. The latter ruptures and the cyst is forced outside the dura.

Stroke and Embolism of Cerebral Arteries

Stroke as a complication of cardiac hydatidosis is described in Chap. 22. Suffice it to say that this type of embolism is seen with ruptured cysts within the left cardiac chambers or wall as well as post excision of such cysts (Vaquero et al. 1982). It may produce multiple secondary brain cysts (Turgut et al. 1997; Ugur et al. 1998; Ait Ben Ali et al. 1999), a stroke (Martín Oterino et al. 1996; Yaliniz et al. 2004; Acarturk et al. 2004) which might be fatal (Byard and Bourne 1991; Ulgen et al. 2000), or both (Abbassioun et al. 1978; El Khamlichi 1993; Benomar et al. 1994; el Quessar et al. 1996; Kocaman et al. 1999).

Infertility

Tiberin et al. (1984) report a case of galactorrhea, amenorrhea, secondary sterility, and gain of weight of 2-year duration in a 29-year-old woman in whom no endocrinologic or gynecologic cause could be found and who recovered with restoration of fertility following the removal of an intact left frontal lobe cyst. Mazor et al. (1986) report on a similar case of a patient aged 31 who got pregnant less than 2 months following the excision of a left frontal lobe hydatid cyst, after 13 years of sterility. Both believe that this condition could be due to pressure exerted by the cyst on the hypothalamic-pituitary axis.

It would be interesting to include under this section the case of an 18-year-old male reported by Ozgen et al. (1984) who had an intrasellar cyst operated through a transsphenoidal approach. The hormonal profile which was on the low side preoperatively returned to normal within 10 months.

Nephrotic Syndrome

Sharma et al. (2010) report on a patient suffering from an extradural intracranial hydatid cyst associated with a nephrotic syndrome. This condition did not respond to the usual medical treatment but subsided when the cyst was removed. They believe that there must be cause-to-effect relationship between these two conditions. This

syndrome was also reported, in the same article, secondary to pulmonary and hepatic hydatidosis.

Complications During the Treatment Period

There are two types of treatment: surgical and medical. These may be used simultaneously or separately, and each has its own set of complications.

Complications Related to the Surgical Act

These complications are many. In a review of 25 cases, Tuzun et al. (2010) reported 20 complications related to the surgical act.

Inadvertent Cyst Punctures During Ventriculography

Puncture of the cyst during ventriculography used to be one of the major complications when that test was about the only one available for diagnosis and localization of brain masses. This brought Brailsford (1931) to condemn its use when hydatid was suspected. When the cyst is punctured, the risk of spillage of hydatid fluid in the brain is very substantial, and recurrences may ensue. Philips (1948) warned against this complication and so did Griponissiotis (1957). Accidental cystography used not to be infrequent (Dew 1934). Fortunately, with the advent of the newer imagery techniques, including CT and MRI, this complication is only of historical importance. This complication is well represented in the following case.

Case 2

NT, a 10-year-old girl, was seen in June 1957 suffering from headache of 7-month duration accompanied by progressive right-sided weakness of 6.5-month duration. On examination, she had tremors in the right hand and crackpot resonance. Plain skull x-ray revealed separation of sutures. Ventriculography was carried out, and the cyst was inadvertently punctured. The films revealed a cyst in the left parietal region (Fig. 17.2). A small craniotomy was performed, and, through the intact dura, the cyst was twice filled with 1 % formalin which was left in the cyst cavity for 5 min each time and then irrigated profusely with normal saline solutions. The dura was then opened and the cyst removed through a small cortical incision. A severe postoperative reaction occurred, accompanied by fever, subsiding on the 13th postoperative day. A month after surgery, the patient was well. No further follow-up was possible.

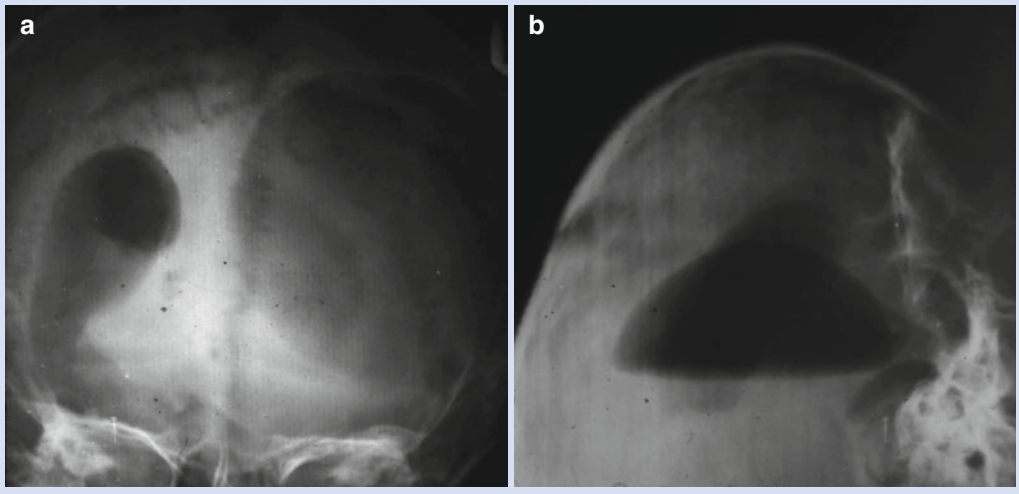

Fig. 17.2 (**a**) Ventriculography showing the injected cyst in AP projection. (**b**) Brow up lateral projection

Intentional Cyst Puncture

Cyst puncture is only indicated in extremis. It should never be carried out to decompress the brain before or at surgery. This is a most dangerous procedure as shown in the following case.

Case 3

RM, an 11-year-old boy, was seen for the first time on January 19, 1980, for headache of 3-year duration diagnosed as migraine. A month prior to his consultation, the headache became very severe, and a plain skull x-ray revealed separation of the sutures, with a decreased uptake in the left frontal area on isotope scanning. On examination there was no papilledema, but a crackpot resonance was obtained. Because of the above and his relatively good general condition, he was suspected of harboring a cerebral hydatid cyst. His family preferred him to be operated in France. His brother, a medical student who was accompanying him, was told that this was most probably a hydatid cyst and was asked to warn his surgeon in Paris not to puncture the lesion and that he, the surgeon, should be aware of that diagnosis and should do his best to deliver the cyst intact. The surgeon did not heed the advice and thought he was dealing with a cystic astrocytoma. When the dura was opened, the brain bulged, and the surgeon introduced a needle in the brain to reduce the pressure. Clear fluid spurted out and the brain relaxed; the surgeon carried out an incision in the cortex and pulled the chitinous membrane, closed the wound, and discharged the child in perfect health. This child was well until 8 months later, August 1980, when he suffered from headaches. CT scan of the brain became available in Lebanon; it was performed and revealed a cyst in the operative field. He was advised surgery but was lost to follow-up until March 28, 1981, at which time he suffered from severe weakness in the upper extremities with bilateral Babinski sign, absent knee and ankle jerks, saddle anesthesia, and urinary retention. He was being treated for a Guillain-Barré syndrome. A cisternal myelogram (CT myelography was not yet in use) revealed a complete block at C6. Following that test, the patient became completely paralyzed from C6 down with a flicker of movement in the left lower extremity. An emergency lumbar myelogram was performed with a puncture at L5–S1 to delineate the lower extent of the lesion. It revealed multiple subarachnoid space-occupying lesions extending from S2 to L2. The contrast medium did not flow beyond L2. The findings were suggestive of multiple subdural spinal hydatid cysts. An emergency surgery was performed on March 31, 1981, first on the cervical spine, from where a 3 cm cyst was removed intact from the spinal subarachnoid space at the C6 level. Then a laminectomy from S2 to L2 was performed, and four cysts were removed, two intact and two ruptured; the latter two had been punctured at the time of myelography (the needle punctures were clearly seen). The cervical and lumbar areas were thoroughly irrigated with 0.1 % cetrimide solution and the wounds closed. The patient gradually recovered his movements and sensations in the upper and lower extremities. Two weeks later, a myelogram, using the residual dye left in the spinal canal, revealed the presence of more cysts in the dorsal region (Fig. 17.3a). On April 16, a third laminectomy, joining the previous cervical and lumbar laminectomies, was performed, and the remaining six subarachnoid cysts were delivered intact from the dorsal region (Fig. 17.3b). The patient made a perfect recovery except for some urgency on urination and was discharged on May 1, 1981. On November 30, 1981, about 7 months after his discharge from hospital, he was readmitted because of bouts of headache and vomiting of 3-week

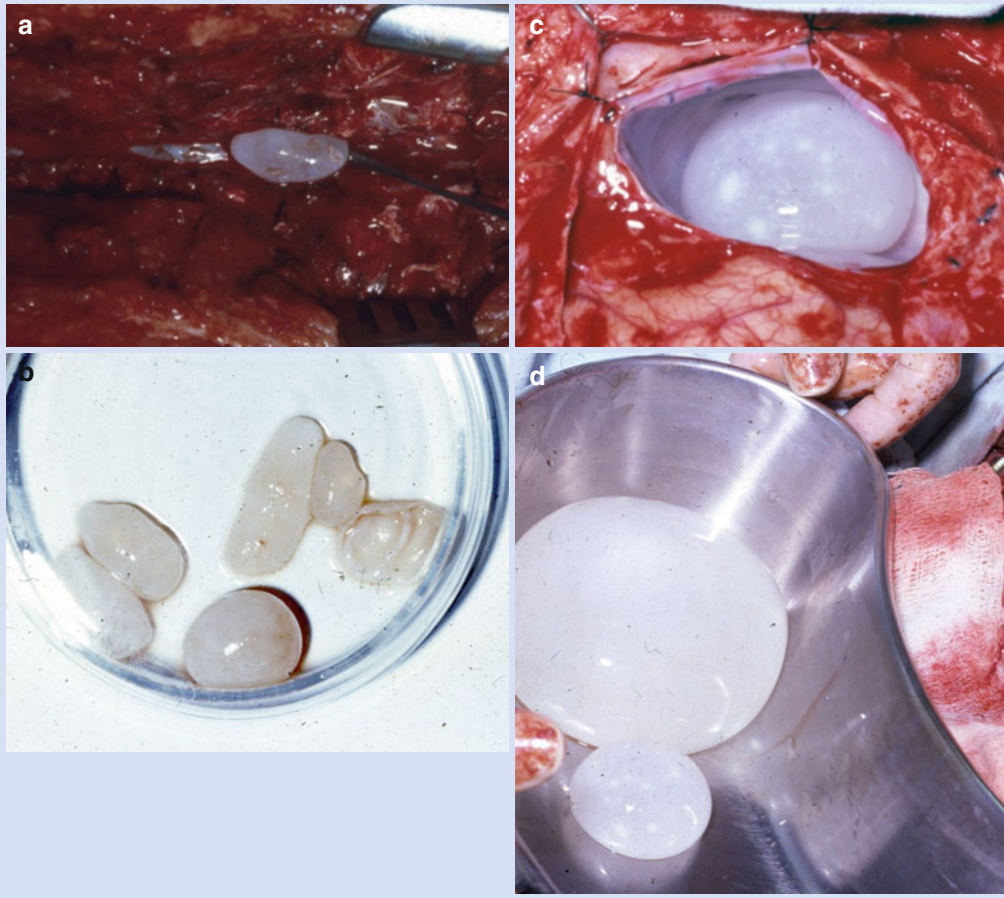

Fig. 17.3 (**a**) Delivery of cyst from the subdural space. (**b**) Cysts lying in a petri dish delivered from the dorsal space. (**c**) Cyst in situ in the cavity left by the previous surgery (note the thickened glistening pericyst). (**d**) Two recurring delivered cerebral cysts in a basin and the cavity left behind

duration. About 23 months from the initial surgery, on December 1, 1981, the left frontal craniotomy was reopened, and two recurrent frontal cysts were removed intact from the bed of the original cyst (Fig. 17.3c, d). Since then he has done well.

Cyst Rupture

The most important and most catastrophic complication in surgery of brain hydatid is the inadvertent or intentional rupture of the cyst in situ at the time of surgery. It is generally estimated that 25 % of all operated cases rupture. Do these cysts have a topographic predilection for rupture during surgery? Deep-seated cysts tend to rupture more often than superficial ones, and cysts around the brain stem are more difficult to deliver intact. Onal et al. (2001) found that cysts in the frontal location were more prone to rupture and seven out of his eight cases, in this location, did rupture.

Most of these cysts are fertile, and, upon rupturing, the brain is flooded with hydatid fluid, disseminating the hydatid sand over a large area. However, only few cysts develop, rarely exceeding a dozen in number. The question which has not yet been answered is why, while such a large number of scolices (it is estimated that one cubic

centimeter of hydatid fluid contains 400,000 scolices) soak the brain, only a few, if any, hatch and only a relatively small number of cysts develop (Case 3). Is it due to the host or to the parasite? Is it that when a scolex hatches, it produces some kind of an enzyme that inhibits the hatching of other scolices? Or is it that the brain develops a certain immunity against the parasite? In some cases, the seeding may reach the spinal subdural space. Case 3 is such an example.

What is the percentage of recurrences following cyst rupture? Griponissiotis (1957) reports on four cysts ruptures out of a total of eight cases, and out of the four there was only one recurrence. He attributes this low incidence of recurrence in ruptured cysts to the fact that he did sterilize the cyst by injecting in it formalin and by washing the cavity left by the cyst with formalin.

It takes an average of 6 months for these recurrent cysts to become fertile and 1 year to produce symptoms. Therefore, the golden rule is: in case a cyst ruptures intraoperatively, it is imperative to investigate the patient within 6 months, even though the patient may be asymptomatic. A negative investigation does not entirely exclude the possibility of a recurrence at a later date. This is why, if the investigations at 6 months are negative, the search should be repeated every 4–6 months for 4 years, as a 4-year period was found to be the maximum time for a recurrence to occur. In case recurrent cysts are found, it is indicated to operate on them before they become fertile, i.e., before 6 months elapse especially that these recurrent cysts usually lie deeper in the brain and their delivery, intact, becomes more difficult. They may at times be found within the lateral ventricle (Case 4) or even in the spinal subarachnoid space (Case 3). In case the cyst recurs in the same place occupied by the original one, often the pericyst is much thicker than usual and is adherent to the adjoining brain and may mimic the appearance of the ectocyst. There may also be fluid between the thickened pericyst and the ectocyst as in our Case 3 (Fig. 17.3c).

To prevent such complications, in case of rupture, it is advisable to adapt surgery in a way to reduced damages to a minimum. As Benjamin Franklin once said "an ounce of prevention is worth a pound of cure." What kind of prevention should be applied? If one adopts the following five rules, one is prone not only to prevent rupture but, in case of rupture, to minimize the damage:

Rule one: Do not allow any sharp instrument or material to be found in or near the surgical field. Cover with wet gauze all Raney clips, and cover all sharp objects in the vicinity of the cyst, like clamps, hooks, bony edges, etc., with a wet gauze.

Rule two: Do not use the cautery (uni- or bipolar) in the vicinity of the cyst. Open the cortex or enlarge the opening using a pair of scissors and applying clips whenever indicated. After the delivery of the cyst is completed, one can coagulate the bleeding points and remove the clips if necessary.

Rule three: Cover all the visible cortex with soft, wet gauze and place a long strip of soft gauze from the edge of the visible cyst to the receptacle which is supposed to receive it intact. Pack the cortex-dura interface with wet gauze to prevent an accidental flood with hydatid fluid from seeping around the cortex and finding its way toward the base of the brain.

Rule four: Enlarge the cortical opening over the cyst using episiotomies in safe directions and excise the pericyst which is quite thin but may impair the normal delivery of the cyst. The pericyst is always present but is translucent and may be difficult to see. It often ruptures spontaneously. The unaware surgeon may believe the ectocyst is starting to rupture.

Rule five: Imbibe all the surrounding gauze with 0.1 % cetrimide solution and in case of rupture irrigate the entire field with the cetrimide solution before and after removing the surrounding gauze. Cetrimide in this concentration is innocuous to the brain but is a powerful scolicidal solution (Frayha et al. 1981; Frayha et al. 1997). Do not use hypertonic saline and certainly not formalin. The use of formalin may be fatal (Kocaman et al. 1999).

If these five rules are followed, the possibility of intact delivery of the cyst is enhanced, and, in case of rupture, recurrences are reduced to a very low percentage.

Cystoperitoneal Shunt

Peter et al. (1994) mention the insertion of a "cystoperitoneal" shunt as an emergency "by a resident." The cyst was removed a year later together with the shunt and the patient developed abdominal cysts.

Cysto-Atrial Shunt

El-Khamlichi et al. (1980) report a case, erroneously diagnosed as an intra-axial tumor, who underwent a cysto-atrial shunt and who developed an infection and meningitis followed by death, and it was on autopsy that the real nature of the disease was discovered.

Anaphylactic Shock

Much has been said and written about anaphylactic shock, especially in case of cyst rupture during surgery; yet there are very few case reports relating to this condition. De Durana et al. (1997) report on a male who was seen in the emergency department with urticaria, angioedema, syncope, and severe hypotension with positive hydatid serological tests, a year prior to the appearance of a cerebral cyst on computed tomography of the brain. It is difficult to accept any cause and effect of these reactions to the cerebral cyst. Kaya et al. (1975) report on a case that died 1 day after surgery, where "the hydatid fluid spilled into the subarachnoid space during the removal of the parapontine cyst; hyperthermia and severe allergic reactions were noted and death was probably due to anaphylactic shock." The authors of the article themselves are in doubt about anaphylactic shock and use the term "probably." Turgut (2001), who reviewed 47 articles in the Turkish literature, collected three deaths from "anaphylactic shock" out of 268 cases but does not describe the facts.

Complications Related to Nonsurgical Treatment

Albendazole and Mebendazole Treatment

If given for a long period of time, they may produce mild to moderate rise in the level of liver enzymes, alopecia, and bone marrow suppression. All these complications are reversible upon the cessation of treatment (Nourbakhsh et al. 2010).

Praziquantel Treatment

I have no experience with this drug and could not find except one reference related to the complications of this drug in humans by Zhang and Zhang (2011) who report on a case of recrudescence of fever following the treatment with this drug. I refer here to Chap. 16 of this book where the authors Dlamini and Ntusi state that "Praziquantel is usually well-tolerated." It may cause abdominal discomfort and nausea. Dizziness, fever, headache, seizures, and malaise have been described. Less commonly, the drug may cause hepatotoxicity, ventricular fibrillation, atrioventricular block, ventricular ectopy, and hypersensitivity.

Complications During the Postoperative Period

Some of these complications are specific to hydatid disease, and others are common to all other craniotomies.

Specific Complications

Recurrence

Recurrence is about the most common complication. It should be differentiated from a de novo cyst. Recurrence comes as the consequence of the spillage of fertile hydatid fluid in or over the brain due to puncture or rupture of the cyst preoperatively or during surgery. Preoperatively, the cyst puncture may be accidental as in ventriculography or for diagnostic purposes or it may be intentional as for preoperative decompression. Intraoperatively its rupture may again be intentional or inadvertent.

Not all cysts that rupture at surgery recur. In the series of Krawjewski and Stelmasiak (1991), only two recurred out of six ruptured cysts; Tuzun et al. (2010) reports one of three cases that recurred. All six ruptured cases of El-Shamam et al. (2001)

recurred, and only two cases recurred out of seven in the series of Ersahin et al. (1993). The major reason why not all ruptured cysts recurred is that those cysts may have been sterile at the time of surgery. Another reason may be that the surgeon sterilizes the cyst before he tackles it using different solutions like hypertonic salt solution, cetrimide, absolute alcohol, silver nitrate solution, or formaldehyde. The latter three solutions are not safe for use, as disability or death may ensue.

The rate of recurrence following cyst rupture is hard to evaluate because most authors report only one or a small number of cases and follow-ups are scarce and inadequate. Statistics in this respect are erroneous because, especially in the Mediterranean regions, if the disease recurs the patient seeks the opinion of another neurosurgeon and the original one may not know of the recurrence. Therefore, these statistics tend to underestimate the true recurrence rate which have been evaluated in a wide range. Ciurea et al. (1995) reported a recurrence rate of 40.7 % in a series of 27 patients, Onal et al. (2001) reported 4 out of 30 (14 %), and Tuzun et al. (2010) reported one recurrence out of 25 operated patients (4 %).

It is interesting to note that the rupture of these cysts was used by many surgeons, to determine the growth rate of hydatid cysts in the brain. They would measure the size of the recurrent cyst at the time of the redo surgery and divide it by the time elapsed between the insemination and delivery thus obtaining the so-called growth factor. None took into consideration that this growth is not a linear one but depends greatly on the intracranial pressure as well as the location of the cyst. Obviously cysts would grow in a virgin relaxed brain quicker that it would in a tense brain.

Case 4

MG, an 8-year-old boy, was admitted to hospital on October 6, 1953, for headache and vomiting accompanied by blurred vision of 4-month duration. Twenty days prior to admission, he gradually developed spasticity on the left side of the body. On physical examination, he was mentally clear and well oriented with crackpot resonance of the skull and a convergent squint. Bilateral papilledema was present. There was spastic paresis of the left side of the body with a left Babinski sign and clonus of the left foot. Plain skull x-rays revealed widening of the sutures. Casoni, Weinberg, and purified protein derivative tests were negative. A ventriculography revealed the presence of a large mass in the left frontal region. As there were no neurosurgeons in the country, a general surgeon drilled a burr hole in the left frontal region, and a cyst appeared under the dura. It was aspirated. The chitinous membrane was pulled out and the reconstructed cyst measured 5.5 cm in diameter. The patient made a good recovery. He was readmitted about a year later to another hospital where we are told another brain cyst was removed. The details of this admission are not available. On October 10, 1955, he was readmitted because of severe bouts of headaches, vomiting, and a left-sided spasticity. The right frontal craniotomy was reopened, and more than 30 cysts were removed, measuring from 1 to 7 cm in diameter. Unfortunately two small cysts ruptured. The area was thoroughly washed with hypertonic saline solution. The lateral ventricle was then opened, and a large intact cyst was removed from within it using a sterile teaspoon. Following this surgery, he was seen at different time intervals for seizures. He was seen about a year ago and is still doing well.

Porencephalic Cyst

Usually the brain reshapes postoperatively and fills the cavity left behind by the cyst so that it may be difficult to tell where the cyst was. However, in a substantial number of cases, especially when the cyst is large (estimated size at 5 cm or more), a porencephalic cavity remains in the field. Tuzun et al. (2004) recorded 4 such cavities out of 25 operated patients and Ersahin

et al. (1993) 2 out of 19. These porencephalic cavities are most usually asymptomatic and need no further attention. However, this was not the case in the second patient of De Villiers Hamman and Joubert (1957) who presented a year later with a right hemiparesis and aphasia (the latter symptom is extremely rare in hydatid disease) and was operated for a possible recurrence. At surgery a large porencephalic cyst was found, and no recurrence was observed. This is the problem we faced with our radiologist who insisted that there was a recurrence and forced our hand to reoperate the following patient.

Case 5

RJ, a 21-year-old female, was operated on March 18, 1994, by a colleague for a right parietal hydatid cyst. The patient reported that her previous surgeon had told her family that "some spillage of the cyst content occurred during delivery." She received albendazole for 3 months after surgery. She was readmitted in our service on November 2, 1994, at which time an MRI revealed "a 2 cm well circumscribed cystic lesion in the right parietal lobe compatible with local recurrence of previously excised hydatid cyst" (Fig. 17.4). The patient was operated, and only gliosis surrounding a cystic area was found. Last seen on July 1, 1998, she was doing well.

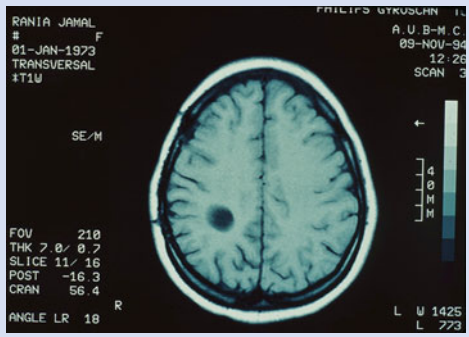

Fig. 17.4 Porencephalic cyst seen on MRI in the right parietal white matter mistaken for a recurrence

Kocaman et al. (1999) reported on two patients who needed a porencephalic cystoperitoneal shunt. These porencephalic cysts may be associated with a subdural effusion. They often last for a very long period of time.

Case 6

HI, a 10-year-old boy, was admitted to the American University Medical Center of Beirut on December 19, 1994, suffering from dizziness and headache of 1 month duration. On examination he had a left hemianopsia, papilledema, and a right Babinski sign. He brought with him an MRI revealing a 10.5×9.5 cm cyst in the right parietotemporal region (Fig. 17.5a). The cyst was delivered but leaked through

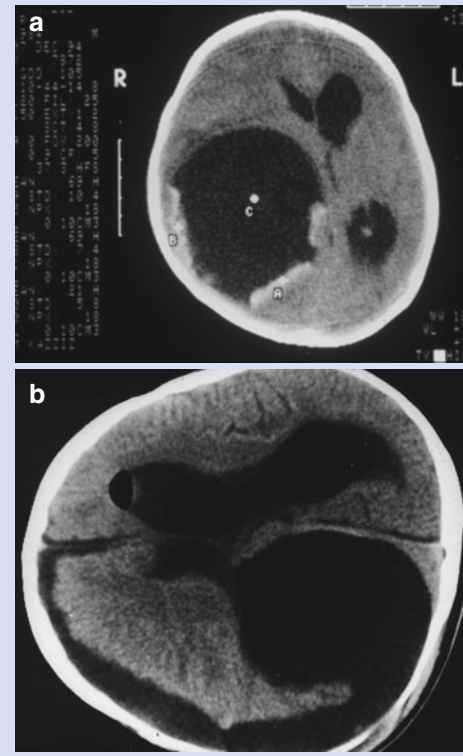

Fig. 17.5 (**a**) Pre-op MRI revealing a 10.5×9.5 cm hydatid cyst with multiple overgrowth of the germinative membrane. (**b**) Post-op MRI showing a large porencephalic cyst in continuity with a subdural hygroma

a pinhole. The entire field was thoroughly irrigated with 1 in 1,000 cetrimide. Readmitted 13 months later on January 17, 1996, because of headache, a large porencephalic cyst was discovered, and a cystoperitoneal shunt was planned. A needle was introduced into the cyst, and the fluid did not flow out; it had to be aspirated. In view of the low pressure in the cyst, it was decided against a shunt. Patient was seen 10 months later, on November 20, 1996; he was still asymptomatic, and his immunohemagglutination was negative.

Subdural Effusion

This is not an uncommon complication (Tuzun et al. 2004; Yuceer et al. 1998). In one report it occurred in three out of five operated patients (Abbassioun et al. 1978) and in another in 7 out of 25 operated cases (Tuzun et al. 2010). It may be connected to a porencephalic cyst as is seen in the case of HI (Fig. 17.5b). Immediately after surgery, this represents the fluid which was injected in the cyst bed just before the final dural closure to eject all the air that had filled the surrounding spaces. This fluid is later replaced by cerebrospinal fluid. Very often this condition does not need any intervention, and the fluid is gradually and spontaneously absorbed within 2–3 months (Abbassioun et al. 1978). The subdural fluid should not be aspirated with a syringe or evacuated by drainage. It is not a helpful procedure because the space will quickly refill with fluid or air. Subdural effusion very rarely produces increased intracranial pressure. In such very exceptional cases, a subdural-peritoneal shunt is of help (Tuzun et al. 2010).

Pneumocephalus

Pneumocephalus has been reported in 12 % of cases in the postoperative period (Tuzun et al. 2004). It is of no consequence and disappears within few days without any specific treatment.

Hydrocephalus

This complication is quite rare. It has been described by Ersahin et al. (1993) who report on one case who needed a ventriculoperitoneal shunt after surgery and so did Kocaman et al. (1999).

Intracerebral Bleed

Intracerebral bleed has been occasionally reported (Tuzun et al. 2004). Griponissiotis (1957) lost a patient from hemorrhage "resulting from an attempt to remove a very thick capsule." Radwan and Khaffaji (1988) reported on a patient who developed an intracerebral, intraventricular, and extracerebral hematoma which was evacuated; but the patient deteriorated progressively, developed hydrocephalus, and died 7 months later.

The etiology of such bleeds is legion, but most frequently bleeds occur after the delivery of a cyst which had leaked, ruptured, or was infected in situ prior to surgery. These three conditions often produce adhesions of the cyst to the adjoining brain tissue through the pericyst rendering delivery difficult and hazardous. Tuzun et al. (2004) lists the following causes of postoperative bleed: uncontrolled bleed from a hidden area, difficult dissection, retraction, vessel injury by needle, bleeding from a residual lesion, local hemodynamic changes, and hypertension during surgery and during recovery from anesthesia.

Postoperative Calcification

St. George et al. (2003) reported a complicated case in whom postoperative calcification occurred. A 9-year-old boy was harboring a 5 cm hydatid cyst diagnosed as a "porencephalic" cyst of the parietal lobe. This was treated with aspiration. The cyst got infected with "mixed organisms," and an Ommaya reservoir was inserted for repeated aspiration and local instillation of gentamicin. The patient also received parenteral antibiotics until the returns from aspiration became culture negative. It is interesting to note that, 6 years later (1981), a multiloculated cyst was found at the site of the original one from which sterile "thick purulent fluid" was aspirated and patient was started on mebendazole. A left parietal craniotomy was performed, and multiple cysts containing scolices and brood capsules were delivered with calcifications in the walls of the larger ones. In 1984, 3 years after the excision of the cysts, a calcification was observed on CT scan at the site of surgery. Twelve years later the

patient developed a malignant glioma at the site of the previously removed hydatid cyst. In this case it is not clear whether this calcification had a direct relation to the cyst or whether it was a consequence of the infection or whether it was part of the glioma.

A real postoperative calcification was seen in the bed of the delivered cyst in one of our patients.

Case 7

HQ, a 23-year-old male, was seen for the first time on October 14, 1981, suffering from generalized headache of 1-month duration. Examination was negative, and he was managed conservatively. The headache persisted, and on December 17, 1981, he had developed papilledema. A CT was performed and revealed a very large cystic mass, in the left parietal region which was considered an abscess or a hydatid cyst. He was urgently admitted to hospital where he was operated, and the mass proved to be a hydatid cyst (Fig. 17.6a) which was delivered intact. On April 14, 1993, i.e., 12 years after surgery, the patient returned complaining of some headache in the left side

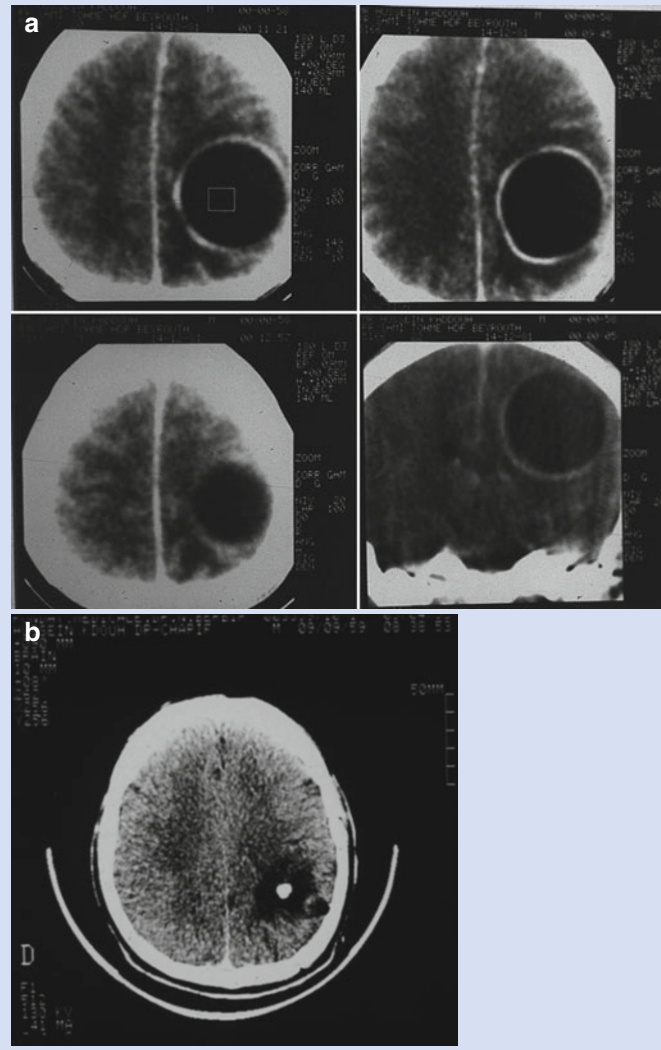

Fig. 17.6 (**a**) Preoperative CT showing the left parietal hydatid cyst. (**b**) Gliosis with central calcification at the site of the hydatid cyst removed 12 years earlier

of the head, and a CT revealed an area of gliosis with a central calcification at the site of the previous hydatid cyst. This calcification is most probably in the pericyst left behind (Fig. 17.6b).

Glioma

St George et al. (2003) report on a case described in the previous section ("Postoperative calcification") of a man who developed a malignant glioma, in the same location from which 22 years earlier a hydatid cyst was removed, and ponder whether it is "possible that the glioma arose as a result of chronic changes induced by previous hydatid?" No other reference for such a transformation has been found in the literature.

Choreiform Movements

These movements were described in the postoperative period in one case in which the cyst was delivered from the basal ganglia area. That patient was free from these symptoms prior to surgery (Turgut 2001).

Delayed Mental Development

It is interesting to note that 3 out of 12 operated children (ages not recorded) reported by Krajewski and Stelmasiak (1991) "showed retardation of mental development." All three children had a persistent porencephalic cyst.

Nonspecific Complications

These complications are common to all craniotomies and are not specific to hydatidosis.

Superficial Wound Infection

Turgut et al. (2007) reported four cases of postoperative infections out of 268 cases retrieved from the Turkish literature, and Griponissiotis (1957) lost a patient because of postoperative infection. St. George et al. (2003) reported a case, described under section "Postoperative calcification", of an iatrogenic infection.

Meningitis and Abscess

Meningitis was reported by Turgut et al. (2007) in 1 case out of 268. Krajewski and Stelmasiak (1991) reported 2 cases of nonbacterial meningitis occurring immediately after surgery, out of 12 operated patients, as well as one case of meningitis appearing a year after the third operation for recurrent hydatid disease. Mircevski et al. (1985) reported on three deaths from a series of nine intraventricular cysts, one of whom, a 5-year-old girl harboring a fourth ventricular cyst, died from purulent meningitis. Samiy and Zadeh (1965) reported a 9-year-old girl who developed meningitis due to a cerebrospinal fluid fistula and died 3 months after surgery. Botteau et al. (2003) describe a case of eosinophilic meningitis which occured following excision of a cerebral hydatid cyst and resolved under chorticosteroid therapy. Ouboukhlik et al. (1994) reported on a case in which an abscess developed in the cavity left by the cyst needing a second operation.

Deep Venous Thrombosis

Turgut et al. (2007) reported 2 out of 268 cases.

Pulmonary Embolism

The case of Tiberin et al. (1984) developed "a delayed massive pulmonary embolism (which) responded well to anticoagulation therapy."

Cerebrospinal Fluid Leak

Turgut et al. (2007) reported 1 out of 268 cases, and Samiy and Zadeh (1965) described one case which led to meningitis (see section "Meningitis and abscess").

The above three subsections are not all inclusive. Although little was found in the literature about these three types of complications, obviously they must have occurred more frequently but have not been reported.

Subdural Hematoma

Subdural hematoma has been described on the opposite side of surgery and proved to be fatal (Garcia-Uria et al. 1980). This is probably due to the decompression that occurred following the

evacuation of the cyst. The positioning of the head during surgery is of paramount importance; were the patient lying on the normal side of the head, the weight of the brain would have avoided this complication. Turgut (2001) reports on 4 cases out of 268 but does not mention the side relative to surgery nor the outcome.

Epidural Hematoma

This complication was reported in one out of 25 operated cases (Tuzun et al. 2010). The extreme decompression within the skull may be inductive to such a complication. This is why it is advisable to place retention sutures from the dura to the pericranium at the start of surgery, which will obliterate the extradural space and will not allow the dura to peel off.

Seizures

Focal cerebral seizures occur in approximately one-third of patients before surgery (Arseni and Marinescu 1974) and show a wide range of frequency from 7 to 48.5 % depending on different authors (Goinard and Descuns 1952; Arseni and Marinescu 1974; Ersahin et al. 1993). The electroencephalography is not pathognomonic of hydatid disease and often shows delta wave activity (Arseni and Marinescu 1974). These seizures frequently improve following surgery. However, de novo seizures do occur postoperatively; 4 out of 59 operated patients were reported by Arseni and Marinescu (1974), 4 out of 30 by Onal et al. (2001), 4 out of 23 by Kocaman et al. (1999), and 10 out of 48 by Ouboukhlik et al. (1994). These patients do require long-term antiepileptic therapy.

Postoperative Mortality

In hydatid disease, like all major intracranial surgery, mortality depends a great deal on the preoperative condition of the patient (our Case 8) and the localization of the cyst(s) (Barjhoux et al. 1970) as well as on the expertise and dexterity of the surgeon. It ranges from zero percent in some series (Tuzun et al. 2010) up to 25 % or 26.6 % in other series (Kaya et al. (1975).

Case 8

FM, a 2-year-old boy, was admitted to hospital for seizures, headaches, vomiting, and right hemiplegia. He was diagnosed as harboring a brain space-occupying lesion. He developed chicken pox, and the pediatrician insisted on discharging him, to be readmitted for surgery in 3 weeks' time. He was lost to follow up until he reappeared, on February 1958, at the age of 5 years, with a right hemiplegia, diplopia, and vomiting. On examination he was drowsy and had fits of unconsciousness accompanied by generalized spasticity with head turning to the right side. He had an enlarged head mainly in the left parietal region with crackpot resonance. He had bilateral papilledema and a bilateral Babinski sign. An emergency right carotid angiogram was performed revealing a large avascular, rounded space-occupying lesion in the left hemisphere mainly in the parietotemporal region. Chest x-ray was negative, and blood examinations revealed zero eosinophils, a negative indirect hemagglutination test, and a 1/4 Weinberg test. By the time the patient was taken to the operating room, his pupils had become dilated and nonreactive to light. A scalp flap was rapidly turned, and the skull was cut with a pair of scissors. When the dura was opened, a large cyst appeared (Fig. 17.7a). It was delivered intact and weighed 1.7 kg (probably the largest cerebral cyst on record) (Fig. 17.7b). Postoperatively the patient started to recover very gradually, his pupils came down, and he began to respond to painful stimuli but passed away on the fourth postoperative day from aspiration pneumonia.

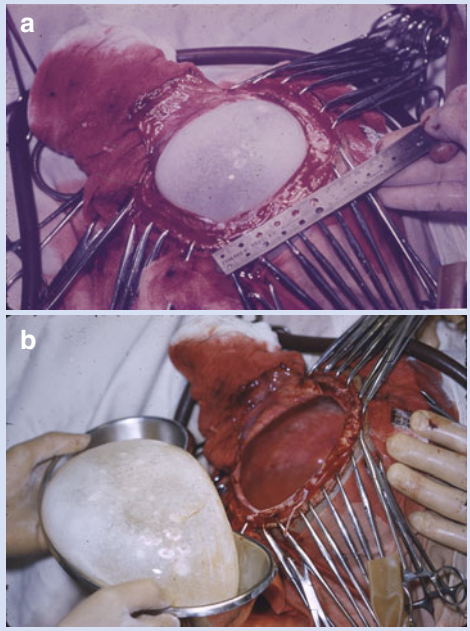

Fig. 17.7 (**a**) Cyst as it appeared upon the reflection of the dura. (**b**) Cyst delivered intact into a basin

Conclusion

Complications of cerebral hydatid disease are multiple. Most of them are avoidable if the nature and progression of this disease is well understood. Although some are of a minor nature, others may be very serious and even lethal.

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Complications of Spinal Hydatidosis

18

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Contents

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Introduction

It has been reported that hydatid disease involving the vertebral body and paraspinal muscles is rare, even in rural areas where echinococcosis is endemic. The treatment of choice for spinal hydatidosis is surgical resection of the affected vertebrae combined with stabilization, followed by postoperative adjuvant chemotherapy. Nevertheless, the recurrence rate is extremely high, and radical resection is often impossible to achieve in cases of extradural lesions involving the spine due to rupture of the hydatid cyst during surgery.

Complicated Hydatid Cysts of the Spine

Epidemiology

Spinal hydatid cysts account for 1 % of all cases of hydatid disease and 50 % of cases of hydatid disease of the bone (Szypryt et al. 1987; Schnepper and Johnson 2004; Herrera et al. 2005). Cysts can be located in the thoracic spine (50 %), lumbar spine (20 %), sacral spine (20 %), or cervical spine (10 %) (Turgut et al. 2007). It has been reported that hydatid disease involving the vertebral body and paraspinal muscles is rare even in rural areas where echinococcosis is endemic (Szypryt et al. 1987; Sudo and Minami 2010).

Epidemiology of hydatidosis is discussed in detail in Chaps. 2, 3, 4, and 8.

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Characteristics of Cystic Lesions

In contrast to the infestation of other body tissues, infestation of the bones including the vertebral column provides an appropriate microenvironment for viable parasites (Turgut et al. 2007). In vertebral hydatidosis, the parasites spread along the intratrabecular spaces, destroying the bone, although intervertebral discs are usually preserved because the disease tends to propagate beneath the periosteum and ligaments (Herrera et al. 2005). In addition, spinal hydatid cysts have thinner walls because of decreased inflammatory response against them and reduced fibrotic reaction (Tali 2004; Turgut et al. 2007). Clinically, unilocular type I cysts, unilocular type II cysts with daughter vesicles or detached membranes, and unilocular type III calcified cysts are frequently observed (Polat et al. 2003; Turgut et al. 2007).

Vertebral Involvement and Pathological Fracture

Hydatid cysts in the vertebral column are usually asymptomatic until a pathological fracture develops. Herrera et al. (2005) reported that only 5 patients showed back or sacral pain out of the 20 operated patients. In a review of 14 cases of spinal hydatidosis, Haddad and Bitar (1997) reported that pain was the most common symptom (13 out of 14 cases). Other symptoms were incontinence of urine, weakness, and sciatica. Signs include weakness and spasticity. The findings on spinal radiography are mostly nonspecific, though they have a characteristic imaging appearance on computed tomography (CT) or magnetic resonance imaging (MRI). Plain spinal radiography sometimes shows an "absent pedicle sign"-like spinal tumor. On CT, a spinal hydatid cyst has a typical appearance of a large non-enhancing cyst of cerebrospinal fluid density, with no pericystic edema and no enhancement after injection of the contrast medium (Turgut et al. 2007). Frequently, they have a honeycomb appearance due to a multiplicity of small cysts within the bone marrow. Large unicystic lesion is very rare; it may be found in the paraspinal area. Absence of osteoporosis and sclerosis in the host vertebrae as well as lack of damage in the adjacent intervertebral disc space also indicates this disease (Turgut et al. 2007).

MRI is the preferred imaging modality for the diagnosis of spinal hydatidosis. On MRI, the involved vertebra has a heterogeneous medium to low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. The daughter cysts are more hypointense than the parent cyst on T1-weighted images, whereas they are of slightly higher signal intensity in comparison with the parent cyst on T2-weighted images (von Sinner et al. 1991; Turgut et al. 2007).

In advanced cases, mild kyphotic deformity of the spine is observed due to compression fracture or collapse of the affected vertebra. Persistent pain and deformity is caused by either collapse of the spine or extension of the process beyond the skeletal confines (Tabak et al. 2007).

This material is discussed in detail in Chap. 8.

Spinal Canal Compromise

Although it is not specific to spinal hydatidosis, radicular pain and myelopathic pain with back pain are the most typical symptoms. Neurological deterioration will result in paraplegia in 25–50 % of cases (Normelli et al. 1998; Schnepper and Johnson 2004). Spinal hydatid cysts can be extradural, subdural, subarachnoidal, or intramedullary (Akhan and Ozmen 1999; Turgut et al 2007) and are usually situated in the dorsal region. They may generate medullary or radicular symptoms according to their location (Karadereler et al. 2002). A primary spinal intradural extramedullary hydatid cyst is extremely rare. Kalkan et al. (2007) reported this lesion in a child as follows: an 8-year-old boy presented with back pain, left leg pain, and difficulty in walking. The patient had no other signs of systemic hydatid cyst disease. An intradural extramedullary cystic lesion was identified with MRI and shown to be a hydatid cyst by histopathological examination after surgical

removal. In MRI examination, an intradural extramedullary hydatid cyst has two dome-shaped ends but no debris in its lumen and has sausage-like appearance. Cyst walls are extremely thin and regular and have no septation (Kalkan et al. 2007).

Hydatid cysts that lack the typical radiographic appearance may be mistaken for arachnoid cysts. Secer et al. (2008) documented these cysts as follows: arachnoid cysts occur as single or multiple cysts. Because they have long T1 and T2 relaxation times, they demonstrate a homogeneous signal pattern similar to that of cerebrospinal fluid: hypointense on T1-weighted and hyperintense on T2-weighted images. One of the differential diagnoses of a spinal arachnoid cyst is a unilocular type 1 hydatid cyst. Unilocular type 1 hydatid cysts usually have thinner walls than their counterparts. However, arachnoid cysts are an exception because of the existence of a decreased inflammatory response.

Paraspinal Extension

When vertebral body destruction and paravertebral soft tissue involvement are observed, tuberculous spondylodiscitis can be confused with hydatid cysts. Tabak et al. (2007) documented a vertebral hydatid cyst mimicking tuberculous spondylodiscitis. They reported that the macroscopic destruction of the vertebrae observed during the surgery was typical of spinal tuberculosis; therefore, antituberculous therapy was initiated before the histopathological reports verifying the presence of *Echinococcus* was obtained. Other differential diagnoses should be established for pyogenic brucellosis, other granulomatous infections affecting the vertebral bodies causing paravertebral abscesses, and tumors (Tabak et al. 2007).

Infection of Cystic Lesion

Turgut et al. (2007) reported that superimposed pyogenic infections involving the spine may develop in some cases, particularly those cases in which cyst rupture occurs spontaneously. In complicated cases, osseous structures, such as vertebrae, constitute a friendly microenvironment for the development of a chronic infection resistant to treatment. On CT or MRI, there may be atypical features such as irregularity of the cyst wall contour, enhancement of the surrounding rim, isodensity, or heterogeneity of the cyst content.

Complications Related to Surgery

Surgical Indications for Spinal Hydatidosis

The treatment goals of spinal hydatidosis are to resect the infested lesion, alleviate pain, prevent neurological deficit, and establish spinal stability. Although the appropriate treatment varies with patient condition and cyst characteristics, including size and location, surgical intervention is mostly indicated in patients with spinal hydatidosis. Patients should be operated as soon as diagnosed unless there is a contraindication for surgery. The earlier the surgery is carried out, the better is the prognosis. One should not wait until surgery becomes a palliative treatment. Conversely, there is no clear consensus regarding which patient should undergo surgical treatment in cases of diffuse spread of the infection within multiple vertebrae and paraspinal muscles (Figs. 18.1, 18.2, 18.3, 18.4, 18.5, and 18.6). Possible indications for palliative surgery in such cases may include vertebral collapse causing intractable pain, spinal cord compression causing progressive neurological compromise, and a life expectancy of at least 3 months, in line with the recommendations regarding palliative surgery for metastatic spinal tumors (Oda et al. 2006).

Surgical Procedures

Laminectomy with complete resection of the cysts is the most frequently performed procedure. A posterior approach should be used to resect the involved posterior element and add

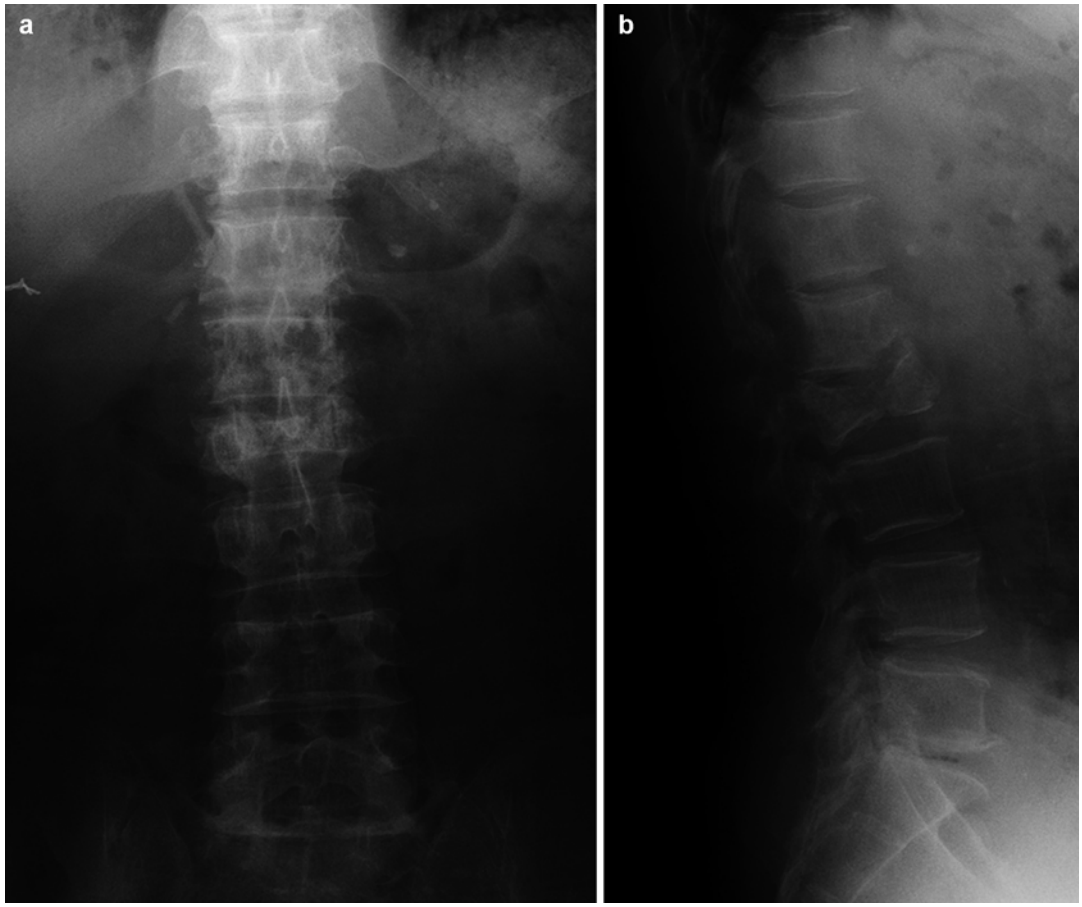

Fig. 18.1 A 73-year-old man presented with increasing low back and leg pain. Plain lumbar spinal radiography showed a compression fracture within the L2 vertebra as well as the "absent pedicle sign" at both L1 and L2. (**a**) Anteroposterior view. (**b**) Lateral view. In this patient, a hydatid cyst of the liver caused by *Echinococcus multilocularis* was surgically resected 30 years before the time of presentation

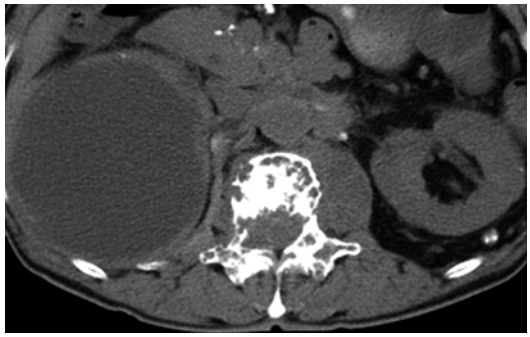

Fig. 18.2 CT shows the presence of multiloculated osteolytic lesions in the vertebral body and posterior elements. Periosteal reactions were observed

posterior fixation. Care should be taken to avoid implant protrusion into the dorsal skin, decubitus ulcer formation, and vertebral fractures in the adjacent segments after posterior spinal reconstruction. An anterior approach to perform total corpectomy and bone grafting with a cage may be used when most of the disease is located in the vertebral body (Charles et al. 1988; Herrera et al. 2005). The anterior approach is useful for curative resection of infected vertebrae; however, care must be taken to avoid spread of the disease to the chest and abdominal cavities (Bhojraj and Shetty 1999). Surgical procedures used in spinal hydatidosis are discussed in detail in Chap. 14.

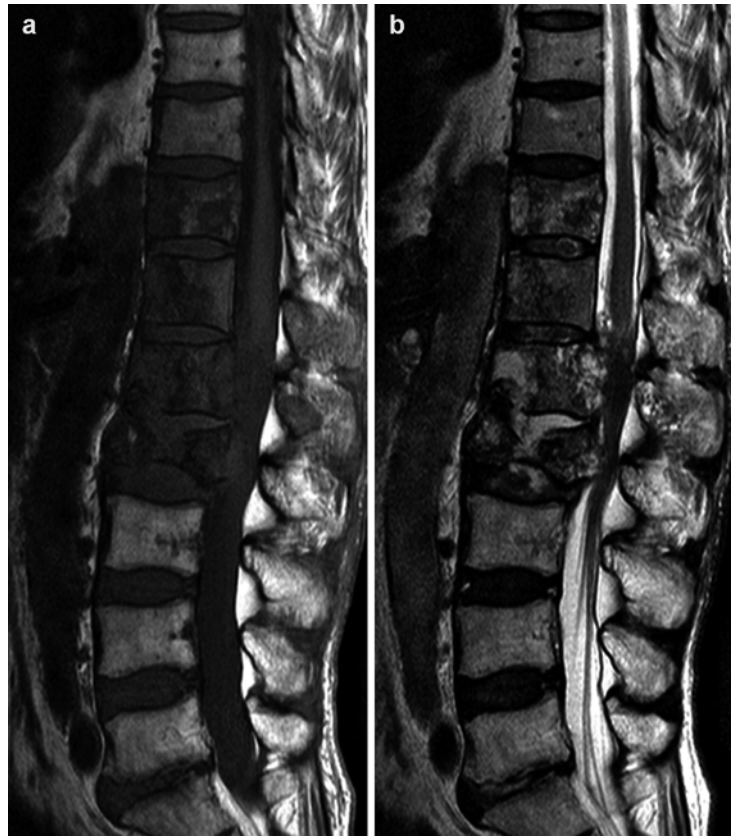

Fig. 18.3 Sagittal MRI views show multiseptated and multicystic lesions. Epidural extension of soft tissue with cord compression is also seen. T1-weighted (**a**) and T2-weighted (**b**) image

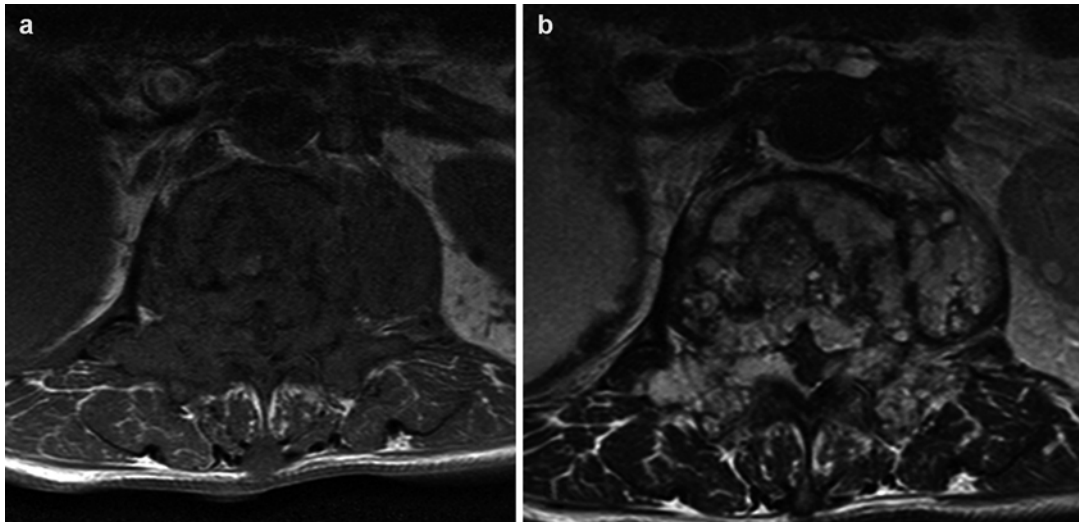

Fig. 18.4 Axial T1 (**a**) and T2 (**b**) MRI demonstrate involvement of neural structures, paraspinal muscles, and the liver

Fig. 18.5 Coronal T2-weighted MRI shows the presence of a complex T2 hyperintense mass in the paravertebral region with multiple septa

Surgery-Related Complications

Surgical Site Infection

In hydatid of the spine, there is not one cyst around which dissection can be carried out. The bone is infiltrated with a great number of minute cysts. In cases where leaked fluid containing parasites is left behind at the surgical site, concerns are raised about delay of skin closure, leading to deep pyogenic infection. It is particularly a cause of concern when surgical intervention is complicated by cerebrospinal fluid leakage. In this case, lumbar drainage may be required. Intensive muscle closure is also required during surgery to avoid fluid leakage. A plastic surgical procedure, such as musculocutaneous flap transfer, is often required for chronic infection. Although there have been few reports about larger series of spinal hydatidosis, Herrera et al. (2005) reported that 50 % of recurrence cases also have chronic wound infection with chronic productive sinuses that required several surgical debridements. Because surgery for spinal hydatidosis is extensive and

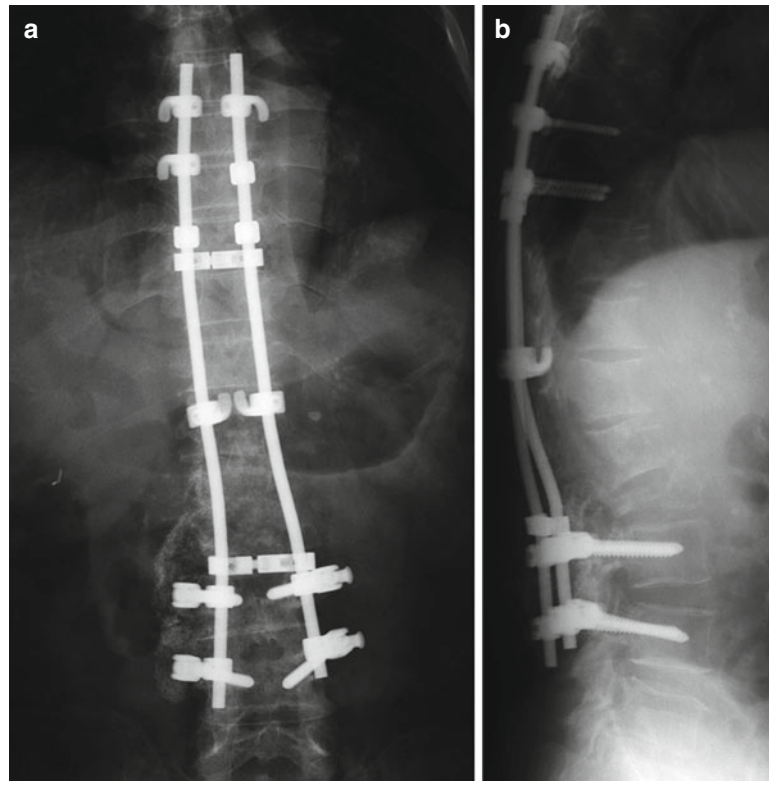

Fig. 18.6 Palliative surgery was performed with posterior decompression and instrumentation for persistent leg pain. Leg pain was significantly reduced. Spinal stability was maintained until the patient died (2 years after the surgery) (Courtesy of S. Satoh, MD) (**a**) Anteroposterior view. (**b**) Lateral view

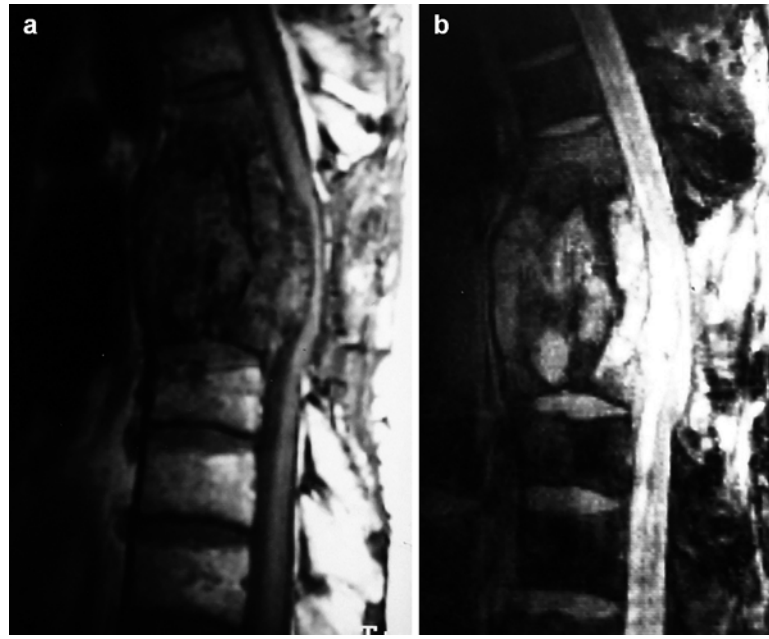

Fig. 18.7 Recurrence of spinal hydatidosis. A 52-year-old man presented with intractable leg pain and motor paralysis. Two years before the time of presentation, anterior mass resection and autologous fibular grafting had been performed, followed by posterior decompression and fusion using an iliac bone graft at T6–T9. MRI shows cysts extending into the canal and compressing the spinal cord. T1-weighted (**a**) and T2-weighted (**b**) image

the reappearance of postoperative surgical wound infection is frequent, perioperative antibiotic therapy is important.

Rupture of Cysts and Allergic Reactions

Another surgery-related complication is allergic reaction caused by rupture of the cyst. This reaction ranges from mild hypersensitivity to fatal anaphylaxis (Kök et al. 1993; Wellhoener et al. 2000; Laifer et al. 2002). Because spinal hydatidosis is usually advanced, rupture of the cyst into the surrounding tissue will already have occurred and the possibility of serious allergy manifesting during surgery is regarded as extremely low. However, this possibility makes close monitoring mandatory during surgery, with facilities available for treating potential complications, particularly anaphylactic shock and laryngeal edema (Khuroo et al. 1997).

Complications After Surgery

Recurrence

Recurrence remains a major problem in spinal hydatidosis (Figs. 18.7, 18.8, 18.9, and 18.10); the literature cites a rate of 30–100 % (Schnepper and Johnson 2004). The thin wall may easily rupture, either spontaneously or due to surgery, resulting in recurrence of multiple cysts (Schnepper and Johnson 2004). It is extremely difficult to resect the extradural lesions involving the spine without rupturing the hydatid cyst because the cysts are contained in narrow spaces within bone boundaries (Schnepper and Johnson 2004; Tabak et al. 2007). Therefore, the management of echinococcal cysts usually involves a combination of surgical resection and antihelminthic therapy.

Adjunctive Chemotherapy

Adjunctive chemotherapy before and after surgery appears to reduce the risk of recurrence by inactivating protoscolices and lessening the tension of cysts for easier cyst resection (Tabak et al. 2007). Administration of either albendazole or mebendazole is recommended to reduce the risk of secondary hydatidosis (Erzurumlu et al. 2000). Chemotherapy for spinal hydatidosis is discussed in detail in Chap. 16.

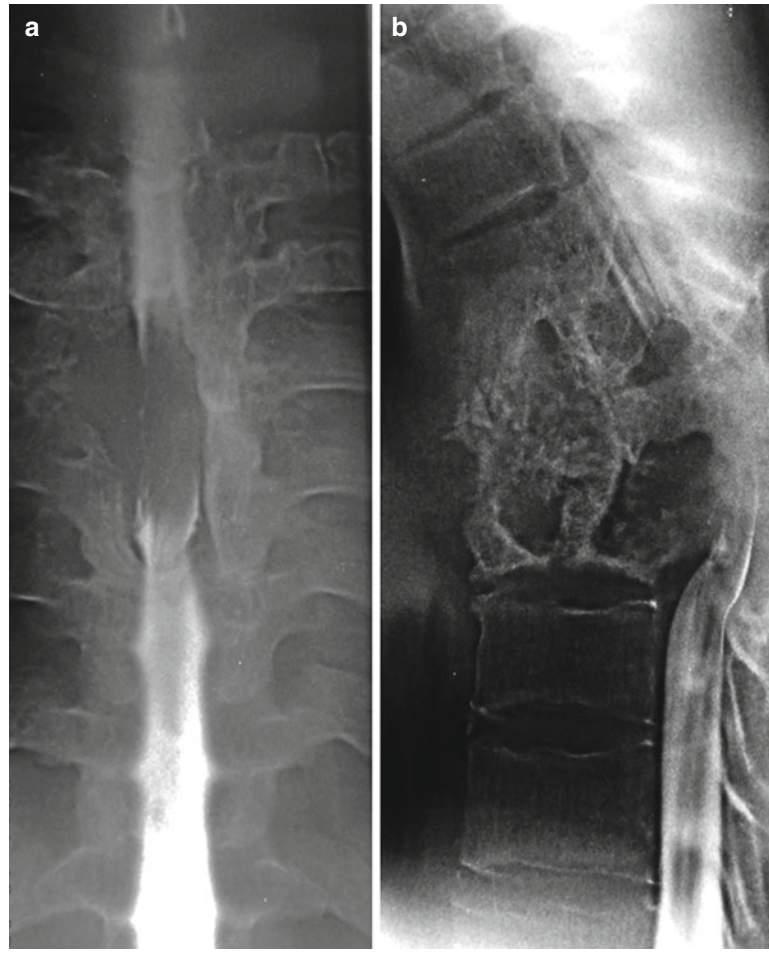

Fig. 18.8 Myelo-tomogram. Note that even after the spinal fusion was completed, the grafted bone was destroyed by recurrent cysts (**a**) Anteroposterior view. (**b**) Lateral view

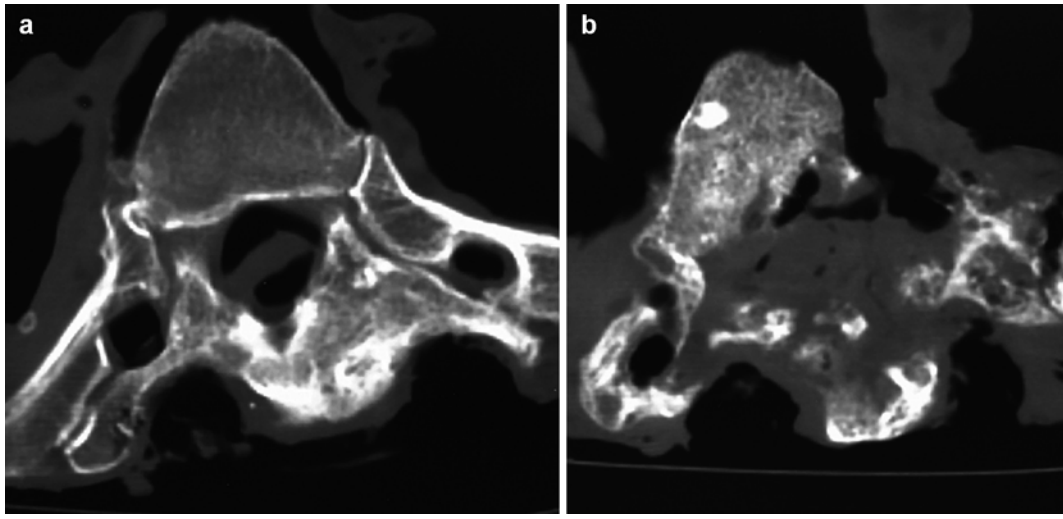

Fig. 18.9 CT showing the completed spinal fusion after the previous surgery (**a**), but recurrence of spinal hydatidosis destroyed the fusion mass (**b**)

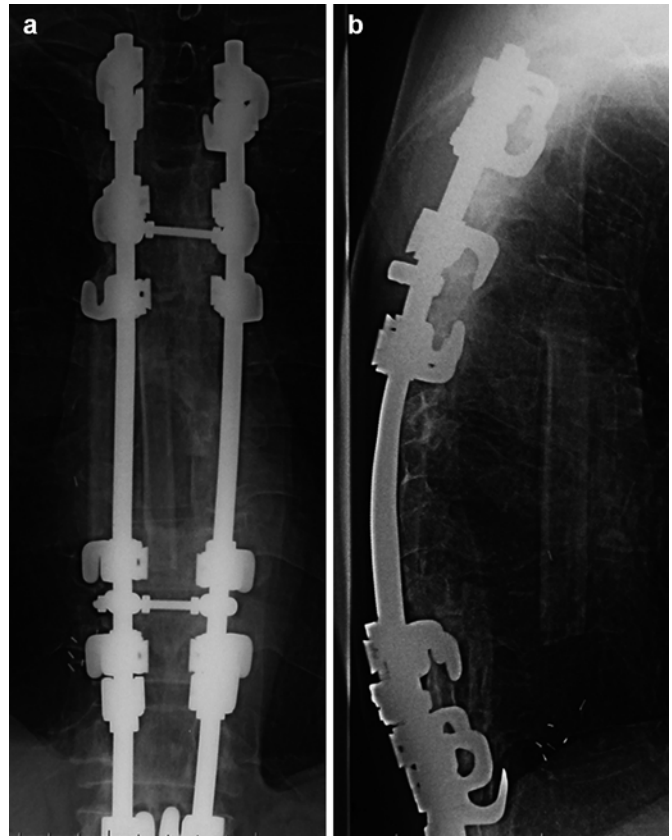

Fig. 18.10 Following posterior decompression and fusion, anterior mass resection and vascularized fibular grafting was performed in a second operation (**a**) Anteroposterior view. (**b**) Lateral view

Other Preventive Measures

Intracystic injections of 10 % formalin, 0.5 % silver nitrate, hydrogen peroxide, 1 % aqueous iodine, and hypertonic saline solutions have been used to destroy the residual larvae (Erşahin et al. 1993), although these remain unproven. Irrigation of the surgical site with hypertonic saline or diluted betadine solution after the cyst resection may help destroy and disrupt the parasite (Schnepper and Johnson 2004; Herrera et al. 2005). Hypertonic saline is a scolicidal agent because the difference of osmolality between the hypertonic saline and the interior of the cyst causes sclerosis of the cyst. Bavbek et al. (1992) documented that the operation area was soaked with 3 % NaCl-wetted patties for a few minutes, which were then removed, and the area was washed with normal 0.09 % NaCl.

Prognosis

Due to the high rate of recurrence, spinal hydatidosis has poor prognosis and has been compared to spinal malignancy. Reported mortality rates range from 3 to >50 % (Bettaieb et al. 1978; Karray et al. 1990; Schnepper and Johnson 2004). Radical resection is sometimes impossible to achieve in cases of extradural lesions involving the spine. Comprehensive evaluation of the patient is important during treatment. Assessment factors should include general complications, other hydatid lesions, prognosis, lifestyle, pain, and the absence or presence of paralysis.

Conclusion

The treatment goals of spinal hydatidosis are to resect the infested lesion, to alleviate pain, to prevent neurological deficit, and

to establish spinal stability. Nevertheless, it is extremely difficult to resect the extradural lesions involving the spine without rupturing the hydatid cyst. Therefore, the management of echinococcal cysts usually involves a combination of surgical resection and antihelminthic therapy. Comprehensive evaluation of the patient is also important to prevent complications of spinal hydatidosis.

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19 Outcome and Follow-up of Patients with Cerebral Hydatidosis

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Introduction

The ideal and generally accepted treatment of hydatid disease involving the central nervous system (CNS) is surgical and that medical treatment should be restricted to nonoperable patients. The outcome of treatment depends on many factors such as the species of echinococcal infestation, whether it is primary or secondary, single or multiple; the anatomical location and dimension of the lesion; the result of surgical intervention; the presence and extent of the disease in other parts of the body; and the type and the duration of drug therapy in cases with rupture of a cyst or of cysts during surgery (Saidi 1976; Altinors et al. 2000; Khaldi et al. 2000; Turgut 2002; McManus et al. 2003; Sayek et al. 2001; Izci et al. 2008; Duishanbai et al. 2010). Prognosis is also different for osseous echinococcal lesions of the cranial bones (or the vertebral column), which secondarily involve the neural elements (Reddy et al. 1972, 1979). The cranial hydatidosis and the vertebral hydatidosis are types of bony hydatid disease which produces few pericystic formations and such lesions confined inside bony tissue enlarge by the formation of a large number of daughter cysts with attendant risk of spillage during their removal and inevitable recurrence of the disease at a later stage. Bony hydatidosis causes few tissue reactions by the host, and the value of drug treatment in such cases is questionable. The outcome also varies with the anatomical location of the lesion, depending upon whether it is epidural,

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subdural, or subarachnoid or it involves the brain or spinal cord parenchyma. Certain locations of hydatid cysts such as cavernous sinus, interpeduncular region, intraventricular region, and brainstem make a total intact excision difficult (Copley et al. 1992; Kiresi et al. 2003; Hamamci et al. 2004; Beskonakli et al. 1996; Gana et al. 2008; Muthusubrahmanian et al. 2009; Guzel et al. 2008; Furtado et al. 2009). The result also depends upon whether calcification is present or not as well as whether an infection is involved (Turkoglu et al. 2005; Abderrahmen et al. 2007).

Species of Echinococcal Infestation

The outcome of therapy mostly depends upon the type of species of the cestode infestation. There are four main species of the larval stage of tape worm, namely, *E. granulosus*, *E. multilocularis* (*alveolaris*), *E. vogeli*, and *E. oligarthus*. *E. granulosus* is the most common infestation worldwide, whereas *E. multilocularis* is prevalent in the northern hemisphere including Alaska, Canada, Siberia, and Central Europe but has recently been increasingly reported in more temperate regions of Eastern France, Nebraska, Illinois, and Turkey (Aydin et al. 1986; Algros et al. 2003). Dog is the host for *E. granulosus* infection; livestock and humans are intermediate hosts. Infection with the remaining types of echinococcosis is rather rare since wild animals such as fox and rodents are the hosts in such types of echinococcal infection (Romig 2003). The presence of fertile scolices and whether they are single or multiple differentiates the first two species of echinococcus infestation. The alveolar echinococcosis is an aggressive disease and eventually invades contiguous structures with tumorlike progression. Usually found in the liver, it can metastatize to the lungs and brain (Kappagoda et al. 2011). Lesions of *Echinococcus multilocularis* in the brain are of firm consistency with a jellylike material, and they mimic brain tumors (Senturk et al. 2006). Infection with *E. alveolaris* has a relatively poor prognosis compared to *E. granulosus* infestations, and in untreated cases it has a mortality of 90–100 % after 10 years (Ehrhardt et al. 2007). In some countries the clinical picture of the hydatid disease may be due to both an *E. granulosus* and an *E. alveolaris* infection. There are reports that there could be infestation by cystic as well as alveolaris types in a single individual (Meade and Barnett 1941). The last two are Neotropic species of echinococcosis which are prevalent in certain parts of Central and South America. Only three cases of *E. oligarthus* and 200 cases of *E. vogeli* cases have been reported from 12 countries in Central and South America (D'Alessandro and Rausch 2008). No cases of cerebral involvement by these species of echinococcal infection have been reported so far, but in other organs they produce invasive lesions like multilocularis, and hence their prognosis should be poor. Single large cysts associated with *E. granulosus* infection can be extirpated without spillage in the majority of cases, and usually the surgical results are better in such cases. For example, in the series of Ciurea et al. (2006), there were only 3 multiple cysts out of 76, and of the single cysts, 56 (73.7 %) could be excised without rupture. There was only one death due to an anaphylactic shock in those 56 cases where as all three patients with multiple cysts died. In contrast cystic lesions which are located in deeper areas or in eloquent regions may not be amenable for complete excision. All cerebral alveolar lesions are secondary, and all patients do have hepatic lesions, and some may have pulmonary lesions too. Sometimes alveolar cerebral lesions had been excised completely, but the patients had succumbed to irreversible liver disease (Wang et al. 2009). In general it may be admitted that all types of cerebral echinococcosis are serious, but the alveolar echinococcosis is worse.

Primary or Secondary

A hydatid lesion in the CNS is classified as primary lesion, when there are no recognizable lesions in other parts of the body (Dew 1928, 1955). Such a hydatid lesion of the brain arises from an onchosphere which is initially deposited

in the brain by the blood stream after a successful passage through the hepatic and pulmonary filtering systems. In contrast the secondary hydatid cysts of the brain are those which originate from scolices or brood capsules belonging to a primary hydatid disease elsewhere. They have landed secondarily in the brain. Obviously management of primary lesions is better than those with secondary lesions affecting other organs. Primary cerebral lesions are usually single, but multiple lesions are reported very rarely. It is supposed that multiple cerebral lesions will develop, if the content of the ruptured cyst gets directly in the arterial circulation (Mancuso et al. 1997; Karadag et al. 2004). Some primary lesions could be in different hemispheres. Some primary lesions especially those involving the spine may develop by spreading through the venous or lymphatic route. Primary lesions are mainly in the cerebral hemispheres in the middle cerebral artery territory, but they have also been reported to occur in the intracranial epidural space (Beskonakli et al. 1996), spinal epidural, vertebral, and rarely in spinal intradural and extramedullary locations. Management of primary lesion in any location results in good surgical outcomes (Pasaoglu et al. 1989; Arif and Zaheer 2009). Favorable long-term outcome has been reported for the excision of primary solitary cerebral lesions in children, and this supports the assumption that these lesions in the pediatric age group are mainly primary (Lunardi et al. 1991). They reported on 12 children, of which one patient suffered from a secondary brain cyst. Eight of the 12 patients who had a mean follow-up of 28 years were still living and enjoying good health at the time of the report. In contrast to primary lesions, the secondary lesions are infertile since they lack brood capsules and scolices (Mancuso et al. 1997).

Solitary or Multiple

Cerebral hydatid cysts are nearly always solitary, and in one series of 135 cerebral lesions, only 2 were multiple (Iplikcioglu et al. 1989). But in a large study which was performed by Turgut (2002), there were 92 (77 %) solitary cases out of 119 and the rest were multiple in 27 (23 %). There were 20 cases with involvement of spine 1 in this series. After surgery there was recurrence in 22 % of cases, in which 6 solitary and 12 multiple lesions occurred. Al-Zain et al. (2002) reviewed all the cases of multiple intracranial hydatidosis and collected 77 cases from the literature. These cases often have serious neurological deficits, and frequently the outcome of surgery was not satisfactory, and in only 46.4 % of cases, a good outcome could be achieved. Overall the mortality in multiple cases was 17.6 %. Five of the patients had more than one recurrence which had appeared from 3 months to 3 years after surgery. Recurrent disease is defined as the appearance of new active cysts after therapy, and a rising titer is of value regarding the diagnosis of recurrence (Sielaff et al. 2001). The chance of recurrence is higher in multiple cases with multiple lesions after surgery. Multiple secondary hydatid cysts can develop by embolism from cardiac echincoccosis and echinococcosis of great arterial vessels (Mancuso et al. 1997; Turgut et al. 1997).

Unusual Locations

Hydatid disease is endemic in many parts of the world, and it can develop in any part of the body. The location is mostly hepatic (75 %) and pulmonary (15 %), and only 10 % other parts of the body are affected (Kiresi et al. 2003). There are some rare sites in the brain where hydatid lesions can occur: cavernous sinus, interpeduncular region, sella, brainstem and cerebellopontine angle, lateral ventricles, and cerebellar hemispheres. Occasionally hydatid could exist along with primary brain tumor (Ozgen et al. 1984; Copley et al. 1992; Beskonakli et al. 1996; Hamamci et al. 2004; Evliyaoglu and Keskil 2005; Gana et al. 2008; Guzel et al. 2008; Furtado et al. 2009; Muthusubrahmanian et al. 2009; Siddiqui et al 2010). The prognoses in cases of hydatid disease involving rare sites especially those in deeper locations are poor.

Laboratory Diagnosis of Echinococcosis

Casoni's test is not very helpful in the diagnosis of hydatid disease involving the CNS (Fairley and Kellaway 1933). However, a positive result with complement fixation test before the first operation on any cyst provides definite evidence of hydatid disease. In the diagnosis of recurrent disease, the skin tests are not helpful. Assessment of the extent of the skin response in such tests is no method for monitoring the disease or adapting the medication. Hence a great number of immunological assays have been developed for the detection of antibodies to anti-hydatid cyst antibodies. Detection of circulating antibodies may be more useful for the immune diagnosis of hydatid disease (Sadjjadi et al. 2009). Tests which are available for the diagnosis of the hydatid disease are enzyme-linked immunosorbent assay, indirect hemagglutination or immunofluorescent assay, radioallergosorbent testing, and latex fixation tests. All of these tests are sensitive but are compromised by nonspecific cross-reactivity with *Helminthes* other than echinococcosis. A positive result of one of these tests should be confirmed by the use of a more specific test. The results of standard serological tests are positive in over 90 % of patients with hepatic cysts but only in about 50 % of those with pulmonary disease and only in 25–36 % in other organs (Karadereler et al. 2002). In a series of 25 cerebral hydatid cysts, the serological tests were positive in only 3 cases (Tuzun et al. 2010). The problems with the laboratory diagnosis of the hydatid disease very often lead to difficulties in the preoperative diagnosis and planning of treatment of the hydatid disease involving the brain in non-endemic areas.

Treatment

The management strategies available for the treatment of echinococcosis depend on the cyst stage and include puncture-aspiration-injection-reaspiration (PAIR), surgery, antiparasitic chemotherapy, and expectant management (Tirnaksiz and Dogan 2004). Positron emission tomography scan and contrast-enhanced ultrasound of the liver involvement might help in guiding the treatment of hepatic lesions by the visualization of metabolic activity and vascularization pattern of echinococcal lesions. Surgical excision and alternative techniques to surgery such as fine needle aspiration and injection of scolicidal drugs and puncture of the cyst, aspiration of the fluid followed by introducing a protoscolicidal agent, and then reaspiration (PAIR procedure) are reported (von Sinner et al. 1995) for abdominal lesions. However, the ideal treatment of intracranial and cerebral lesions is their total surgical excision. PAIR procedure may be necessary in cases of deep-seated or difficult cerebral cystic lesions. Medical treatment is indicated when a cyst ruptures or the disease involves the other organs. Intracranial hydatid cysts grow very rapidly, and some may grow as much as 10 cm per year, and hence their excision is preferred as a mode of therapy (Kirimlioglu et al. 2001). The rate of growth of cerebral hydatid cysts is variable; it can be 1–10 cm per year according to various reports (Vaquero et al. 1982; Sierra et al. 1985).

Surgical Treatment

Surgical treatment remains the preferred management for active hydatid disease, and the aim of the surgery is to excise the cyst or cysts in toto without soiling and complete obliteration of the resulting dead space (Dowling and Orlando 1929; Normelli et al. 1998; Kirimlioglu et al. 2001; Abdel Razek et al. 2009; Tuzun et al. 2010; Mohindra et al. 2011) (Figs. 19.1, 19.2, 19.3, 19.4, and 19.5).

Sometimes successful excision of the alveolar lesions which are in an accessible location followed by a piecemeal of those in difficult locations resulted in good neurological recovery (Wang et al. 2009). Alveolar type of hydatid disease may sometimes mimic a brain tumor, and its total excision may be difficult (Senturk et al. 2006; Ma et al. 2009). Rarely granulosus lesions could be multiple and may be present in different hemispheres, and such cases need planned

excision in one or more stages (Yuceer et al. 1998). Liver and lung disease may be responsible for delayed deaths later on in spite of chemotherapy. In a Chinese study, two of the six surgically treated cases of cerebral hydatid disease of the alveolar type died due to end-stage liver disease (Wang et al. 2009). In a recent study, injection of 0.04 % chlorhexidine into the cysts (hepatic) for 5 min had been shown to kill all the live scolices and there was no recurrence over a follow-up period of 2 years (Topcu et al. 2009). However, this method is yet to be tried in cerebral and cranial hydatid disease. One has to study the deleterious effects of 0.04 % chlorhexidine to the brain, if that were to get spilled over accidentally during the operation. Effective scolicidal agent is useful especially while removing the cysts containing fertile scolices. Viability and fertility of the protoscolices and viable germinal layer determine the recurrence of the disease at a later date (Manterola et al. 2006). Orbital location of hydatid disease is a rare type of infestation, and total extirpation of the cysts without rupture may be difficult, and in such cases recurrence is the result (Fig. 19.6; Ghosh et al. 2008). Endoscopic approaches are available in the management of orbital hydatid disease. Cranial and vertebral hydatid disease invariably recurs because of spillage of large numbers of daughter cysts. Long-term chemotherapy preferably a combination of albendazole and praziquantel is recommended in such cases. Recurrence of spinal disease even with chemotherapy may benefit

Fig. 19.1 Enormous numbers of cysts of different sizes in a case of cranial hydatid disease in frontal region involving orbit with spread into the intracranial epidural space. Recurrence of the lesion occurred 1 year later in spite of prolonged chemotherapy

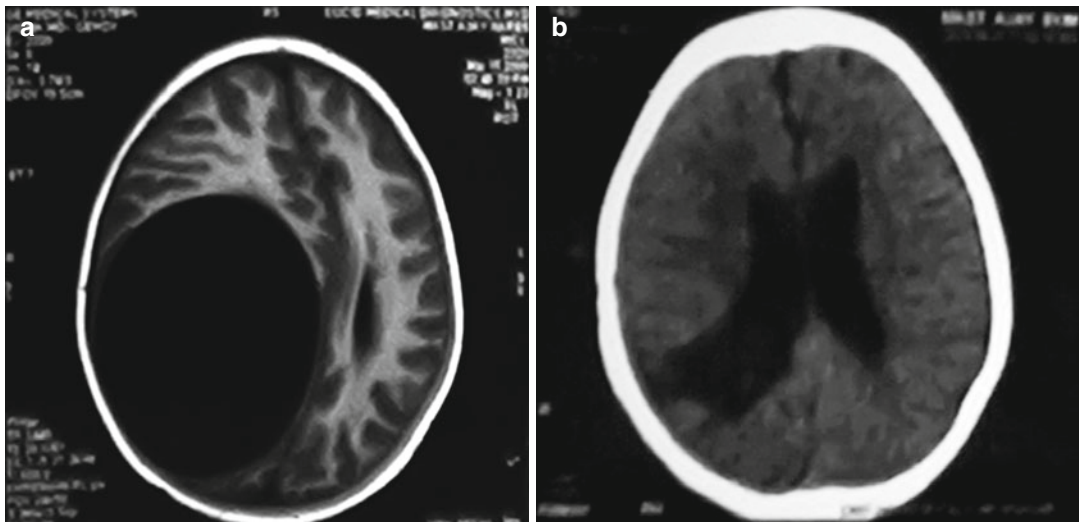


Fig. 19.2 (**a**, **b**) Single primary **c**ystic lesions of the type depicted above, even if large reaching on to the surface in accessible areas are amenable for complete excision with a cure. Preop scan on the left and post-op scan on the right side

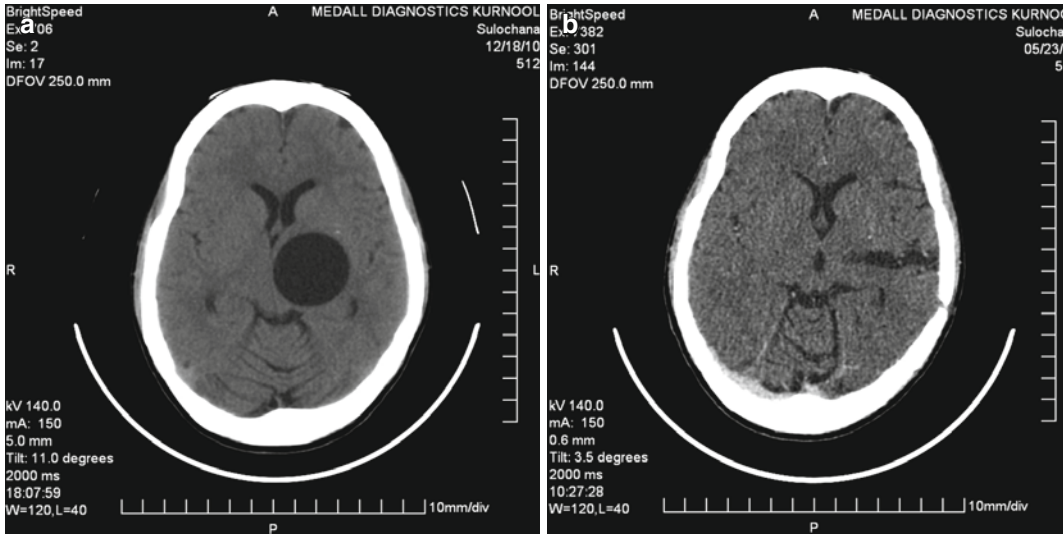


Fig. 19.3 (**a**, **b**) The best surgical outcomes are recorded also in cases of hydatid disease of the central nervous system when the lesion is primary solitary and even if it is located in deeper areas of the brain as shown above. This kind of lesion needs planning and requires microsurgical methods for excision without spillage. Same is true for rare primary spinal epidural and intradural and extramedullary lesions. Scans shown in this figure belong to a 24-year-old lady from an endemic area of hydatid disease. Picture on the left is before surgery, and the scan on the right side is after the total excision of solitary primary lesion. Microscopic excision is helpful in these cases which provide good illumination and careful dissection. Adults seek treatment earlier, and the lesions tend to be smaller in size as compared to those of children where the cysts grow to a large size and their excision without breaking of the cyst may sometimes be difficult due its sheer size with thin walls especially towards the ventricle

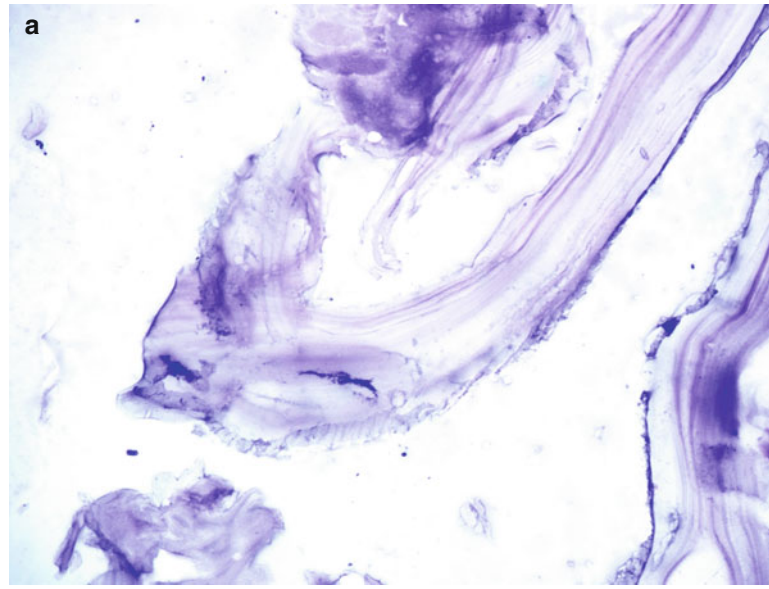
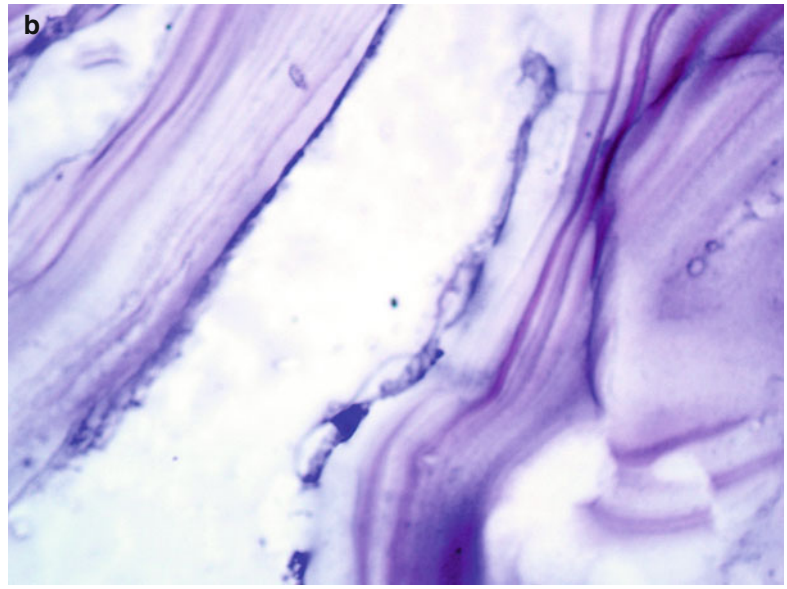


Fig. 19.4 (**a**, **b**) Laminated membrane of the hydatid cyst wall with an inner germinal layer. Hematoxylin and eosin magnification 110× on left (**a**) and 200× (**b**) on the right side, respectively

Fig. 19.4 (continued)



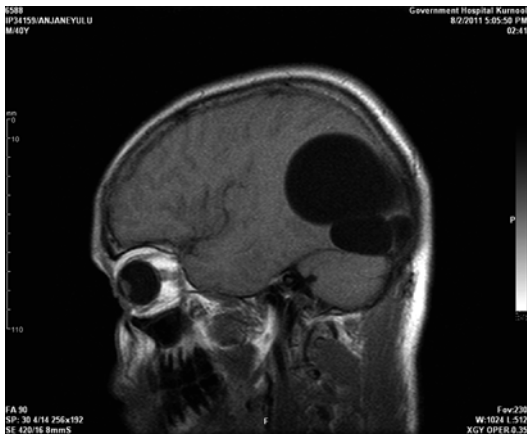


Fig. 19.5 A 40-year-old male with right parieto-occipital primary multiple hydatid cysts in close proximity

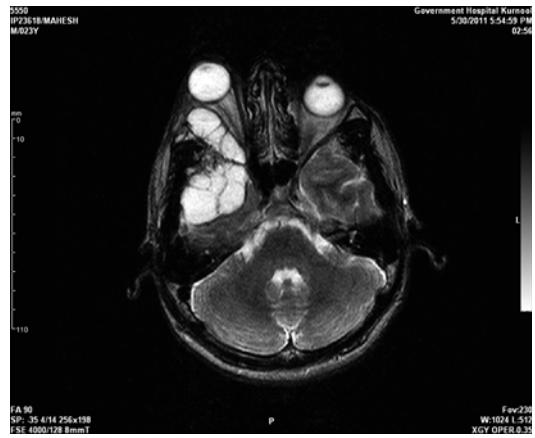


Fig. 19.6 A 23-year-old male with recurrent hydatid cysts involving the orbit, frontal, and temporal regions

from reoperative surgery since the recurrent cysts may be without a brood capsule and hence they may not recur again. Intact excision was possible in 119 cases out of 137 cases of cerebral hydatid disease (Turgut 2002). In 22 % of cases, recurrence was noted and surprisingly recurrence occurred in 7 of the cases which were removed intact. Recurrence was expected in such of those cases which ruptured during surgery, and these were 7 out of 31 (Turgut 2002). Recurrence in those cases depends upon the presence of live protoscolices, and these can be estimated per field, and it is also known that fertile cysts contain malate fumarate along with other resonances. Greatest number of viable protoscolices was observed in multiple cysts in comparison to single cysts (Manterola et al. 2006). Preoperative studies will help in planning the surgery as well

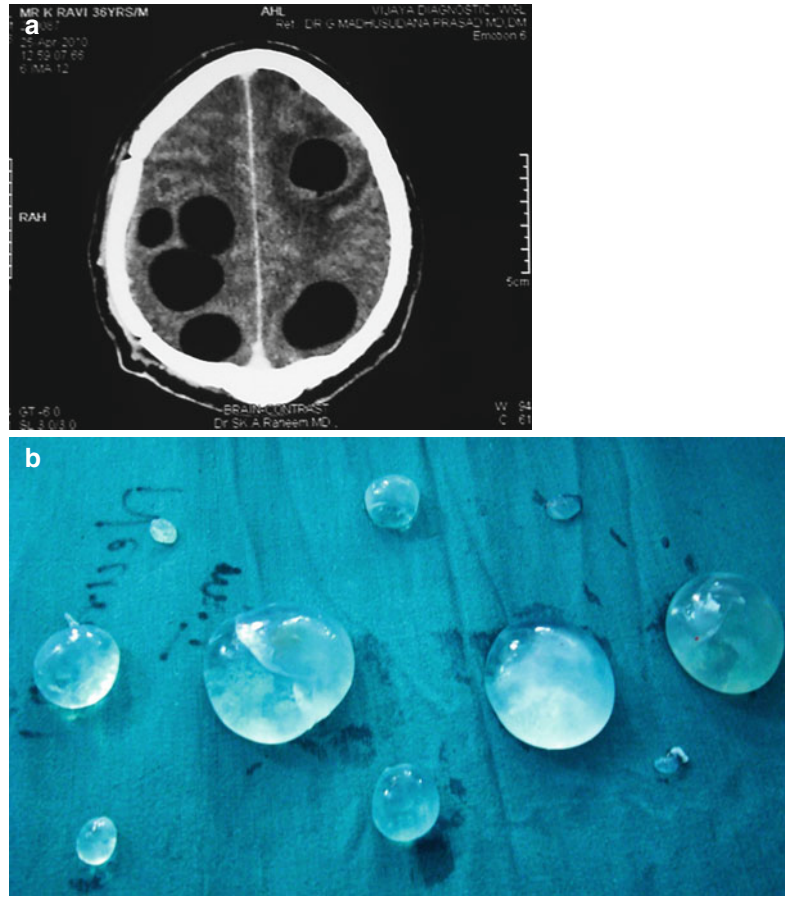


Fig. 19.7 (**a**, **b**) A 34-year-old male with recurrence after rupture during first operation. There were six large lesions and a few smaller lesions which were all removed with good outcome

as the precautions that should be taken to avoid risks of surgery. Microscopic surgery gives good illumination and helps in proper dissection of the cysts. Cyst rupture during surgery is always critical, and the recurrence depends upon whether the lesion is primary or secondary. In one study with long-term follow-up, out of 29 cases operated, 18 were removed intact and 8 cases ruptured, of which 5 are dead (63 %) and they were all primary. In contrast 3 cases also ruptured and they were secondary and they are alive proving that secondary lesions are not fertile. Recurrence after rupture is a problem, and even if there are many lesions, they should be removed and the results can be gratifying (Fig. 19.7). The complications of cerebral hydatid cyst surgery are not uncommon which require prompt diagnosis and treatment (Tuzun et al. 2010). Subdural effusion and porencephaly are the delayed complications, whereas hemorrhage in the operated site and extradural hematomas are immediate problems. Rarely there could be infected hydatid cysts which need antibiotic coverage (Obrador and Urquiza 1948; Arana-Iniguez and Julian 1954).

Medical Treatment

Medical treatment may be chosen if patients are not eligible for surgery or the cysts are present in many organs. Albendazole, mebendazole, and praziquantel are the main drugs used as antiparasitic medication for the treatment of echinococcal infection (Davis et al. 1989; Gil-Grande et al. 1993). Albendazole is a broad-spectrum benzimidazole which is preferred over mebendazole because it is better absorbed and achieves higher blood, cyst wall, and fluid

concentrations. Both act by inhibition of tubulin polymerization resulting in the loss of cytoplasmic microtubule formation inhibition and the inhibition of the glucose uptake of the parasites leading to cell autolysis (Silva et al. 2004; Kappagoda et al. 2011). Albendazole sulfoxide, the active metabolite, reaches predictable levels in serum after an oral dose; cyst fluid levels are slowly reaching therapeutic levels and are less predictable; thus a prolonged duration of treatment is required. It is effective against the larval forms of echinococcal infection. Albendazole results in disappearance of up to 48 % of cysts and a substantial reduction in size of the cysts in another 28 %. It is another drug for the treatment of hydatid disease, but it does not produce adequate serum levels which are able to kill the germinal membrane alone and can be used along with albendazole. It increases serum concentrations of albendazole to the fourfold and can be used in combination, which is advisable (Sihota and Sharma 2000; Jamshidi et al. 2008). The duration of anthelmintic treatment could be up to 5 months or longer. Anthelmintic therapy is beneficial and indicated in patients with spillage or in those patients with disease in other parts of the body, like the liver and lungs. Severe disease in organs other than the CNS may be responsible for delayed deaths. The response to albendazole treatment for cerebral hydatid disease can be monitored with CT and MRI imaging (Kalaitzoglou et al. 1998). There are reports that a viable residual spinal hydatid cyst disappeared with albendazole therapy (Baykaner et al. 2000). Preoperative combination chemotherapy is more effective for post-spillage prophylaxis than albendazole or praziquantel alone (Morris 1987). There are also reports claiming that albendazole is not effective in the treatment of hepatic hydatid cysts (Kapan et al. 2008).

Hydatid Disease in Other Parts of the Body

Presence of hydatid lesions in other parts of the body also determines the outcome of treatment (Fig. 19.8). In a recent study, six cases of intracranial hydatid cysts were operated, but two of these subsequently died from severe forms of liver involvement sometime later (Wang et al. 2009). These cases had no recurrence of cerebral lesions even though they were removed piecemeal. Liver transplantation is now possible in cases with hepatic hydatid disease. Same may also happen in the cases with involvement in other parts of the body such as the lungs. Turgut (1997) reviewed the hydatid disease of the spine in Turkey and reported that 14 out of 18 cases of hydatid disease had pulmonary involvement. Naturally, disease in other parts of the body dictates the outcome of hydatid involving the CNS.

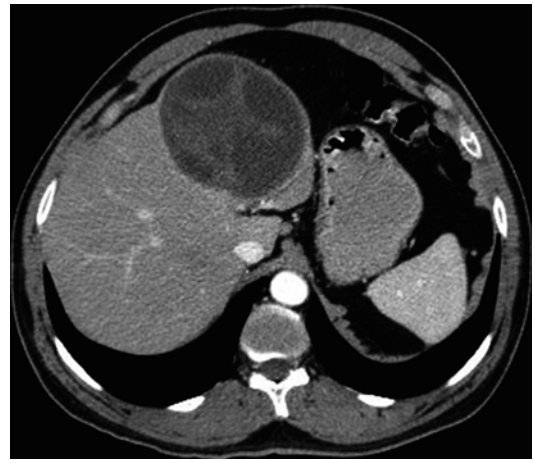


Fig. 19.8 Central nervous system hydatid disease with involvement of liver that determines the ultimate outcome of the patient. Echinococcosis of the alveolaris type invariably has the liver involvement, and their survival depends upon the liver status

Delayed Complications

Sometimes hydatid cyst could be associated with other primary lesions of the brain such as acoustic neurinoma and glioma. Prognosis depends upon the other associated disease (Cohen et al. 1997). Delayed development of glioma at the same site of previous hydatid cyst raises the doubt whether constant irritation may be responsible for its development (George et al. 2003). But glioma development in this case could have been incidental also.

Outcome and Prognosis of Hydatid Disease Involving the Central Nervous System

Hydatid disease causes considerable mortality and morbidity, and a large population around the world is affected by the disease (McManus et al. 2003). Surgical removal of the clinically symptomatic primary cysts is curative, and treatment with anthelmintics in nonoperable cases is only palliative. Long-term experience of the treatment of alveolar types of hydatid disease is not rewarding (Pau et al. 1987; Reuter et al. 2001; Buttenschoen and Buttenschoen 2003; Buttenschoen et al. 2009). Forty-two percent of cases were cured, and in the remaining 58 %, palliative treatment alone was possible.

The Australian Hydatid Registry contained 1,802 cases by the end of 31 March in 1945, and only 16 of the cases showed a brain involvement. The registry estimated the deaths from hydatid disease as 16.6 %, but they cautioned that this number was fallacious since this was the number of patients with hydatid disease who died in hospitals (Barnett 1936). In a survey the number of hydatid deaths till then were given as 276, but the actual number of dead was 534 because more deaths occurred in the homes of the diseased. Probably the best strategy of any public health policy should be prevention and control of the hydatid disease. Each country needs to find the echinococcal species causing the disease and the definitive and intermediate hosts responsible in the life cycle of the parasite (Palmer et al. 1996). In some countries both forms of the disease, *E. granulosus* and *E. alveolaris*, may be prevalent. For India the definitive host is the domestic dog and the intermediate hosts are sheep, goat, and cattle. In a study on the incidence of hydatid infestation in intermediate hosts in Kurnool of Andhra Pradesh, India infection rates of goats, sheep, and cattle were 16.96, 21.75, and 60.94 %, respectively. 33.3 % of dogs were positive in Kurnool region (Reddy et al. 1968; Reddy and Murthy 1986). These facts emphasize the importance to control the disease in intermediate hosts and definitive hosts to contain the hydatid disease (Reddy 2009).

Conclusion

Long-term outcome of cerebral hydatidosis can be summarized as follows: (1) Surgical treatment remains the preferred management of active hydatid disease involving the brain; (2) the best surgical outcomes are recorded in cases of cystic hydatid disease where the lesion is primary solitary and is located in an accessible area which can be excised without rupture; (3) the excision of alveolar type of echinococcosis is only palliative in nature; and (4) the presence of hydatid disease in other parts of the body besides the brain determines the long-term outcome of cerebral echinococcosis.

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Outcome and Follow-up of Patients with Spinal Hydatidosis

20

Lukas K. Postl and Chlodwig Kirchhoff

Contents

Introduction

The following chapter focuses on outcome and follow-up of patients suffering from spinal hydatidosis, i.e., the cystic as well as the alveolar form. In general, intraspinal hydatidosis differs from the intracranial form not only regarding the primary manifestation and treatment but also regarding follow-up and recurrence. Although several characteristics apply to the cystic as well as the alveolar form, detailed information is provided separately in each specific section.

The intraosseous growth of hydatid disease progresses relatively slowly and asymptomatically, developing diverticulated cysts along the intratrabecular spaces. Usually hydatid disease becomes clinically symptomatic in the extraosseous stage, when cysts excavate into the extradural and paraspinal regions, compromising nerve roots and the spinal cord causing objective sensory and motor disturbances at the level of the involved vertebrae (Herrera et al. 2005; Sengul et al. 2008; Belhassen-Garcia et al. 2011). However, local recurrence of hydatid disease does not typically begin in the vertebral body. But it also can relapse in the paravertebral, paraspinal, or intraspinal portion and therefore become clinically apparent early after negative restaging. Several authors describe a "malignancy" or "white cancer" when reporting on hydatid disease (Haddad et al. 1963; Turgut 1997; Viljoen and Crane 2008).

According to our opinion every patient suffering from hydatid disease needs a clearly structured aftercare and follow-up calendar including

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physical examination, imaging, as well as serologic tests. This follow-up should also be individualized and consider the surgical progress, i.e., in case surgical spreading of the echinococcosis is likely, the follow-up needs to be adapted. Regarding the best follow-up imaging modality, it can be stated that hydatid extension into the extradural space or para-osseous soft tissues may not be detected by spine radiographs (Bron et al. 2007; Celik et al. 2010).

The imaging features of intraspinal hydatid cyst usually comprise multiple spherical lesions with clearly defined borders, containing fluid that is similar to cerebrospinal fluid (CSF) in intensity on both computed tomography (CT) scan and magnetic resonance imaging (MRI). Due to the need for repetitive scanning on a regular basis, for several reasons, we regard MRI as the imaging technique, since it allows for an early diagnosis of spinal cord compression and for a more accurate localization of intra- and paraspinal manifestation if multiplanar images are acquired (Pamir et al. 2002; Limaiem et al. 2010). On MRI it is possible to detect both the exact anatomical location of the lesion and the viability of the hydatid cysts. On T2-weighted images, a cystic lesion has a high intensity, whereas a decrease in signal indicates a necrotic cyst. Thus, a decreased signal in this sequence is a characteristic indicator for a necrotic cyst. Furthermore, the layers of the cyst can only be demonstrated by MRI, and the pericyst may show enhancement after contrast material administration due to its rich vascularization. Figures 20.1 and 20.2 demonstrate MRI findings.

Localization

The outcome of hydatid disease significantly depends on the location of the lesions. In this context the classification of Braithwaite and Lees provides an initial reference for the expected outcome (Braithwaite and Lees 1981). According to their anatomic location, cysts can be divided into intramedullary, intradural-extramedullary, extradural, spinal (vertebral), and paraspinal lesions extending into spinal structures. Besides these anatomic references, especially the spinal level influences the neurologic outcome. There is a remarkable difference regarding the outcome between cervical, thoracic, lumbar, and sacral manifestations of the spinal hydatid disease, especially in advanced stages when irreversible nerve tissue damage exists.

Aftercare

Surgical decompression and chemotherapy are the principal forms of treatment in pediatric and adolescent cases of spinal hydatidosis. Unfortunately even with extensive surgery, results are far from being curative. The recurrence and mortality rates for intraspinal hydatid disease range up to 50 and 15 %, respectively (Taratuto and Venturiello 1997; Toussaint et al. 2001; Wang et al. 2009). Up to 40 % of patients are reported to have recurrent symptomatology within 2 years after the initial operation (Spies et al. 2008; Takci et al. 2008; Taghipoor and Razmkon 2009). As the recurrence rate is high, adjuvant anthelmintic agents are recommended following surgery. Anthelmintic drugs are strongly recommended in case of recurrence, systemic disease, intraoperative rupture or puncture, poor suitability for surgery, and prophylaxis (Papagelopoulos et al. 1997; Schnepper and Johnson 2004; Romig 2009; Sharma et al. 2011). However, a clearly structured aftercare and follow-up calendar including physical examination, imaging, as well as serologic testing is mandatory. In parallel to the aftercare of soft tissue sarcoma, we recommend restaging every 3 months for the first 2 years. This should include CT scans of the abdomen and MRI of the spine. In the following the intervals can be reduced to twice a year up to year 5 and once a year until year 10 after onset of the disease.

The imaging features of intraspinal hydatid cyst usually comprise multiple spherical lesions with clearly defined borders, containing fluid with similar CSF intensity on both CT and MRIs. Though, due to the need for repetitive scanning on a regular basis, we regard MRI for several reasons as the best imaging technique, since it allows early diagnosis of spinal cord compression and

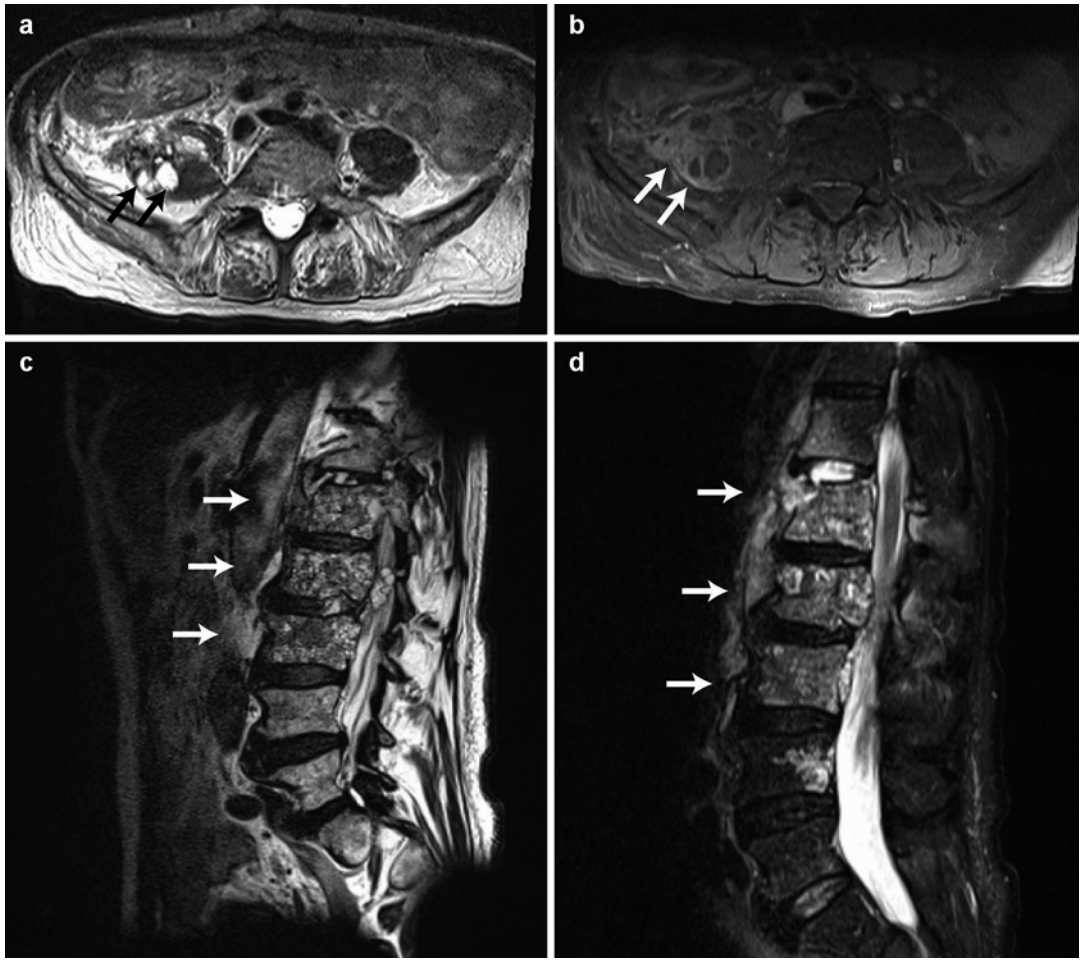

Fig. 20.1 The figure demonstrates the MRI findings of an 80-year-old male patient, initially presenting with recurrent abdominal pain and pain in the upper lumbar spine from lumbar vertebrae L1 to L3 without neurological deficit. (**a**) The T2-weighted axial MRI shows multiple small hyperintense lesions in the right psoas muscle (*arrows*). The corresponding fat-suppressed T1-weighted image after gadolinium administration (**b**) confirmed the diagnosis of a multicystic mass and delineated the thickened, contrast-enhancing septations around the cystic components (*arrow*). T1-weighted image (**c**) and T2-weighted STIR image (**d**) of the lumbar spine show the bone marrow replacement within the first, second, and third lumbar vertebrae (*arrows*). The lesions comprise of cystic and solid components

more accurate localization of intra- and paraspinal manifestation if multiplanar images are acquired. On MRI it is possible to detect the exact anatomical location of the lesion and to show the viability of the hydatid cysts. On T2-weighted images, a cystic lesion has a high intensity, and a decrease in signal indicates a necrotic cyst. Thus, a decreased signal in this sequence is a characteristic indicator of a necrotic cyst. Furthermore, the layers of the cyst can only be demonstrated by MRI, and the pericyst may show enhancement after contrast material administration due to its rich vascularization. In particular positron emission tomography scanning in combination with CT scan or MRI might show active lesions at a time when clinical symptoms are absent or unspecific and recurrence of parasitic tissue is not detectable by conventional imaging (Brunetti et al. 2010). Imaging of spinal hydatid disease is discussed in Chap. 12.

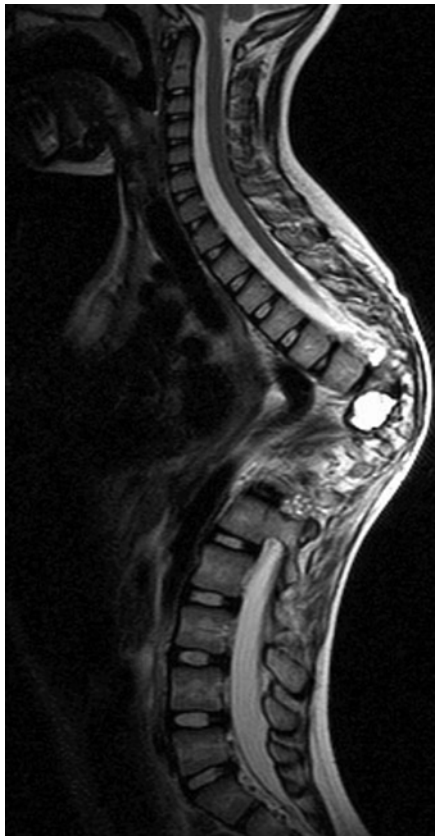

Fig. 20.2 The figure presents the MRI of a 6-year-old girl with primary *Echinococcus granulosus* infection of the spine being treated with various interventions. Now presenting recurrence of infection due to incomplete cyst resection and inappropriate surgical measures causing progressive kyphoscoliotic deformity, spinal stenosis, cord compression, and neurologic injury. At the presentation at our institution, she was wheelchair bound. The clinical investigation revealed gibbus in the middle thoracic spine with a Cobb angle of 110°, cord compression at the apex, and paraplegia with Frankel Grade C

Blood tests should include benzimidazole blood levels as well as serological tests (Nell et al. 2011). Determination of benzimidazole blood levels, 4 h after the morning dose, is recommended 1, 4, and 12 weeks after initiating drug therapy. Detection of antibody directed to echinococcal polypeptide antigens has the highest degree of specificity. Enzyme-linked immunosorbent assay (ELISA), indirect hemagglutination, and complement fixation tests are reported to be 80–100 % sensitive and 88–96 % specific in abdominal disease. However, the sensitivity decreases abruptly to 25–56 % in extrahepatic disease which limits their use in the diagnosis or follow-up for primary bone disease. Second-line tests like immunoblotting (antigen 5 precipitation: arc-5 test) may be used for confirmation after ELISA and hemagglutination. Laboratory findings of patients with spinal hydatidosis are discussed in Chap. 10.

Benzimidazole Treatment

Albendazole should be administered orally at a dose rate of 10–15 mg/kg/day divided into two doses (WHO 1996). In practice a daily dose of 800 mg is applicable to adults. Intermittent or cyclic treatment is no longer necessary, since albendazole treatment is well tolerated and it has been reported that a dose rate of 20 mg/kg/day is tolerated for up to 5 years. Alternatively if albendazole is not enough tolerated or available, mebendazole could be administered at a daily dose rate of 40–50 mg/kg/day. Benzimidazoles are generally well tolerated. Adverse reactions include hepatotoxicity, alopecia, gastrointestinal disturbances, and leucopenia (Vuitton 2009). Moreover the only contraindication for benzimidazoles is pregnancy. Albendazole is the most widely used benzimidazole worldwide. Benefits of albendazole are a better bioavailability to achieve higher plasma levels, an easy administration, and an overall better efficacy. However, benzimidazoles in general are only parasitostatic and do not erase *E. multilocularis* metacestodes.

Cystic Echinococcosis

Neurological Deficit

The neurological and orthopedic symptoms can often be reduced or eliminated by surgery and/or anthelmintic treatment for a certain time, but very often only a short follow-up is reported, and it remains doubtful if the patient was cured (Arif and Zaheer 2009; Kotil et al. 2010; Thaler et al. 2010; Scarlata et al. 2011). In recurrent cases multiple interventions can be reasonable to

preserve or even improve the spinal stability and the neurological status, but cure of disease is usually not possible (Keller et al. 1997).

Treatment Characteristics

Benzimidazole treatment is recommended for a period of at least 3 months. Although these drugs are well tolerated, Pamir et al. (1984) do state that there is no clear evidence that further administration is lowering the recurrence rate. Nevertheless, Turgut (1997) report that the drugs could effectively keep the disease asymptomatic for a prolonged time.

Several authors stress that imaging should not be the only means for diagnosing a recurrent disease, because a residual cavity is very hard to differentiate. In this regard symptoms seem to have a certain impact. Lawn et al. (2004) found that during post-surgical follow-up, the immunoglobulin G subclass IgG2 antibody response provides a reasonable correlate of disease activity, and Nouir et al. (2008) found that immunoblotting can be a useful approach for monitoring post-treatment follow-up.

Recurrence Rate

Recurrence During Anthelmintic Therapy

Conservative treatment seems to be effective and the recurrence rate of conservatively treated patients is significantly lower than the rate of surgically treated patients without chemotherapy. Nevertheless, very often patients present with neurological symptoms that urgently require surgical decompression.

Recurrence After Surgery

Total excision of the cysts should be the aim of treatment, but in the majority of cases, this cannot be obtained and recurrence is reported. Therefore up to 40 % of cases show recurrence within 2 years of initial operation (Turtas et al. 1980). Nevertheless, the excision of intradural and extradural lesions without osseous involvement could theoretically be curative when the cysts remain intact (Bettaieb et al. 1978; Pamir et al. 1984). But in most cases a complete removal of cyst cannot be performed without damaging the nerve roots (Turgut and Turgut 2010). Osseous involvement causes a multivesicular and diffuse infiltration of the vertebrae (Ozek 1994). Due to this fact the surgery at the vertebrae will lead to spillage of the scolices (Baysefer et al. 1996; Islekel et al. 1998). In this context Turgut (1997) were able to show that the recurrence rate of spinal lesions is significantly higher (33 %, $n=41$) than the rate of intraspinal lesions without or minor bone involvement (<6 %, $n=27$). Both surgery and anthelmintic therapy should be considered. Some authors recommend administering lifelong chemotherapy. Most patients suffer from multiple recurrences, worsening of disease, and very often restoration of the spine to improve and preserve neurological status and spine stability.

Prognosis

The recurrence rate is reported in up to 40 % of all cases, but the recurrence probability for a single case depends very much on the localization of the lesion and in case of a surgery on the progress of the intervention. The literature does provide case reports and reviews, but larger studies on echinococcosis of the spine are scarce. Most publications only report on a period of a few years post operation, and reliable data on, e.g., the survival time for cases with spine affection, is missing.

Alveolar Echinococcosis

Treatment Characteristics

Although postoperative benzimidazole therapy is obligatory in all cases, generally accepted guidelines concerning presurgical anthelmintic treatment and the duration of treatment after surgery are not available. Brunetti et al. (2010) recommended temporary treatment after complete

resection. Reuter et al. (2000a, b) require a benzimidazole treatment for a period of at least 2 years post surgery, since residual echinococcosis might remain undetected and follow-up of patients should be at least 10 years. In cases of a subtotal surgery or in inoperable cases, long-term or even lifelong benzimidazole therapy is necessary. Ammann and Eckert (1996) provided evidence that long-term benzimidazole therapy in subtotal resected lesions causes a significant improvement of the 10-year survival rate. According to the authors the 10-year survival rate in an untreated historical control group was found to be 6–25 % and could be increased to 80–83 % in patients receiving long-term benzimidazole therapy. Further long-term anthelmintic treatment also lowers the recurrence rate (Torgerson et al. 2008).

Serological tests in the follow-up seem to be predicative. Scheuring et al. (2003) reported that anti-Em2 and anti-Em18 antibodies rapidly decreased after total resection of lesions and became undetectable. Serological analysis in the follow-up provides reliable information about clinical status and efficiency of treatment of patients with alveolar echinococcosis; thus there is a close relationship between clinical regression and specific serology (Tappe et al. 2009). But unfortunately in patients with subtotal resections and under benzimidazole treatment, the interpretation of serological test is more complex.

Recurrence Rate and Prognosis

Reliable data on recurrence prognosis of the spinal alveolar echinococcosis is even scarcer than data on the prognosis of the cystic echinococcosis. Only a few cases have been published so far (Claudon et al. 1987; Duewell et al. 1990; Merkle et al. 1997; Reuter et al. 2000a, b; Sudo and Minami 2010). For alveolar echinococcosis in general (for all lesions and not only for lesions of the spine), it has been stated that treatment had improved average life expectancy at time of diagnosis—while it had been 3 years in the 1970s, it has reached 20 years in 2005 (Nouir et al. 2008). The recurrence rate seems to be lower under benzimidazole treatment.

Conclusion

Based on our experience and literature data on spinal hydatidosis, the following points are concluded:

1. The outcome will differ for cases of cystic echinococcosis and alveolar echinococcosis.
2. The location of the lesions will strongly influence the outcome and should be considered regarding follow-up.
3. Structured aftercare and follow-up calendar including physical examination, imaging, as well as serologic tests are crucial.
4. Surgical decompression and chemotherapy are the principal forms of treatment in cases of spinal hydatidosis. Unfortunately, even with extensive surgery, results are far from being curative.

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Unusual Presentations of Hydatidosis of the Central Nervous System

21

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Contents

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Introduction and General Data

Hydatid disease is an anthropozoonosis caused by the larval cysts of *Echinococcus granulosus*, a small, cosmopolite, cyclophyllid cestode (tape worm) currently found throughout the world.

History of hydatidosis is given in detail in Chap. 1 of the book.

Morphology and Classification

Currently, the *Echinococcus* genus (of the *Taenoides* family) is represented by four subspecies which were found in human beings: (1) *E. granulosus*, (2) *E. multilocularis*, (3) *E. oligarthus,* and (4) *E. vogeli* (Eckert et al. 2001).

The subspecies of hydatidosis in the world are discussed in Chaps. 2, 3, and 4.

Unusual Manifestations of Craniocerebral Hydatid Disease

By unusual presentations of hydatid disease, we understand the extremely rare situations that some clinicians might never actually see in their practice. The cases mentioned here come as a result of personal experiences of the authors and a review of the world literature.

Hydatid disease can theoretically be positioned anywhere within the skull, thanks to its hematogenous dissemination. From the known data in the literature, we mention hydatid disease

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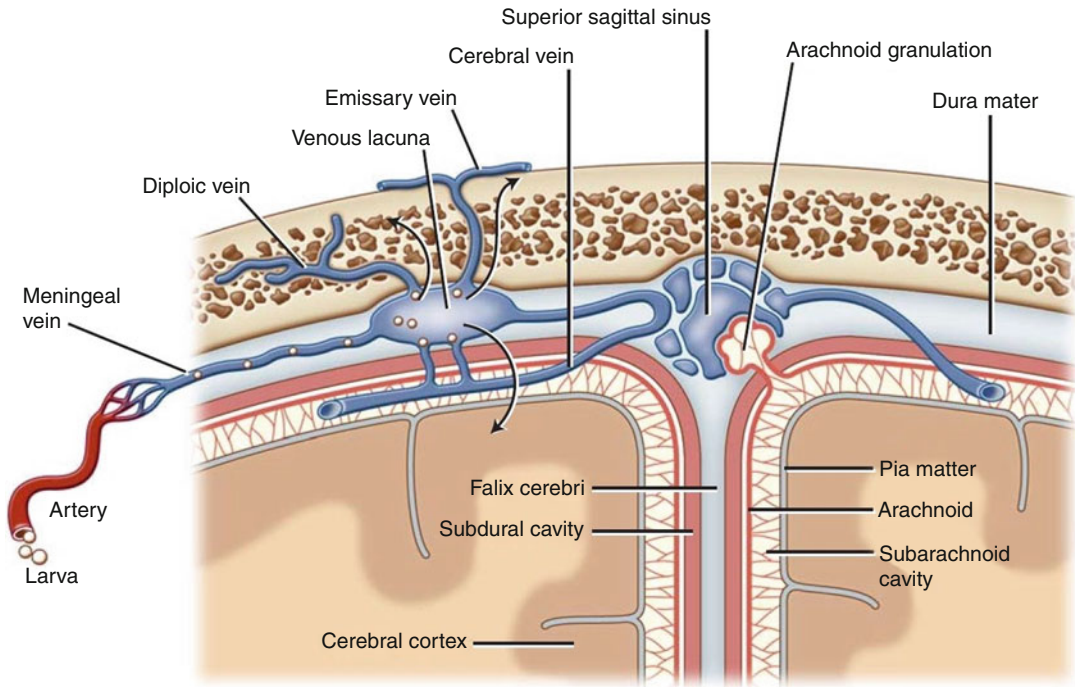

Fig. 21.1 The vascular dissemination of hydatidosis

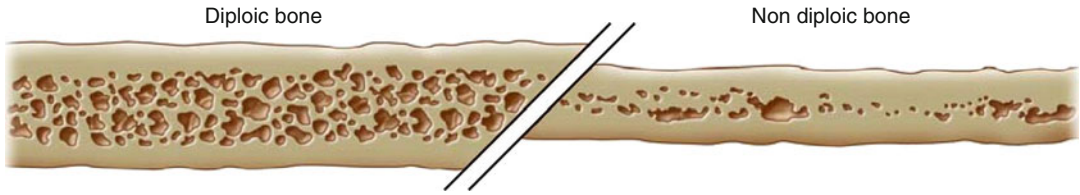

Fig. 21.2 Diploic vs. nondiploic sagittal bone section

positioned in the epidural space, within the meninges (intradural), subdural, subarachnoid, intracerebral, intraventricular, periventricular, cisternal, intrasinusal (vascular), in the brainstem, in the thalamus, and in the bony skull. All these manifestations are considered to be completely unusual. Among these, the most frequent are those located within the tissue of the central nervous system (CNS) due to the intense vascularization of the brain and better conditions for the larvae of *E. granulosus* (Fig. 21.1).

Calvarium

Hydatid disease in the calvarium is usually the rarest in the CNS. Anatomically, the bones of the calvarium, which has a protective function toward the brain, are made of one layer of spongious bony tissue flanked on the outside and on the inside by two other layers of compact laminar bone tissue such is the case of diploic bones (Figs. 21.2 and 21.3).

The bones of the base of the skull are nondiploic and the core spongious bony tissue may be very little represented or absent. While bones of the calvarium are more prone to destruction by hydatid cysts, the bones of the skull base can also be involved, although this situation is much rarer (Fig. 21.4). The first one to describe bone destruction as a consequence of hydatid cysts in the skull was Monro in 1811 (Arseni et al. 1981). There were other scarce presentations in the literature of hydatid disease in the diploe (in 1872 by

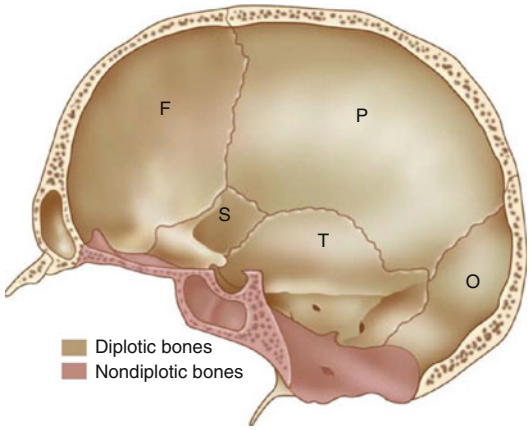

Fig. 21.3 Sagittal cut-through section of the skull showing the distribution of the diploic and nondiploic bones. *F* Frontal bone, *P* parietal bone, *T* temporal bone, *S* sphenoid bone, *O* occipital bone

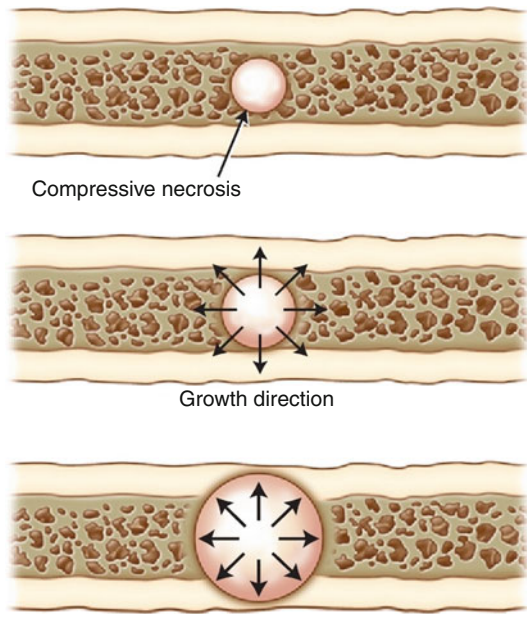

Fig. 21.4 Hydatid cyst growing in the diploe. The inner and outer tables are gradually spread apart by the eccentrical growth of the cyst

Verdale, in 1901 by Herrera and Cranwell, in 1909 by Goyanes). Felix Deve himself managed in 1949 to gather 637 cases of hydatid disease in the skeleton, of which 22 cases were positioned at the level of the calvarium (quoted from Arseni et al. 1981). Another peculiar manifestation of hydatidosis is in the petrous part of the temporal bone. Three such cases were presented in the literature by Schroeder et al. 1953 (quoted from Arseni et al. 1981).

The pathogenic mechanism of hydatid disease in the calvarium is quite difficult to explain. Arseni and Samitca mention in 1957 in their monograph regarding hydatidosis a single case of hydatid disease in the cranial vault. As to the bones of the skull base, researchers such as Arana Iniguez showed that 7.6 % out of 145 cases of cerebral hydatid disease attacked the bony structures, especially the petrous portion of the temporal bone (quoted from Arseni et al. 1981). Recently, a case in which an *E. granulosus* cyst produced a brain abscess in a 28-year-old patient has been reported (Llanes et al. 2008). In this case, the evacuation of the brain abscess was performed with a combined otolaryngologic and neurosurgical procedure (canal wall down mastoidectomy and temporal craniotomy) (Llanes et al. 2008). Another rarity we found in skull vault-related unusual presentations of hydatidosis is the presence of the disease in the viscerocranium – especially the sinuses. The maxillary sinus (Goldsher et al. 1983) and maxillary antrum (Copley et al. 1992) are two of the rarest locations for hydatidosis in the skull even in the endemic areas across the world.

The surgical approach for hydatid cysts in the skull vault doesn't present too many surgical difficulties. Many authors recommend an oval incision in the skin, in the form of a horseshoe to provide an intact removal of the hydatid cyst penetrating the calvarium. In endemic areas, the diagnosis must be clearly made, absolutely without biopsy and without compromising the integrity of the cyst in the subjacent structures including the bone and meninges. In non-endemic areas, a case of multifocal hydatidosis, metastasized or polycystic, has to be correctly diagnosed. In this respect, all the investigative data has to be correlated so that the diagnosis and surgical approach are not carried out inappropriately (Fig. 21.5). One case stands out. It is the case of a 14-year-old boy which after birth started showing a particular progressive deformity of the calvarium. Despite what looked like hydrocephalus or scaphocephalus, the child showed satisfactory results in school. The child started suffering from latero-cervical

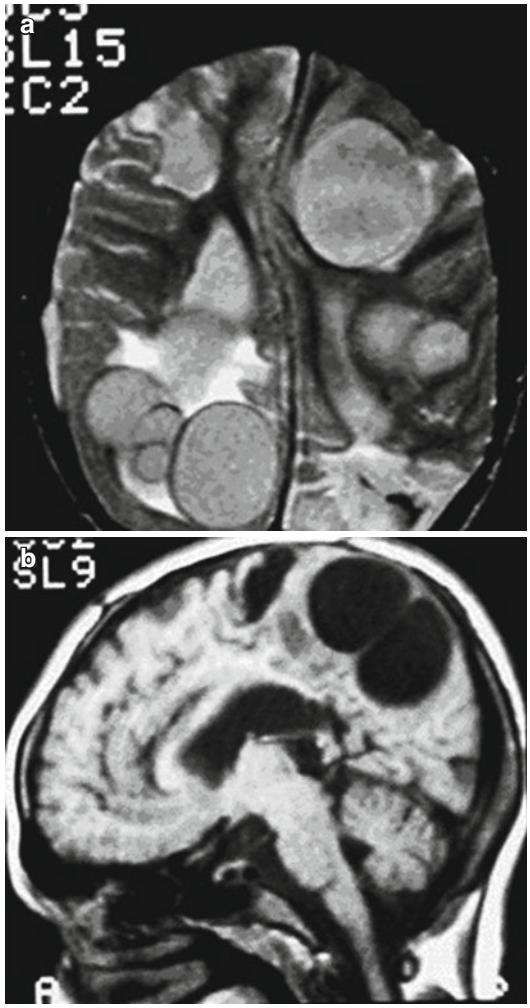

Fig. 21.5 Axial (**a**) and sagittal (**b**) MRIs of multiple hydatid cysts in the brain

pain which irradiated to the back of the head and associated with nausea and lately with intermittent vomiting. The radiograph showed a characteristic cyst-like formation 12 cm in length and 5 cm thick. Once opened, the calvarium contained more than 80 microcysts ranging from 3 mm to 5 cm. At the periphery of the cyst, the calvarium measured 1.5 cm in thickness. The depressed inner sheath of the bone was also removed (thus complete craniectomy was achieved) with a minimal blood loss and well-tolerated surgery. A few hours after surgery, shock installed; however, the patient managed to withstand due to glucose serum and blood perfusions. Twelve hours postoperative the patient started showing right-sided hemiplegia with cerebral edema. Gradually the patient recovered and left the hospital with a minimal deficit which was completely resolved 4 months after surgery (Fig. 21.6).

The hydatidosis of the skull is discussed in Chap. 5 in detail.

Craniocerebral Extradural

Extradural hydatid disease occurs at the moment when one or more *E. granulosus* oncospheres end up via the bloodstream in the epidural space of the cerebrospinal axis; this includes the skull and spine. The space we are referring to consists of the space enclosed between the outer surface of the dura mater and the internal surface of the skull which continues through the foramen magnum downward with the internal surface of the spinal canal, lined by the tectorial membrane, posterior longitudinal ligament, and yellow ligament and is filled with the peridural adipose tissue (Figs. 21.7, 21.8, and 21.9).

After the larva has penetrated the inner bone layer, it will grow outside of the dura mater, developing into a substantial cyst of viscous consistency. The cyst will then compress the brain matter leading to the characteristic symptoms. The clinical features of this manifestation are dominated by the slow evolution of the cyst which is translated into a raised intracranial pressure syndrome and diminished visual acuity. Patients usually end up at the hospital when the cyst has exaggerated dimensions (Arseni et al. 1981). Sporadic manifestations of extradural hydatidosis in the literature have also been found more recently (Sharma et al. 2010). The extradural meningeal space is generally affected during a multifocal hydatid disease (Siddiqui et al. 2010).

Interesting enough is the fact that more and more unusual manifestations of extradural hydatid disease appear in the literature. We mention only for historical purpose six cases (Arseni et al. 1981).

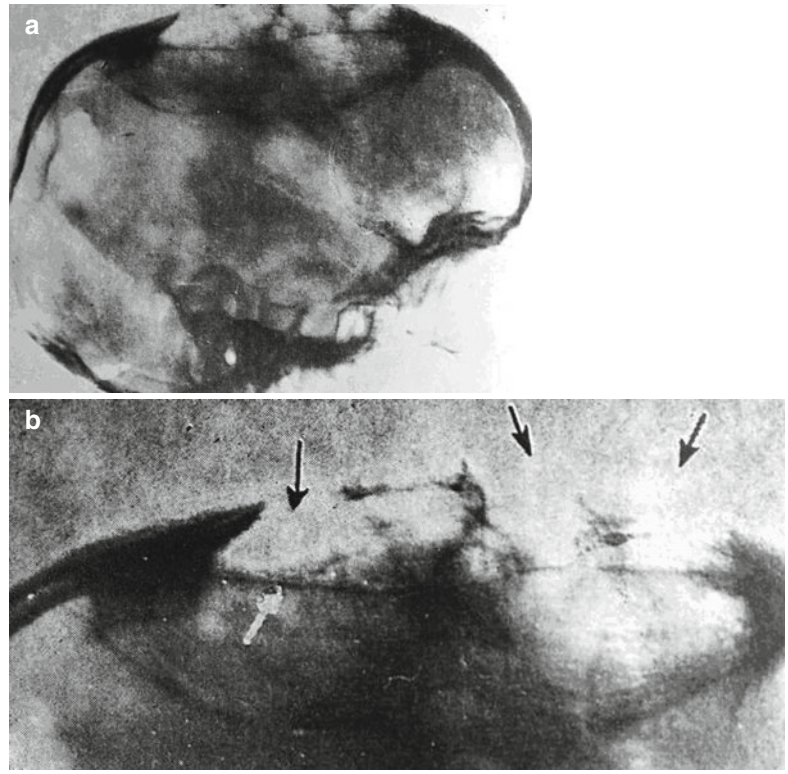

Fig. 21.6 (**a**) Lateral radiograph showing the cyst. Note the length and the width of the displacement of the inner and outer sheath of the calvarium. (**b**) Radiograph centered on the cyst. *Arrows* represent areas where the hydatid cyst has destroyed the outer sheath of the calvarium

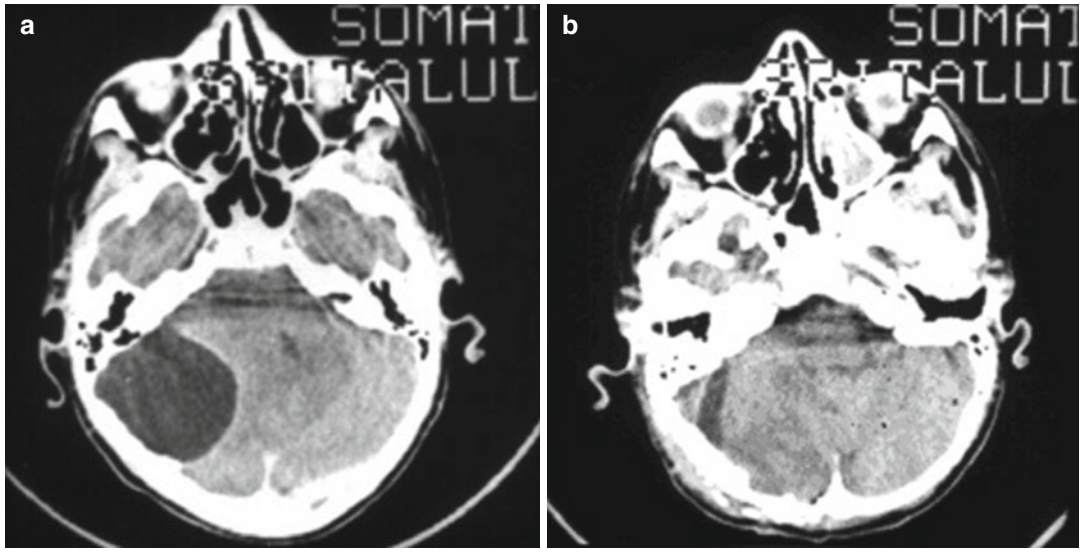

Fig. 21.7 Preoperative (**a**) and postoperative (**b**) aspects of an extradural hydatid cyst in the posterior fossa

We describe two such cases: one is mentioned in the literature in 1949 (Arseni et al. 1981). Here, the patient, a young child, had a large destruction of bony substance associated with an enormous cyst 425 cm^3 in volume that contained nine daughter cysts which varied in size. The child died 4 days after surgery as a result of violent epileptic seizures triggered by 100,000 units

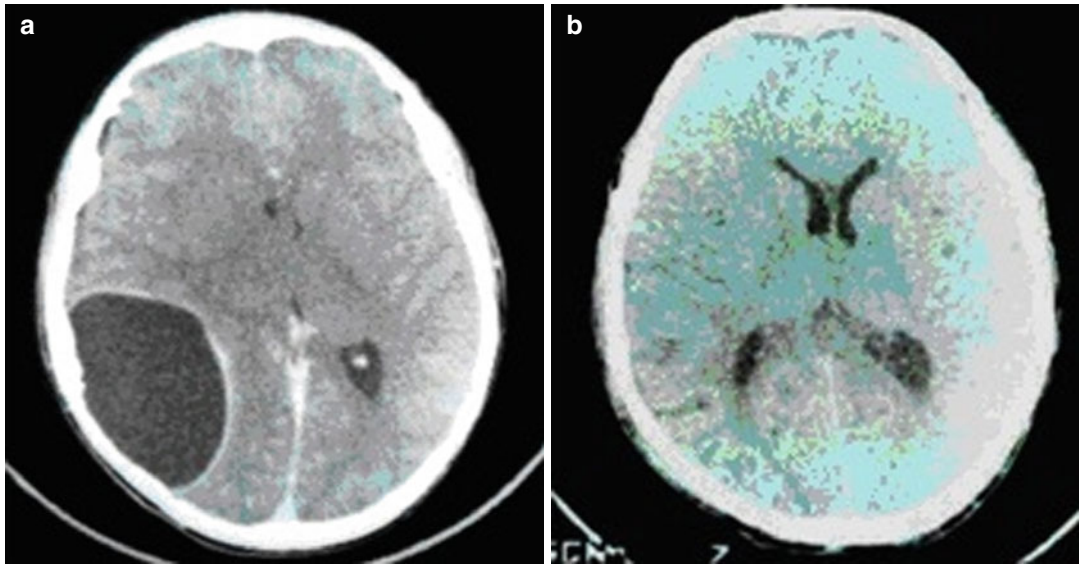

Fig. 21.8 Preoperative (**a**) and postoperative (**b**) aspects of an extradural hydatid cyst in the parietooccipital region of the brain

of penicillin administered at the site of the cyst. The second case was published in 1959 (Arseni et al. 1981). The patient showed a left frontal pulsatile tumefaction. The cyst had drilled through the walls of the left frontal sinus, and the secondary sinusitis masked the presence of the cyst. Three such cases are presented by Arseni et al. (1981) as part of their personal list of cases.

Craniocerebral Extradural Sellar

An extremely interesting case was signaled in the Maghreb where a young Bedouin woman became fertile again 13 years after a hydatid cyst that was pushing against her pituitary stalk was removed. The removal of the cyst returned full hormonal functions (Mazor et al. 1986) (Fig. 21.10).

We are familiar with one other case of such nature, taken from the literature, in which a 38-year-old woman manifesting hypothalamic stupor and absolute mutism presented a hydatid cyst in the area between the diencephalon and pituitary gland. The patient unfortunately died and the cyst was found at autopsy, lying behind the optic chiasmus and in front of the pons. The cyst was herniating between the hemispheres and was the size of a pigeon egg (Arseni et al. 1981). The cyst developed in the tissue of the pituitary gland, the ceiling of which got atrophic and resorbed through a slow process of compression which was doubled by a flattening of the neural portion as well as the whole infundibulo-tuberian area. One such case was also depicted by Arseni et al. (1981) as part of their personal experience in Fig. 21.11.

Craniocerebral Extradural Parasellar

Another case of multiple hydatid cysts was spotted in a patient from an endemic area, a 21-year-old man presenting with multiple cranial nerve palsy, impaired eyesight, raised intracranial pressure, and a computed tomography (CT) image showing a hypodense mass with septations and a hyperdense rim. The case pointed out the presence of a parasellar hydatid cyst (Behari et al. 1997).

The recommended surgical approach in such situations is the pterional basal one or the fronto-temporo-orbito-zygomatic one, which can be extended to the needs of the surgeon. The approach is executed in such a way that it will allow the widest exposure of the cyst to permit a complete intact cyst removal. Under no circumstance should the integrity of the cyst be disrupted (Fig. 21.12).

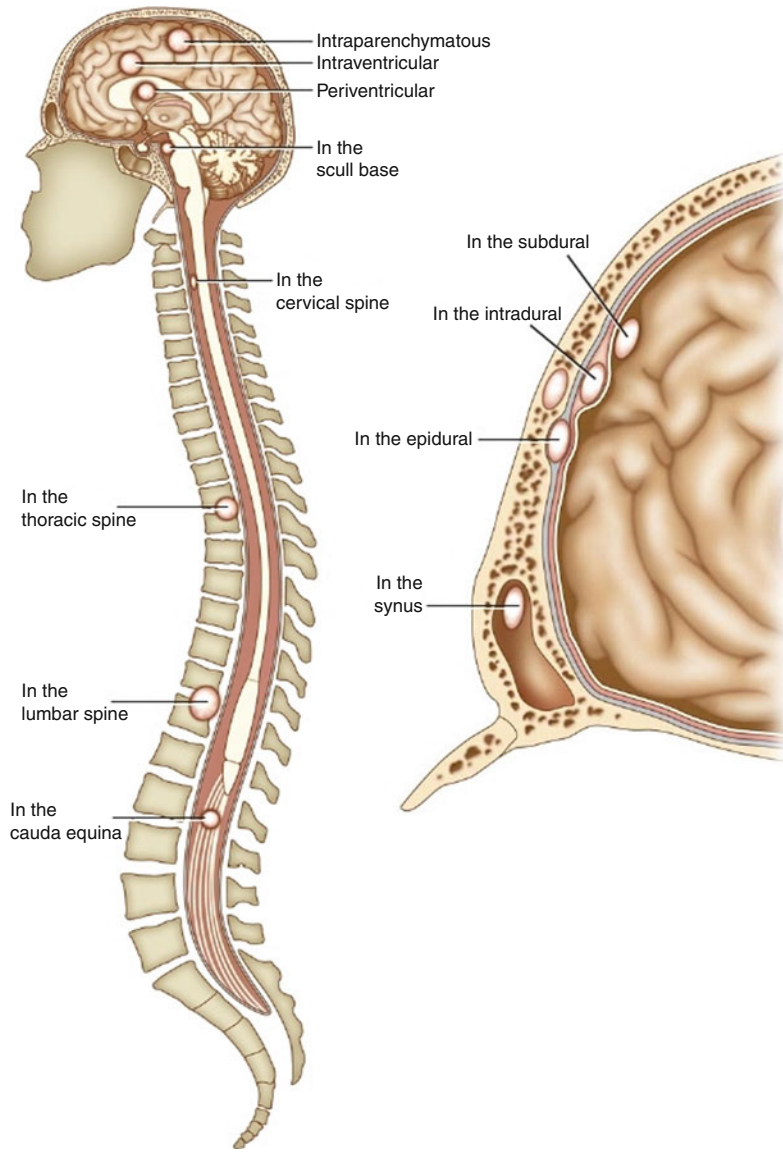

Fig. 21.9 Distribution of the dura mater and the development of various hydatid cysts

Craniocerebral Intradural and Subdural

Unlike neurocisticercosis, literature data shows extremely few cases of intradural manifestations of hydatidosis. Not even data from endemic areas is significant. We describe the case of a 6-year-old child, in which an *E. granulosus* cyst developed between the dura mater and the arachnoid membrane. The cyst had destroyed the frontoparietal skull as it had grown in all directions unhindered (Arseni et al. 1981) (Fig. 21.13).

One other interesting case we found is that of a hydatid cyst which laid both extradurally and subdurally. The larva which traveled via the middle meningeal artery positioned itself in the dura mater. Given the particularities of the dural blood network, the parasite most likely stopped in the deepest layer, which is very similar to the lymphatic capillaries. From here on, the parasite starts to grow and develop more or less as in the case we invoked, in the tissue underneath the dura mater, separated from the cortex by the leptomeninges (Arseni et al. 1981). It is most likely

that after the larva perforated the dura mater, it was able to grow both subdurally and epidurally. We feel forced to mention that usually hydatid cysts remain attached to the inner surface of the dura mater.

The surgical approach in such situations is conducted via a wide skin incision that will encircle the whole surface of the cyst. The craniotomy/craniectomy should resect a surface of the skull wider than the cyst. These rare situations cannot be handled through a minimally invasive approach as the purpose of the procedure is to expose the cyst and the adjacent and subjacent structures. The removal of the cyst will be made via the intact enucleation of Arana Iniguez. It consists of delivering the cyst by introduction of a flexible catheter between the cyst and the receiving cavity while injecting hypertonic fluid (Kalangu et al. 2011). A general rule for the

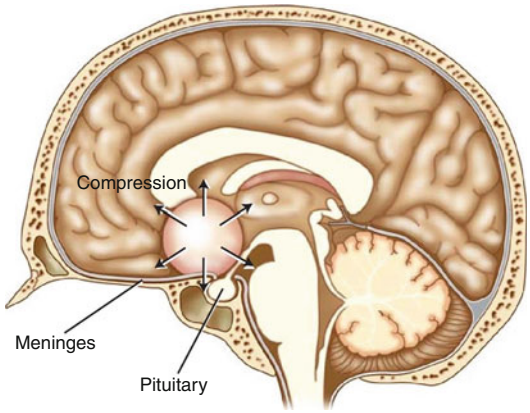

Fig. 21.10 Example of hydatid cyst compressing against the pituitary stalk

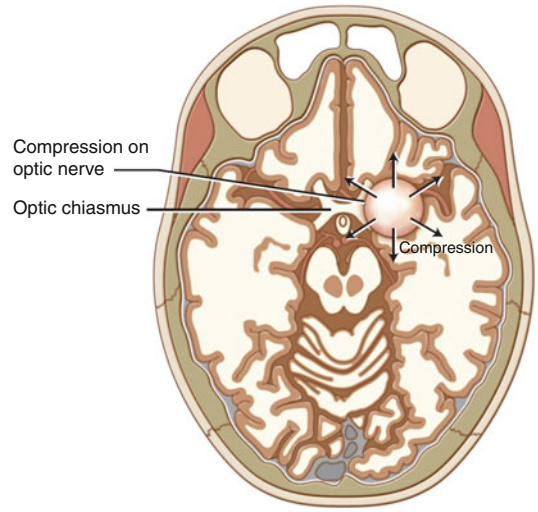

Fig. 21.12 An artistic illustration showing a hydatid cyst in the right parasellar area

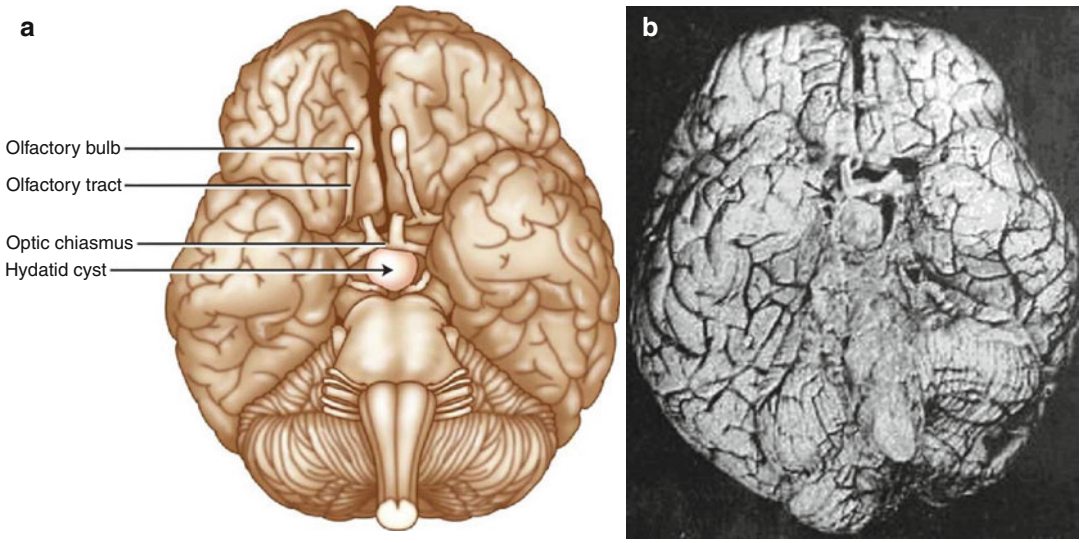

Fig. 21.11 (**a**) Pathology finding of a hydatid cyst behind the optic chiasmus and in front of the pons. Courtesy of the C. Arseni pathology museum. (**b**) Pathology finding of a hydatid cyst behind the optic chiasmus and in front of the pons (Courtesy of the C. Arseni pathology museum)

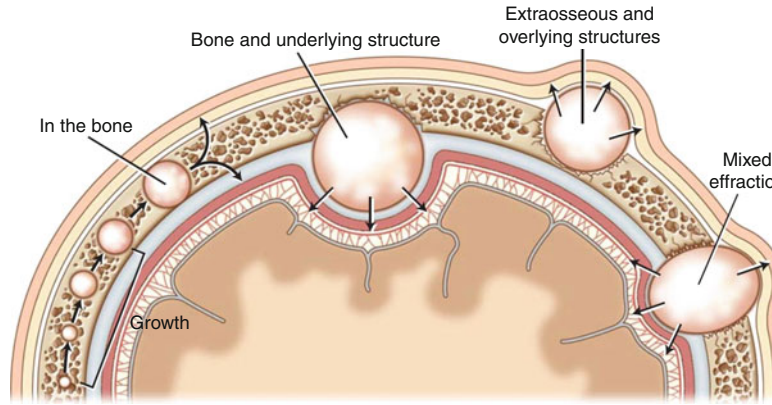

Fig. 21.13 Possibilities of evolution for a hydatid cyst

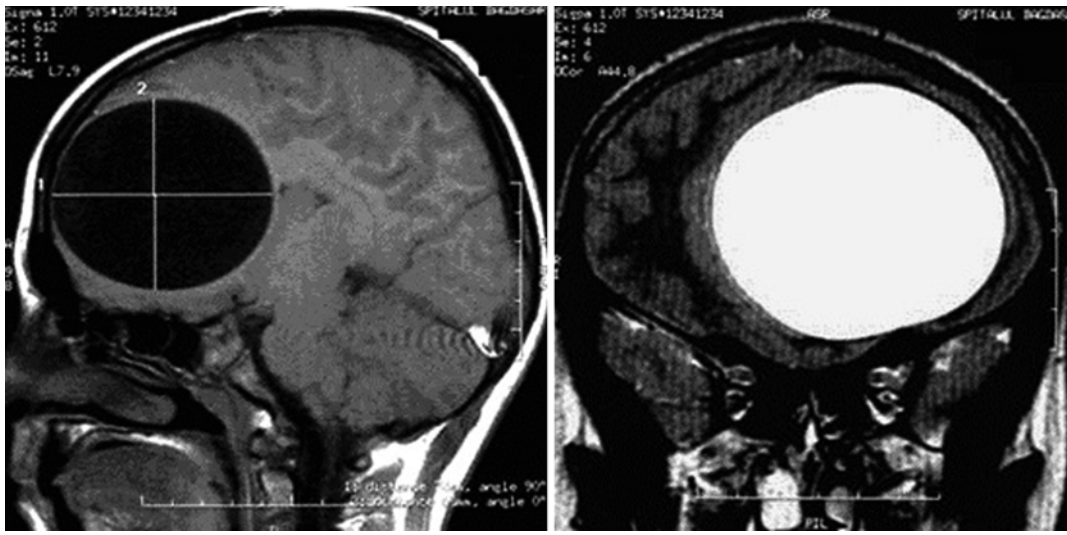

Fig. 21.14 A gigantic frontal cyst

removal of the cysts: preserve the integrity of the cyst at all costs.

The case of subdural hydatid disease is the same as intradural hydatidosis. These are very rare manifestations (Arseni et al. 1981). In the series reported by C. Arseni and V. Marinescu, there are no cases of such nature (Arseni et al. 1981).

Intraencephalic

All the literature data mention the prevalence of hydatidosis in the cerebral hemispheres. Most of the cases of intracerebral hydatidosis are present in the left hemisphere. These cysts can reach tremendous dimensions and volumes, for example, 770 g, as described by Bahloul et al. (2009) (Figs. 21.14 and 21.15).

Cerebral

There is a series of articles worth mentioning in this chapter, as hydatid cysts can take various forms and can come in a wide array of presentations. In one case the hydatid cyst had the unusual appearance of a hemorrhagic infarct (Kanj et al. 2010).

Another strange appearance of a hydatid cyst brought into discussion a strange area of edema resembling a cystic astrocytoma involving a cerebral hemisphere (Bahloul et al. 2009).

The most extreme situation we ever came across was that of a 7-year-old girl. The first manifestation of hydatid disease was raised

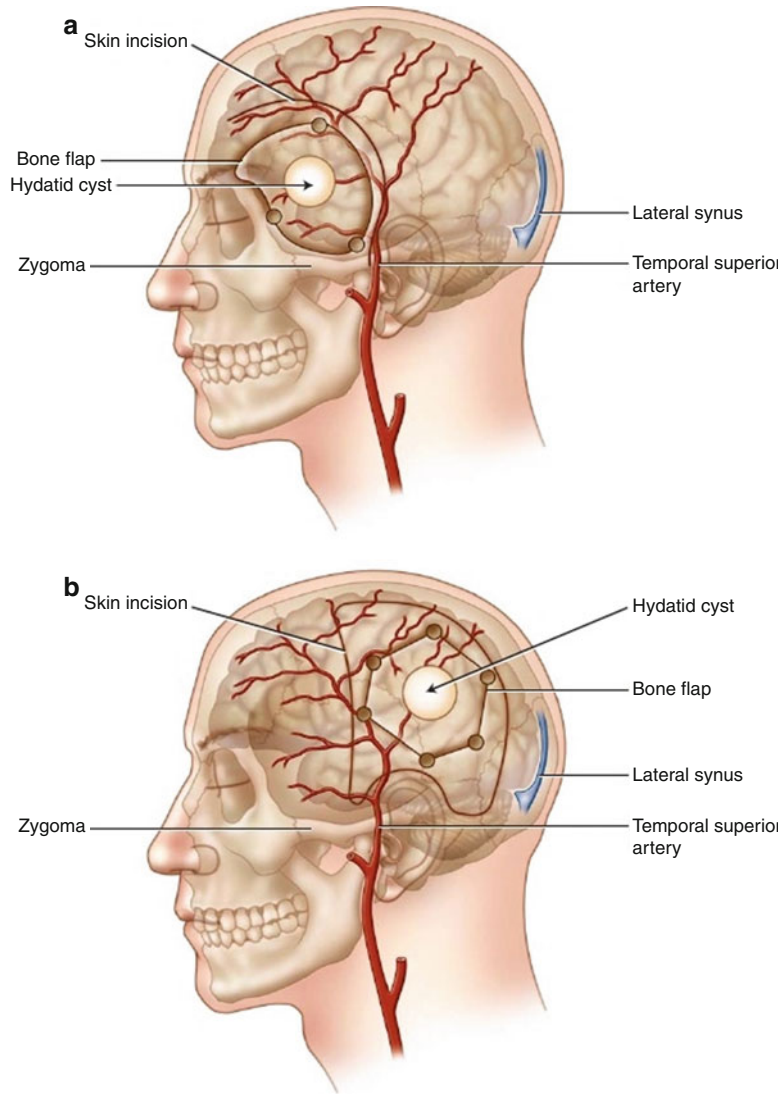

Fig. 21.15 The surgical approach for the craniotomy. (**a**) Frontotemporal hydatid cyst. (**b**) Parietal hydatid cyst. Note: Remember the necessity for large bone flaps

intracranial pressure syndrome. Unfortunately, before the primary ruptured *E. granulosus* cyst was detected in the myocardium of the left ventricle, the patient underwent nine operations over an 8-year period for hydatid embolism affecting the brain among other clinical manifestations. The case was reported by Turgut et al. (1997). The multiple hydatid cysts were the result of a hydatid embolus coming from the heart. Such a possibility must always be taken into account when multiple hydatid cysts are present. Cardiac hydatid disease can generate emboli which in turn can determine reinfections of the brain (Turgut et al. 1997). Stroke as a complication of cardiac hydatidosis is discussed in Chap. 22 in detail.

Cerebral alveolar echinococcosis is a rare but possible manifestation that has a poor prognosis. We report having found in the literature an unusual case presenting with disseminated intracranial lesions secondary to primary hepatic infection (Piotin et al. 1997).

Cerebellar

All the literature data that presents wide series of cases show hydatid cysts in the cerebellum,

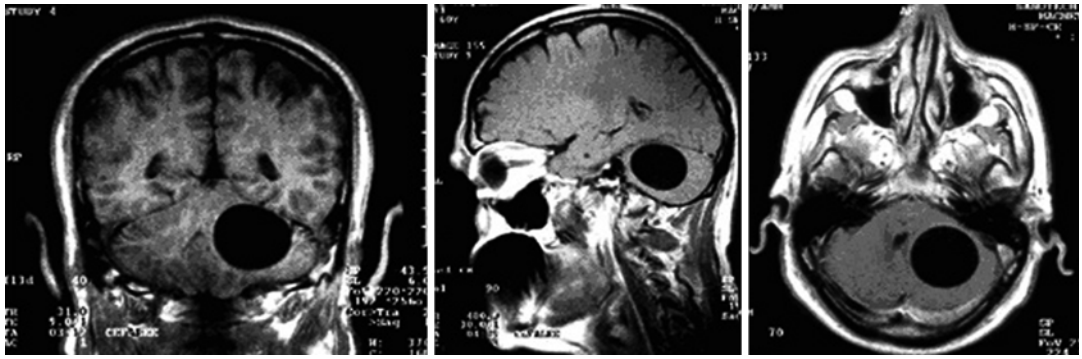

Fig. 21.16 Different views showing a unique cerebellar hydatid cyst

occurring mostly in children. Arseni et al. (1981) collected all the cases in the literature reporting only one case of unique primary cerebellar manifestation of hydatid disease.

In such cases neuroimaging is conclusive just as in cerebral manifestations of hydatid disease (Fig. 21.16). We have personally come across hydatid cysts in the cerebellum. One of our patients was a 9-year-old boy presenting with ataxia and cerebellar syndrome. The investigations showed a large dimension hydatid cyst which was completely excised without incident. Given the young age of the patient, no loss of function occurred and the overall recovery was favorable (Figs. 21.16 and 21.17).

We also report here having found in the modern literature one case involving the cerebellum and the maxillary antrum, a case first described by Copley et al. in 1992.

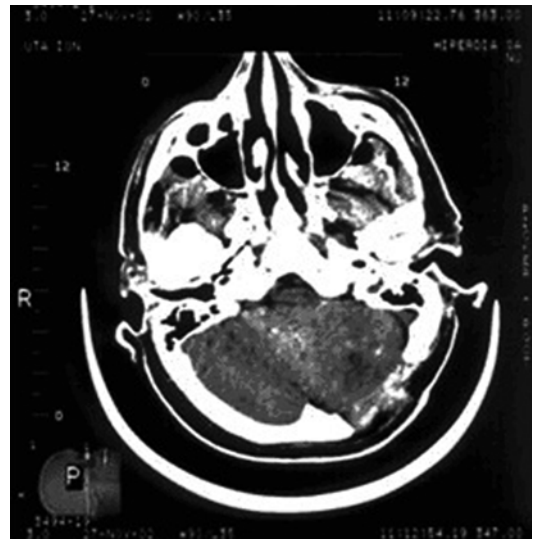

Fig. 21.17 Postoperative aspect of the intervention

Ventricular and Periventricular

Hydatid cysts in the ventricles are reported in all the literature. Of course, this situation is much rarer than in neurocisticercosis (Arseni et al. 1981). In the personal series presented by Arseni et al. in 1981, we noticed five cases of hydatid disease in the lateral ventricles – one in the third ventricle and four cases in the fourth ventricle with a total of ten. This stands for 8.4 % of all intracranial hydatid cysts in Romania at the time.

We present two cases involving the ventricles. The first one is that of a 45-year-old female patient with two primary cerebral hydatid cysts, each one of them being positioned in a separate hemisphere. Imaging studies revealed no evidence of hydatid disease elsewhere in the body. The cysts were removed during two separate interventions. Though the cyst in the right posterior parietal lobe was delivered unruptured, 7 months later, a new cyst was detected in the same cavity, which seems to show relatively rapid growth in a year. The latter was also delivered intact. This case is presented here for its unusual features such as having two primary cerebral hydatid cysts simultaneously in separate hemispheres, one of which partly localized intraventricular, and the occurrence of a new cyst in the

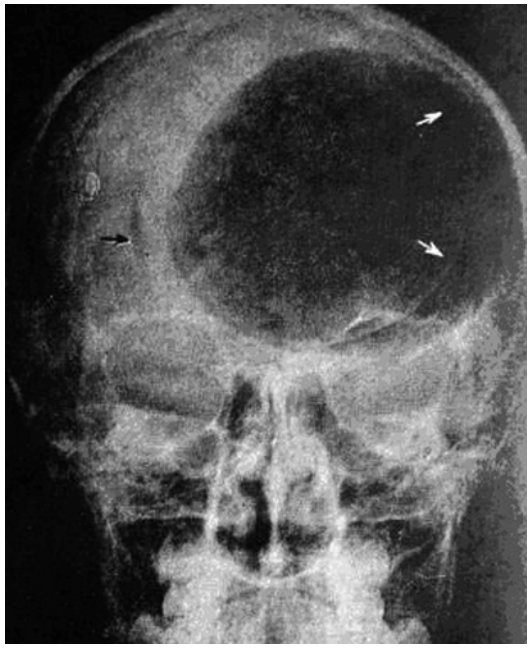

Fig. 21.18 Ventriculography showing a gigantic hydatid cyst in the left ventricle. The right lateral ventricle (*black arrow*) and the contour of the cyst (*white arrows*)

same cavity following intact removal of the previous cyst (Karadağ et al. 2004).

Another reported case shows that hydatid disease can manifest through hemichorea. The discovered cyst was situated periventricular (Iplikçioğlu et al. 1992).

The last article we quoted for this topic shows three children with hydatid disease of the central nervous system. In two patients the lateral ventricles were involved, while one case involved the cerebellar hemisphere. In addition, one child presented with a deposit in the maxillary antrum (Copley et al. 1992) (Fig. 21.18).

The intraventricular hydatidosis is discussed in Chap. 7 in detail.

Brainstem and Basal Ganglia

Such a location is exceptional, even regarding hydatid disease. Even wide series of cases such as those of Paillas and Bonnal or Arseni and Marinescu contain no such cases (Arseni et al. 1981).

In the last years reports from endemic areas have shown sporadic manifestations of such difficulty. Without regard to all difficulties concerning diagnosis and surgical treatment, total removal and good global outcome were achieved.

We present three such cases in which the brainstem and basal ganglia were involved. The first case presents an extremely rare case of a thalamic cyst with a successful total removal via contralateral transcallosal approach (Kurtsoy et al. 1999). The second case (Muthusubramanian et al. 2009) shows a hydatid cyst in the brainstem of a 40-year-old female. She presented with headache, progressive right-sided weakness, double vision, and unsteadiness of gait of 1-month duration. On examination, she had a left one-and-a-half syndrome, right hemiparesis, and left cerebellar signs. CT and MRI scans of the brain revealed a solitary, cystic lesion in the brainstem more toward the left side with features suggestive of hydatid cyst. A left retromastoid craniectomy was performed, followed by a left middle cerebellar peduncle approach. Aspiration of the cyst and total excision of the cyst followed. Postoperatively, the patient improved progressively and was asymptomatic with minimal left cerebellar signs at 1-year follow-up. Last but not least, the third case comes with a completely exceptional manifestation: pontine hydatid cyst in association with an acoustic neurinoma (Mascalchi et al. 1991).

Unusual Positions in the Venous Sinuses

During a multifocal infection with *E. granulosus*, there is an extremely low chance that the larva will position itself in the cavernous sinus generating all the associated symptoms. Such a situation is more than exceptional, but we found a case in the literature coming from Turkey (Kireşi et al. 2003).

Cisternal

The existence of hydatidosis in the cisternal spaces must not be neglected given the capacity of *E. granulosus* larvae to disseminate via the cerebrospinal fluid (CSF) (Andronikou et al. 2002).

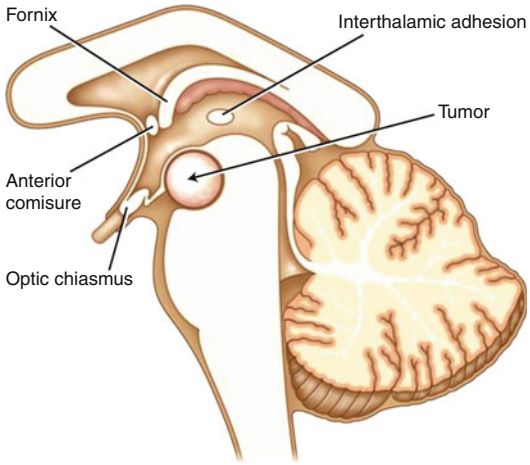

Fig. 21.19 A hydatid cyst in the interpeduncular cistern

Generally any case of multiple hydatid cysts must be carefully investigated for any overlooked hydatid cysts in the skull. This includes the cisternal spaces as well.

We present two cases. The first one is the case of an isolated multilocular hydatid cyst occurring in the basilar cisterns, with nondependent levels of different signal intensities shown on MRIs. Three portions were visualized on T1-weighted images: the hyperintense inferior aspect, the isointense central part, and the superior aspect of lower signal intensity. The inferior portion was hypointense on T2-weighted images. This unusual appearance was caused by layering of hydatid sand and may represent a characteristic feature of hydatid disease (Rumboldt et al. 2003). The second one is the first case in the literature of a hydatid cyst in the interpeduncular cistern (Beskonakli et al. 2005) (Fig. 21.19).

Orbital

Orbital hydatid cysts are known in the entire world as rare manifestations of *E. granulosus* infection. There are various references in the literature regarding the primary orbital manifestations of hydatidosis or orbital manifestations of hydatidosis during multiple dissemination. We will not insist upon these due to their description in Chap. 23 (Figs. 21.20 and 21.21).

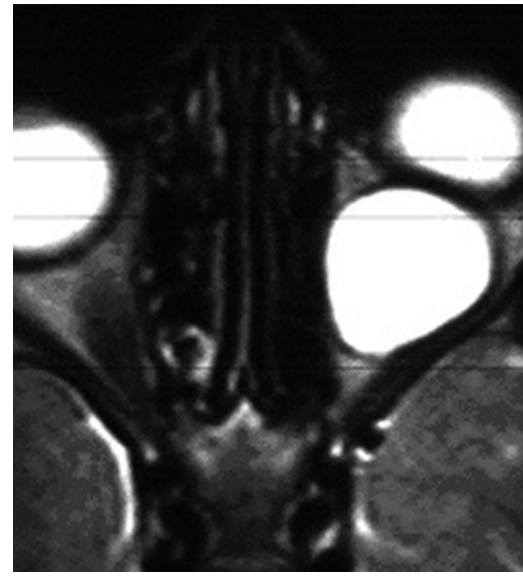

Fig. 21.20 A hydatid cyst in the orbit

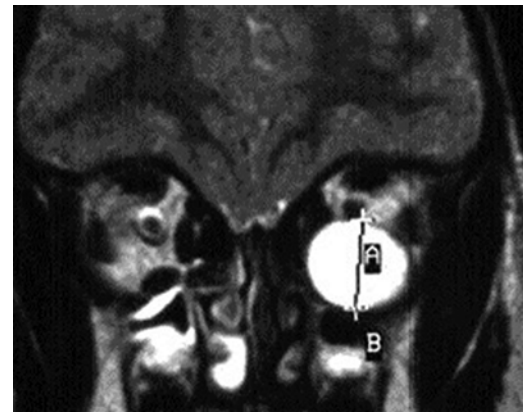

Fig. 21.21 A hydatid cyst in the orbit. *A* represents the coronal diameter of the presented cyst, *B* represents the cyst itself

Unusual Manifestations of Vertebromedullary Hydatid Disease

Although it accounts for 0.5–2 % of all the cases in the literature involving bone dissemination (Papakonstantinou et al. 2011), spinal hydatid disease is much more frequently met than that of the skull given the capacity of the protoscoleces to disseminate via blood and CSF. A second fac-

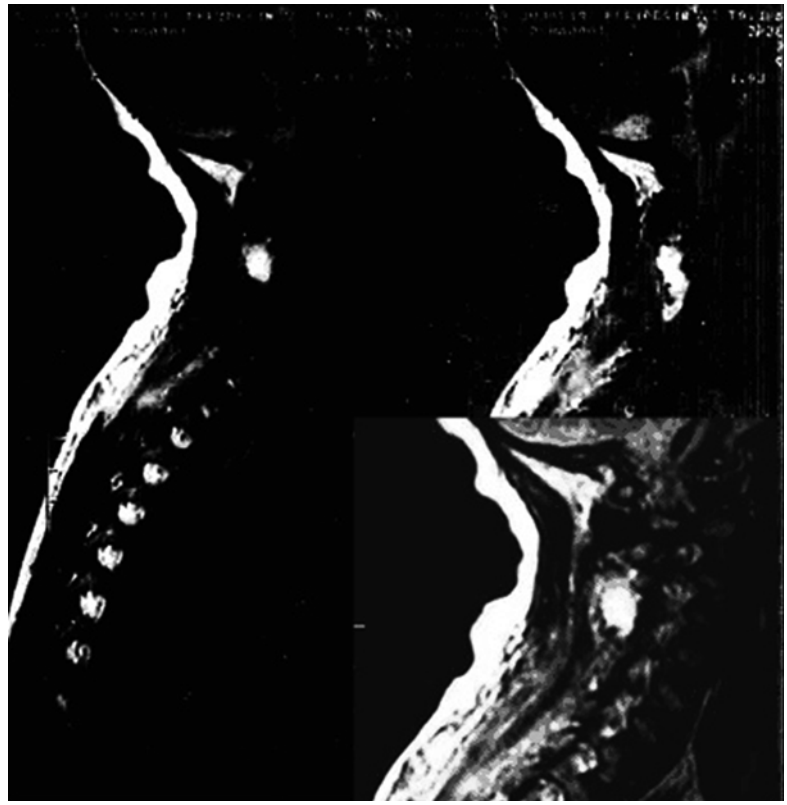

Fig. 21.22 An extreme hydatid cyst in the spine

tor facilitating this migration is the intense vascularization of the spine which often proves to be a dissemination pathway for several pathologies including cancer and polio.

In Deve's series from 1949 there are 281 cases of hydatid disease in the spine – including the sacrum (quoted from Arseni et al. 1981). This stands for 44.2 % of all the manifestations of hydatidosis in the skeleton. Research data advocates for the preponderant disposition of hydatid disease in the thoracic vertebrae.

All the classic authors – Arana Iniguez, Acquaviva, Arseni, and Marinescu – describe multiple cases of hydatid disease in the spine, with a maximum of incidence at patients well past their third decade of life and of male gender. In all these situations multiple hydatid cysts were present in all the patients.

It is Deve who suggested two possible pathways of spinal infestation (quoted from Arseni et al. 1981). One pathway is the pathogenic dissemination of the parasitic embolus from the lung, for example, to the spine via the blood and the other via effraction from the pleura to the extraosseous space.

In the actual literature spinal hydatid disease is widely mentioned. A noticeable aspect is the danger posed by infections with alveolar hydatid disease which has a more severe prognosis. The hydatidosis of the spine and spinal cord is discussed in detail in Chaps. 8, 9, 12, 14, and 20.

Vertebral (Bone Involvement)

Although vertebral hydatid disease has been mentioned in all the studies regarding parasitoses, in the western European countries and in the United States, cases like these are now considered true curiosities. Hydatid disease in the spine attacks all levels – including the cervical spine and lumbar spine – and if untreated can lead up to multilevel vertebral instability as a result of progressive bone destruction. We personally came across one case of hydatid disease manifesting itself in the cervical spine (Fig. 21.22).

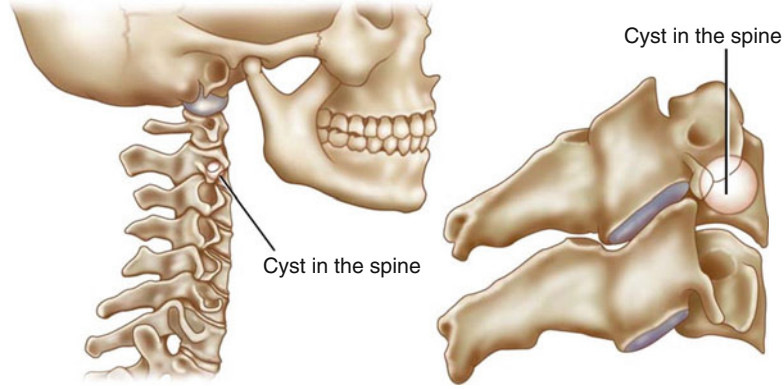

Fig. 21.23 Artistic illustration of the cyst we describe based on the image above

The case we present is old. At the time of the surgery, the true nature of the cystic lesion was only suspected. The diagnosis was confirmed intraoperatively (Fig. 21.23).

Spinal Extradural

Ever since the papers of Deve 1926 mentioning only two cases (quoted by Arseni et al. in 1981), extradural manifestations of hydatidosis were mentioned despite its very low frequency; these cases are reported in the endemic areas. In 1946, two Romanians (Cosacescu and Vereanu) reported a cyst, the size of a chicken egg, which had eroded the spinous processes and the laminae of the S1 and S2 vertebrae (quoted from Arseni et al. 1981). Benhamou and Goinard (1929) mention seven such cases (quoted from Arseni et al. 1981). Chitkara and Colab mention a 17-year-old male with a hydatid cyst positioned at the level of the T1-T2 vertebrae, extradural, on the left side (quoted from Arseni et al. 1981). The cyst formed a cavity at the level of the intervertebral foramen and had an unfortunate evolution which left the patient paraplegic. The pathology findings showed a 3.81 cm cyst. Lagrot and Colab found in an 8-year-old female patient a hydatid cyst the size of a walnut at the level of the L1 vertebral body (quoted from Arseni et al. 1981). The literature of the twentieth century contains sporadic cases of extradural hydatid cysts; however, we feel that we need to present twenty-first-century cases.

In this respect we came up with a series of cases we found in the literature which are perfect for the illustration of extradural space involvement with hydatid disease of the spine. The first case we present is a study on four patients. Out of those four, hydatid disease involved the lumbar spine in two patients, the thoracolumbar spine in one patient, and the lumbosacral in the last patient. All four patients had extensive involvement of the extradural space (Papakonstantinou et al. 2011).

The youngest patient ever met was a 4-year-old boy. He manifested a primary spinal extradural hydatid cyst in the thoracic spine (Eloqayli et al. 2010). For didactic purposes we mention the fact that primitive manifestations of hydatid disease in the spine are referred to as "Hydatid Pott Disease."

According to Arseni et al. (1981) the vertebral body implications manifest as follows: 45 % of all parasitic involvement is placed in the vertebral body, 19 % attacks the posterior arch of the vertebra, and 36 % of all parasitic disseminations at this level attack both the body and the arch. A modern study however shows that hydatid cysts can attack the vertebral laminae, the spinous processes, the pedicles, the articular processes, and the transverse processes as well.

Spinal Intradural and Subdural

The medical literature contains sporadic cases of intradural hydatid disease of the spine. These cases are considered to be exceptional. Most of the cases reported to present intradural manifestations of hydatidosis in the spine have

their authenticity discussed. A multivesicular hydatid disease could easily be mistaken for a neurocisticercosis case. In 1932 Deve presented only three cases (quoted from Arseni et al. 1981). Goinard and Descuns (1952) presented another three (quoted from Arseni et al. 1981). Grossiord et al. (1955) noted in a female patient in Ethiopia several crowded hydatid vesicles in a tight web made out of arachnoid fibers (quoted from Arseni et al. 1981). The roots of the cauda equina were stuck together. The postoperative evolution of the patient was positive in spite of anal sensitivity impairment and paraplegia. The pronounced adhesive arachnoiditis explained the absence of the parasite in the cephalic subarachnoid spaces. A more recent case describing an intradural cyst was reported by Fahl et al., in 1994.

Spinal Intramedullary

Intramedullary hydatidosis is known and reported by all the classic authors including Acquaviva, Arseni, and Colab. Research data is consistent showing affections mostly at thoracic levels. In the Arseni-Marinescu-Ciurea statistics, out of 35 cases of hydatidosis in the spinal cord, 20 are at the thoracic level (Arseni et al. 1981). In the number of reported hydatid disease manifestations in the spine, there are some unusual cases worth mentioning.

Arseni et al. (1981) reported a single such case of spinal manifestation. The patient was a 41-year-old female previously operated for a pulmonary hydatid cyst 1 year earlier. The patient was admitted for motor deficit of the legs, trophic disturbances, sphincteric disturbances, and impaired sensitivity. She manifested flask paraplegia, abolished osteotendinous reflexes, urinary incontinence, and xantochromic CSF.

A wide T_6-T_{12} laminectomy was performed. The dural sack was incised widely. A series of yellowish, fragile membranes that had been wrapped around the medulla were removed. Having proceeded lower, toward the inferior pole of T_{12}, the surgeon was able to identify a white milky membrane that had developed caudally for 12 cm in the shape of a cyst and another one of 10 cm which was side by side with the first one. The medulla had holes in it, and after the surgery, the patient did not improve.

The existence of two cysts in the spine comes as a hint toward the idea that a first cyst had ruptured and disseminated either in the spinal or cephalic CSF. In the current data available, intramedullar hydatid cysts behave exactly like a perfectly delimited medullar compression. In this respect the differential diagnosis must be made with any kind of cystic tumor at this level.

The perfect targets for this affection are young people coming from the rural parts of countries in endemic areas. Multiple disseminations and perfectly delimited cystic lesions indicate the diagnosis and the treatment. The cyst's integrity must be preserved. The surgical treatment imposes a gentle delimitation with cottonoid and the delivery of the cyst via hypertonic fluid injection in the receiving cavity with a flexible catheter.

Conclusion

The following is concluded: (1) Hydatid disease classically involves the liver, lungs, and brain but can involve almost any organ and numerous organs simultaneously. (2) Whether hydatid disease is discovered incidentally or by intentional imaging, extended imaging is recommended to identify multifocal disease. (3) All patients with one known cyst should undergo a minimum CT scan of the abdomen, chest, and brain. The combination of clinical history, imaging findings, and serologic test results usually helps the diagnosis. (4) Imagistic findings are pathognomonic for hydatid disease. (5) Hydatid cysts represent a delayed emergency due to their compression on the central nervous system. (6) Any kind of hydatid cyst – single or multiple – must be immediately removed surgically. (7) There is no temporization and the treatment must not be delayed. Through anthelmintic medication the cysts die but they remain as physical compressive elements. (8) The treatment of hydatid disease is prophylactic – targeted on disrupting the vicious circle taking place between dogs and men. A good sanitary education and hygiene will lead rapidly to the lowering of the number of people infested.

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Stroke as a Complication of Cardiac Hydatidosis

22

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Introduction

Hydatid disease is still a serious disease in some regions of the world such as Australia, New Zealand, North Africa, Europe, Asia Minor, the Middle East, and South America, while it is not a major public health problem in most Western countries (Byard and Bourne 1991; Turgut and Bayülkem 1998; Turgut 2001, 2002). The epidemiology of *Echinococcus* in the world is discussed in Chaps. 2, 3, and 4.

Hydatidosis is commonly caused by *Echinococcus granulosus*. The normal life cycle of the tapeworm *E. granulosus* involves passage from definitive carnivore hosts, with transmission of eggs to an accidental intermediate host. Infection of humans with the cestode is usually caused by inadvertent contamination with eggs from infected dogs as follows: (1) by eating contaminated vegetables, (2) by soiling their mouth after patting infested dogs, or (3) by inhaling dust carrying dried ova (Haddad and Haddad 2005). The ova hatch in the intestine, and the larvae reach the liver, through the portal system, where a hydatid cyst may be formed, but the ova may bypass the liver and settle in the lung (Haddad and Haddad 2005). Routes of infestation and site of primary echinococcal cysts in man are the intestine (very rare), liver (75 %), lungs (8.5 %), and heart (0.5 %), and then muscles (5.5 %), spleen (2.5 %), kidney (2.0 %), brain (1.5 %), bone (1.5 %), and miscellaneous parts (3.5 %) via systemic circulation (Peters et al. 1945). Thus, it is obvious that the heart and brain are quite infrequently affected

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organs, although multiorgan involvement is common in hydatid disease.

Cardiac Hydatidosis

Cardiac involvement by *E. granulosus* is rare and has a reported incidence of 0.5 % of cases in the literature (Peters et al. 1945), because contraction of the heart provides natural resistance to the maintenance of viable hydatid cysts. The first report of hydatidosis of the heart dates from 1836, and the first successful surgical operation for hydatid disease in the left ventricular wall of the heart was performed in 1932 (quoted from Peters et al. 1945).

At present, it is commonly accepted that the oncosphere reaches the cavities of the heart through the coronary arteries by traveling through the myocardium or through pulmonary veins. In cases of cardiac hydatidosis, the most common location is the left ventricle (60 %), followed by the right ventricle (17 %), interventricular septum (9 %), right atrium (8 %), left atrium (4 %), interatrial septum (2 %), and pericardium (very rarely) (Fig. 22.1) (Aleksic-Shihabi and Vidolin 2008; Byard 2009). Amongst these anatomical chambers of the heart, a high frequency of left ventricular hydatidosis is possibly due to various factors including dominance of the left coronary artery, the presence of a big myocardial mass in the left ventricle, and different pressure gradients (Thameur et al. 2001). It has been suggested that hydatid cysts in the pericardium generally occur as a result of rupture of a primitive cardiac cyst (Deve 1946).

As a rule, left-sided cysts tend to grow subepicardially, while right-sided cysts have a tendency to expand subendocardially (Dursun et al. 2008). There are five patterns of hydatid disease of the heart: (1) dead calcified cysts, (2) living intact cysts, (3) ruptured pericardial cysts, (4) pediculated intracavitary cysts, and (5) ruptured intracavitary cysts (Peters et al. 1945). A ruptured cyst is a serious complication of cardiac hydatidosis. It is important to know that right ventricular cyst rupture leads to pulmonary embolus, severe anaphylactic shock, or sudden death (Dursun et al. 2008). The ruptured hydatid cyst results in systemic emboli in organs supplied by the aortic circulation such as the (1) brain (64 %), kidney (17.5 %), spleen (17.5 %), and liver (1 %) (Peters et al. 1945).

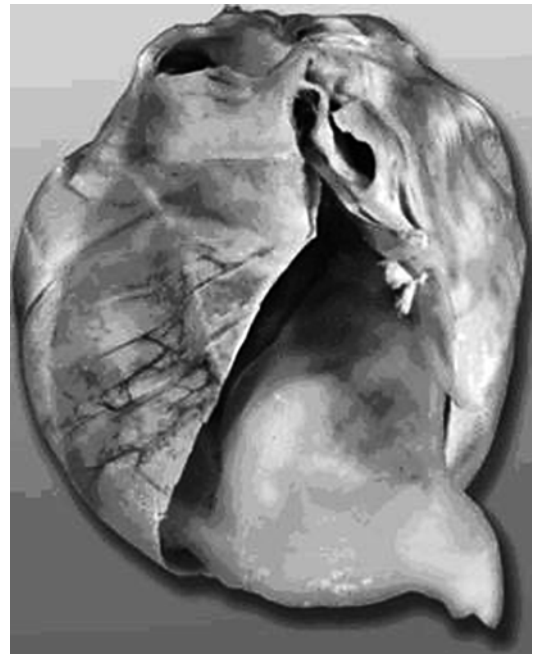

Fig. 22.1 Macroscopic photo of the heart at autopsy demonstrates hydatid cyst filling the left ventricle as a cause of sudden death (From Byard (2009), with permission)

Clinically, the following sequential stages of the hydatid disease develop after direct rupture of a primitive cyst of the heart:

1. Onset stage, characterized by general malaise with signs of anaphylaxis ranging from only a rash to an allergic shock
2. Asymptomatic stage, characterized by embolic dissemination of the parasite into various organs in the body through the pulmonary or systemic aortic circulation
3. Metastatic stage, characterized by development of pulmonary or visceral secondary hydatidosis within the host
4. Complication stage, characterized by development of various complications such as bacterial infection of the pericyst cavity, related to the secondary localization of the hydatidosis (Deve 1946)

Importantly, it has been noted that the aforementioned four stages are independent of the location of the rupture (intracavitary, intramyocardial, or intrapericardial) (Thameur et al. 2001). It has been reported that the intrapericardial location occurs as a result of rupture of a primitive hydatid lesion (Dursun et al. 2008). The early diagnosis and treatment of cases with cardiac

hydatidosis during the initial phase of rupture characterized by the history of allergic reactions is very important to prevent possible fatal risk of rupture. As expected, the diagnosis of cardiac hydatid cyst is easy when the secondary location is symptomatic (Thameur et al. 2001).

In the cases of cardiac hydatidosis, chest pain and cough are the most common initial signs, followed by fever, arrhythmias, cardiac syncope, acute myocardial infarction, pulmonary hypertension, pericarditis, pulmonary embolism, anaphylactic shock, or unexpected death (Aleksic-Shihabi and Vidolin 2008). The sudden death in cases with cardiac hydatidosis results from "obstruction" of the chambers of the heart or "embolism" of pulmonary or carotid arteries by migrated cyst fragments, following intracavitary rupture of the cyst in the right or left heart (Thameur et al. 2001).

The symptoms and signs depend on the anatomical location of the hydatid embolus, including the cerebral arteries, the abdominal aorta, or its branches including the extremity arteries. Imaging studies such as plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US) provide very useful information for the diagnosis of cardiac hydatid disease, although echocardiography (EC) remains the most efficient diagnostic method (Aleksic-Shihabi and Vidolin 2008). In clinical practice, hydatid cyst of the heart is generally sterilized before removal with 30 % hypertonic saline solution or other scolicidal agents including 0.1–1 % cetrimide, 2 % formalin, 1 % iodine, or 0.5 % silver nitrate (Maroto et al. 1998).

Cerebral Hydatidosis

Cerebral hydatid cyst can be single fertile "primary" containing hydatid sand or multiple metastatic "secondary," which is sterile and does not have a germinative layer, due to spontaneous, surgical, or traumatic rupture of a primary cyst (Fig. 22.2) (Turgut and Bayülkem 1998; Turgut 2001, 2002; Byard 2009). It is well known that the sterile cysts do not form secondary cysts in case of rupture, if no sand is present in the cyst (Haddad and Haddad 2005). Nevertheless, there is no consensus as to the route the larvae take from the gut to the brain for primary hydatidosis: the larvae

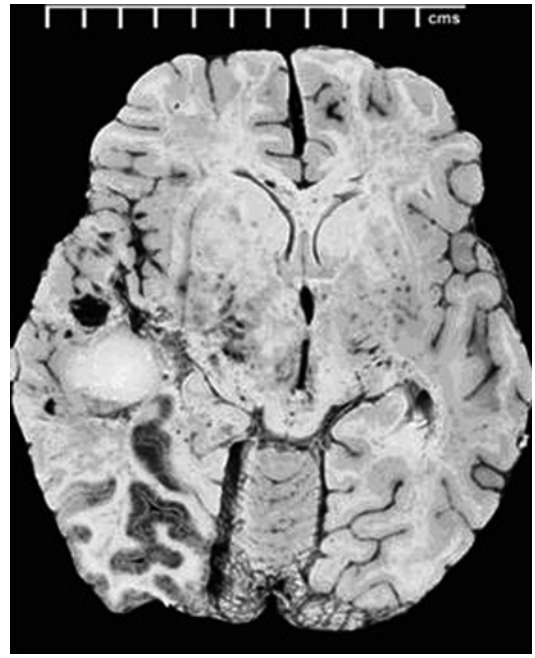

Fig. 22.2 Macroscopic photo of the brain at autopsy reveals a large hydatid cyst in the left temporal lobe (From Byard (2009), with permission)

reach the right heart through the inferior vena cava and the brain in case of a patent septal cardiac foramen or arteriovenous channels in the lung (Haddad and Haddad 2005). On the other hand, as described above, secondary cysts in the brain result from the rupture of the primary cysts localized in the left compartments of the heart.

In general, the clinical picture is dominated by the symptoms of increased intracranial pressure (IICP) with or without hydrocephalus in children, while in adults, the focal neurological signs related to infarcts or cysts located in the watershed of the abovementioned cerebral arteries, such as hemiparesis, epileptic seizures, and aphasia, are usually the first to appear (Abada et al. 1977; Turgut and Bayülkem 1998; Turgut 2001, 2002). It has also been reported that children with multiple hydatid may present with focal neurological signs (Turgut and Bayülkem 1998; Turgut 2001, 2002).

Neuroimaging modalities, such as CT and MRI, are the most valuable diagnostic tools for diagnosing cerebral hydatid disease. Typically, hydatid cyst has a density similar to that of cerebrospinal fluid on CT scans and MRI (Haddad and Haddad 2005). It is important to know that multiple cysts are more often seen in cases secondary to cardiac embolization

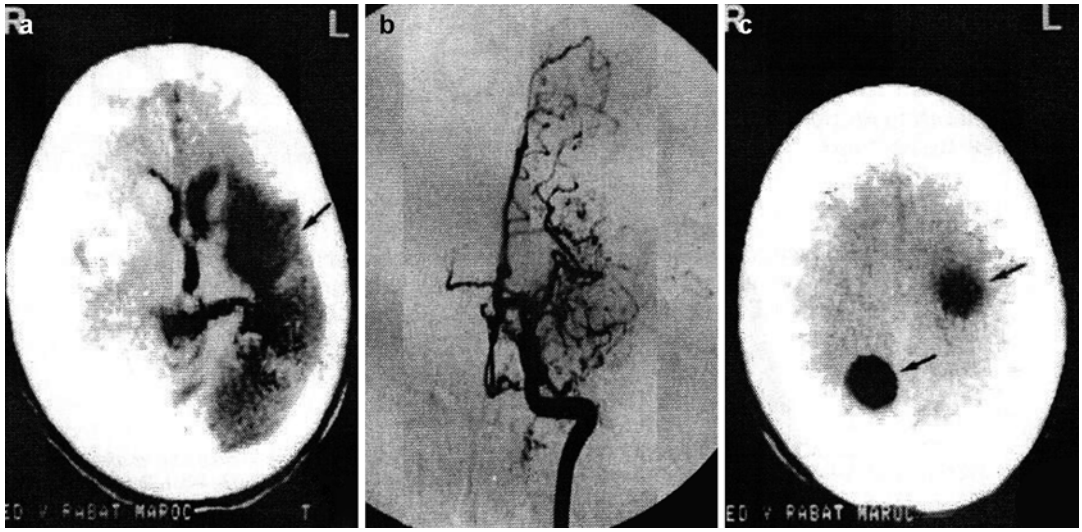

Fig. 22.3 Development of cyst in a previously infarcted region of the brain following hydatid occlusion of the cerebral artery. (**a**) CT shows infarct (*arrow*) of the left middle cerebral artery (MCA). (**b**) Angiogram demonstrates occlusion of the left MCA. (**c**) CT displays cystic lesions (*arrows*) in the infarcted region of the brain (From Benomar et al. (1994), with permission)

through the vascular system (Turgut et al. 1997). In some cases with hydatidosis, the pericyst layer may be calcified owing to the calcium deposition, and there is no peripheral enhancement of the cyst. Recently, it has been suggested that the differentiation of fertile and sterile cysts may be possible with proton MR spectroscopy (Garg et al. 2002).

Today, the treatment of choice is surgical removal of the cysts if possible. In complicated cases, various techniques including tapping of the cyst and injection of a devitalizing solution such as formalin or hypertonic saline other than the Dowling-Orlando technique may be useful before removal of the cyst (Turgut 2001). Rupture of the cyst into the subarachnoid space as complication of surgery may result in severe anaphylactic response (Buris et al. 1987).

Anthelmintics are recommended in patients with multiple cysts and in those unfit for surgery or suffering from recurrent disease (Turgut and Bayülkem 1998; Turgut 2001, 2002). In such instances, anthelmintics such as mebendazole, liposomal and tablet albendazole, or praziquantel should be administered during the perioperative period, although the efficacy of medical treatment is questionable in hydatidosis. Nonetheless, large and symptomatic cysts should be surgically treated first, and the patient should be closely followed up for the need for reoperation in the future.

In addition to different chemotherapeutical agents, clinical and imaging findings of cerebral hydatidosis are discussed in detail in Chaps. 6, 11, and 16.

Stroke as a Complication of Cardiac Hydatidosis

"Stroke" as a complication of cardiac hydatidosis, a cause of ischemic or hemorrhagic infarction and multiple metastatic cyst formations, is an extremely rare entity (Byard and Bourne 1991; Turgut et al. 1997; Turgut and Bayülkem 1998). It results from spontaneous, traumatic, or surgical rupture of a fertile cardiac cyst and embolization of the germinative membrane, scolices, or portions of endocyst. Basically, there are two pathological types of "stroke" from cardiac embolization: (1) acute obstruction of a cerebral artery, partial or complete, with a piece of embolized cyst membrane and (2) development of multiple cyst formations in the infarcted area following embolism of scolices during the course of several months. In young patients with the diagnosis of stroke, subsequent development of "cerebral cyst" within the necrotic area of the brain tissue, called "cerebral infarct," strongly suggests embolism of ruptured cardiac hydatid

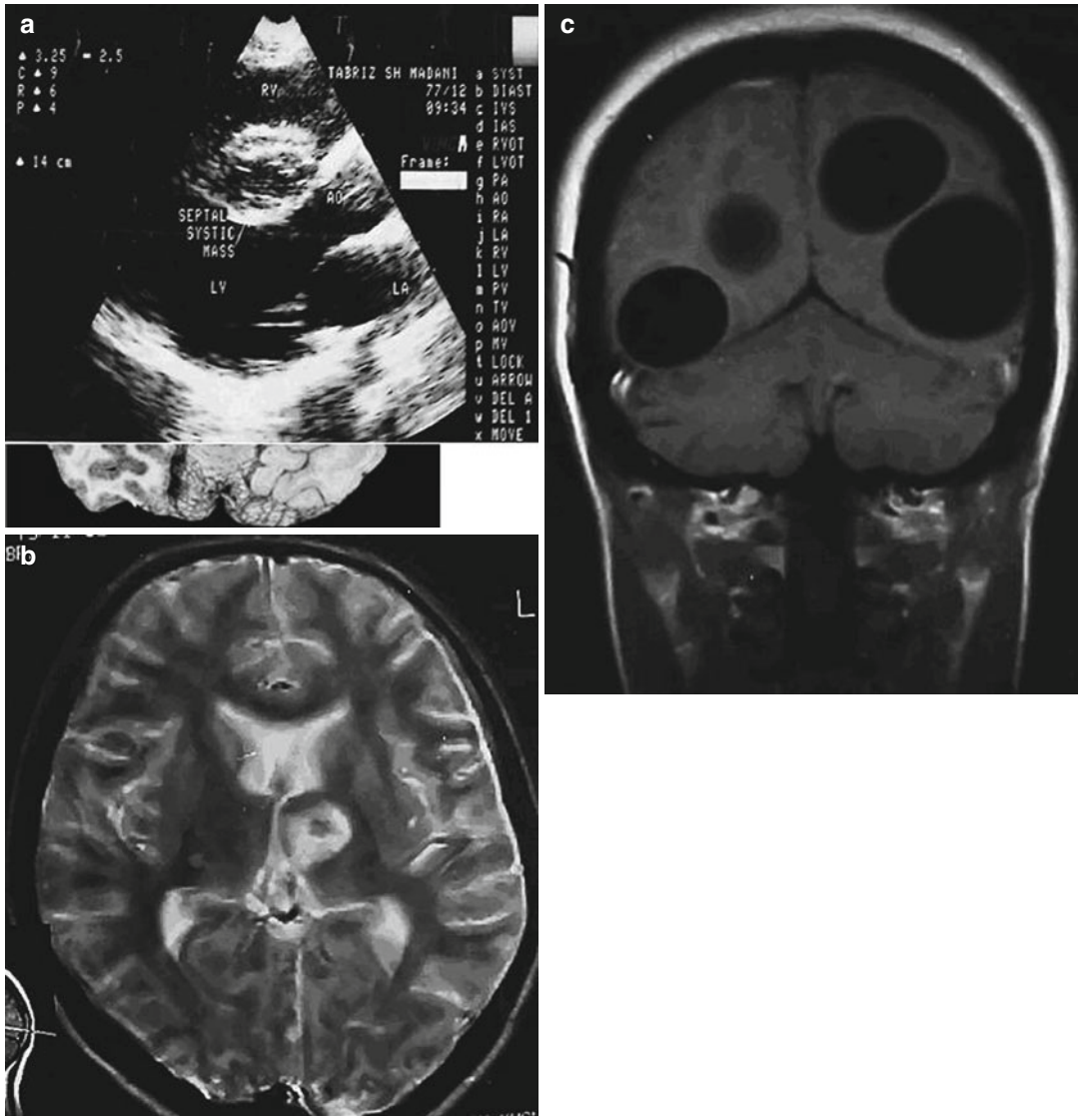

Fig. 22.4 Stroke as a complication of cardiac hydatidosis with an interval of 2 years between infarction and cyst formation. (**a**) Echocardiography shows a cystic mass in the ventricular septum of the heart. (**b**) Axial T2-weighted MRI demonstrates hyperintense cystic foci in the left basal ganglia. (**c**) Axial T2-weighted MRI shows multiple cystic cerebral lesions in both hemispheres (From Lotfinia et al. (2007), with permission)

cysts (Figs. 22.3 and 22.4) (Benomar et al. 1994; Lotfinia et al. 2007). As a rule, the cerebral embolism called "stroke" usually occurs when portions of a ruptured hydatid cyst travel from the left side of the heart to the brain (Turgut et al. 1997). For this reason, a routine investigation for cardiac hydatidosis as a possible source of a cerebral embolus should be undertaken, if patient has hydatid disease in other organs.

We reviewed the scientific literature for all published articles containing cases of "stroke" as a complication of cardiac hydatidosis with/without multiple metastatic hydatid cysts of the brain published to date. In this review, all published case reports, case series, and abstracts found in congress abstract books on stroke as a complication of cardiac hydatidosis were included. If a case appeared in more than one paper on this subject, the earlier report was omitted. Also, dubious cases with no data available to the authors were excluded (Gessini and Giammusso 1957; Preda et al. 1963; Thameur et al. 2001; Díaz and Maillo 2002).

Altogether, 41 articles were selected, containing 41 cases of "stroke" as a complication of cardiac hydatidosis with/without multiple metastatic hydatid cysts of the brain (Peters et al. 1945; Paillas et al. 1962; Chin et al. 1981; Vaquero et al. 1982; Petrov 1987; Borisenko et al. 1990; Byard and Bourne 1991; Benomar et al. 1994; Talaslioglu et al. 1994; el Quessar et al. 1996; Turgut et al. 1997; Evliyaoglu et al. 1998; Kabbaj et al. 1998; Marcì et al. 1998; Ugur et al. 1998; Maffeis et al 2000; Ulgen et al. 2000; Kemaloğlu et al. 2001; Cakir et al. 2002; Trehan et al. 2002; Singh et al 2003; Acarturk et al. 2004; Bükte et al. 2004; Karabay et al. 2004; Pillai et al. 2004; Yaliniz et al. 2004; Itumur et al. 2006; Yaliniz et al. 2006; Lotfinia et al. 2007; Aleksic-Shihabi and Vidolin 2008; Ašanin et al. 2008; Goz et al. 2008; Kumar and Hasan 2008; Byard 2009; Kanj et al. 2010; Kojundzic et al. 2010; Sabouni et al. 2010; Cansu et al. 2011; Ekici et al. 2011; Fabijanić et al. 2011; Potapov et al. 2011). Nevertheless, the cases cited in this chapter do not constitute all of those in the literature because of the unsuitability of some of the reports for proper analysis and the inaccessibility of certain papers. The details of the 41 cases of "stroke" as a complication of cardiac hydatidosis with/without multiple metastatic hydatid cysts of the brain are listed in Tables 22.1 and 22.2.

In this meta-analysis, only 7 (17 %) of the 41 patients of "stroke" as a complication of cardiac hydatidosis in the literature were reported in the period of 1945–1987 and the remaining 34 (83 %) cases in the period of 1990–2011. Importantly, 33 (80 %) of the 41 cases reported were from the Middle East, Mediterranean, or Eastern Europe countries. In all these patients the cerebrovascular condition was caused by rupture of an intracardiac hydatid cyst. There were 24 (59 %) male and 17 (41 %) female patients. Their ages ranged from 4 to 70 years, and 30 (73 %) of the 41 patients reported were clustered in the age between the first and third decades inclusively (Table 22.1).

Locations of Cyst(s)

In all but only two cases, detailed information for the cardiac anatomical location of the hydatid cyst(s) was available. In the cases of cardiac hydatidosis complicated with "stroke" in the literature, there was more than one cyst in the heart, and the most common location of the cyst(s) was the left ventricle (57 %), followed by the septum (13 %), left atrium (13 %), pericardium (11 %), and right atrium (4 %). With the exclusion of only one case without any information, the condition was caused by spontaneous rupture of a primary intracardiac hydatid cyst in 36 (90 %) patients and by surgical rupture of a primary intracardiac hydatid cyst in four (Table 22.1).

Out of 41 cases of "stroke" as a complication of cardiac hydatidosis, 24 (59 %) have single/multiple ischemic/hemorrhagic infarct(s), while 27 (66 %) have single/multiple hydatid cysts. In a total of 10 patients, however, single/multiple hydatid cyst(s) developed within the infarcted cerebral tissue with an interval ranging from a few months to 5 years (Table 22.2). Anatomically, cerebral hydatid embolism from the rupture of a fertile intracardiac hydatid cyst affected the regions of middle cerebral artery, the internal carotid artery, the basilar artery, or peripheral arterial branches (Table 22.2).

Other organs involved by hydatidosis as a result of systemic embolization from the ruptured cyst were the liver in 14 cases, kidney in 8 cases, spleen in 5 cases, lung in 3 cases, eyeball in 2 cases, and thyroid and cecum in 1 case each, in addition to obstruction of the distal branches of the aorta including the renal artery, splenic artery, and femoral artery (Table 22.1).

Clinical Features

Clinical, neuroimaging, and surgical findings are summarized in Table 22.2. Motor weakness, hypoesthesia, IICP, epileptic seizure, and unconsciousness were the most common presenting symptoms in patients with single/multiple infarct(s) and/or metastatic hydatid cysts of the brain. The presenting symptoms were related to (1) embolization from heart with cerebral ischemia and infarction or (2) the mechanical effects of growth and compression of adjacent parenchyma by intracranial hydatid cysts, although they were nonspecific.

Table 22.1 Summary of the 41 reported cases with stroke as a complication of cardiac hydatidosis published in the world literature to date: demographic data and cardiac findings

Author(s)	Country	Year of publication	Patient age (years), sex	Systolic murmur	EC	Location of cyst(s) in the heart	Other organ involvement	Result of serological study	Type of rupture
Peters et al.	USA	1945	5, F	NS	NS	LV[e]	Liver	NS	Spontan
			24, M	NS	NS	LA[e]	NS	NS	Spontan
			45, F	NS	NS	LA, P, IVS, LV[e]	Kidney, spleen, thyroid, ICA, MCA, superior mesenteric artery, renal artery, splenic artery	NS	Spontan
Paillas et al.	France	1962	17, M	(−)	NS	LV[e]	ICA, eyeball, foramen ovale	NS	Spontan
Chin et al.	Australia	1981	37, M	NS	(−)	P	(−)	(+)	Spontan
Vaquero et al.	Spain	1982	37, M	NS	(−)	P, LV	NS	NS	Surgical
Petrov	Bulgaria	1987	32, M	NS	(−)	LV[e]	(−)	NS	Spontan
Borisenko et al.	USSR	1990	11, F	(+)	(+)	LV	(−)	(+)	Spontan
Byard and Bourne	Australia	1991	7, M	NS	(−)	LV	Liver	NS	Spontan
Talaslıoglu et al.	Turkey	1994	19, F	NS	(+)	NS	NS	NS	Spontan
Benomar et al.	Morocco	1994	21, F	NS	(−)	P, LA, LV	Kidney, liver, spleen	NS	Spontan
			40, F	NS	(+)	LV	Kidney, liver, spleen	(+)	Spontan
el Quessar et al.	Morocco	1996	21, F	NS	(−)	P, LV	Kidney, liver, spleen	NS	Spontan
			40, F	NS	(+)	LV	Kidney, liver, spleen	(+)	Spontan
Turgut e al.	Turkey	1997	7, F	(+)	(+)	LV	Femoral artery	NS	Spontan
Ugur et al.	Turkey	1998	18, F	NS	(−)	IVS	NS	NS	Spontan
Kabbaj et al.	Morocco	1998	28, M	NS	(+)	LV	Kidney, liver	(+)	Spontan
Evliyaoglu et al.	Turkey	1998	24, M	NS	(+)	LV	NS	NS	Spontan
Marci et al.	Italy	1998	26, F	(+)	(+)	LV	(−)	(+)	Spontan
Ulgen et al.	Turkey	2000	70, M	NS	(+)	IVS, LV	Liver	(+)	Spontan
Maffeis et al.	Brazil	2000	57, M	NS	(+)	LV	NS	NS	Spontan
Kemaloglu et al.	Turkey	2001	7, F	NS	(+)	LV	NS	NS	Spontan
Cakir et al.	Turkey	2002	6, F	(−)	(+)	LV	(−)	(+)	Spontan
Trehan et al.	India	2002	13, M	(+)	(+)	RA, LA, IAS	Liver	(−)	Spontan

(continued)

Table 22.1 (continued)

Author(s)	Country	Year of publication	Patient age (years), sex	Systolic murmur	EC	Location of cyst(s) in the heart	Other organ involvement	Result of serological study	Type of rupture
Singh et al.[a]	India	2003	13, M	(+)	(+)	RA, LA, IAS	Liver	(+)	Spontan
Acarturk et al.	Turkey	2004	15, M	NS	(+)	LV	Liver, abdominal aorta	NS	Spontan
Pillai et al.	UAE	2004	36, F	NS	(+)	LV	Eyeball	NS	Spontan
Karabay et al.	Turkey	2004	19, M	NS	(+)	IAS, RA, LA	Liver	NS	Spontan
Yaliniz et al.	Turkey	2004	16, M	NS	(+)	LV	Liver	(+)	Surgical
Bükte et al.[b]	Turkey	2004	7, F	NS	(+)	LV	NS	NS	Spontan
Itumur et al.	Turkey	2006	24, M	(+)	(+)	LV	(−)	NS	Spontan
Yaliniz et al.[c]	Turkey	2006	16, M	NS	(+)	LV	Liver	(+)	Surgical
Lotfinia et al.	Iran	2007	17, F	(+)	(+)	S	(−)	NS	Spontan
Aleksic-Shihabi and Vidolin	Croatia	2008	27, M	(+)	(+)	LV, P	(−)	(+)	Surgical
Kumar and Hasan	India	2008	4, M	NS	(−)	LV, P	Lung	(+)	Surgical
Goz et al.	Turkey	2008	24, M	NS	(+)	LV	NS	(−)	Spontan
Ašanin et al.	ME	2008	22, M	NS	(+)	LA	Liver, mediastinum	(+)	Spontan
Byard[d]	Australia	2009	12, M	NS	(−)	LV	Liver	NS	Spontan
Kanj et al.	Lebanon	2010	32, F	NS	(−)	NS	NS	NS	NS
Sabouni et al.	Iran	2010	12, M	NS	(+)	IVS	Kidney, cecum	(+)	Spontan
Kojundzic et al.	Croatia	2010	34, M	(+)	(−)	LV	Lung	(+)	Spontan
Cansu et al.	Turkey	2011	7, M	(−)	(+)	LV	Liver	(+)	Spontan
Potapov et al.	Russia	2011	21, M	NS	(+)	LV	Kidney	(+)	Spontan
Ekici et al.	Turkey	2011	12, M	NS	(+)	LA	(−)	(−)	Spontan
Fabijanić et al.	Croatia	2011	24, F	(−)	(+)	LV	Lung	(−)	Spontan

Abbreviations: *NS* not stated, *USSR* Union of Soviet Socialist Republics, *UAE* United Arab Emirates, *USA* United States of America, *ME* Montenegro, *F* female, *M* male, *LV* left ventricle, *LA* left atrium, *P* pericardium, *S* septum, *IVS* interventricular septum, *IAS* interatrial septum, *RA* right atrium, *ICA* internal carotid artery, *MCA* middle cerebral artery, *EC* echocardiography, *Spontan* spontaneous

[a]The case reported by the authors had already been described by Trehan et al. earlier

[b]The case reported by the authors had already been described by Kemaloglu et al. earlier

[c]The case reported by the authors had already been described by same authors earlier

[d]The case reported by the author had already been described by Byard & Bourne earlier

[e]In these cases, location of the cyst(s) in the heart was determined at autopsy

Table 22.2 Summary of the 41 reported cases with stroke as a complication of cardiac hydatidosis published in the world literature to date: cerebral findings, treatment, and outcome

Author(s)	Presenting symptoms	Imaging study	Kind of cerebral lesion(s)			Location of cerebral lesion(s) (No. of cysts)[e]	Anthel treatment	No. of surgery (cardiac/cerebral)[g]	Outcome
			Infarct	Cyst	Interval				
Peters et al.	NS	NS	(−)	(+)	(−)	Cerebral (1)	NS	0/1	Died
	IICP, right hemiparesis, aphasia	NS	(−)	(+)	(−)	Left T, right O, left P (6)	NS	0/3	Died
	Seizure, coma	NS	(+)	(−)	(−)	Right MCA and ICA	NS	0/0	Died
Paillas et al.	Vertigo, IICP, left hemihypoesthesia and hemiparesis, visual loss and proptosis on right side, seizure	Angio, EEG	NS	(+)	(−)	Right FT (3)	NS	0/1[h]	Died
Chin et al.	IICP, fever, neck stiffness, right hemiparesis	CT	(+)	(−)	(−)	Right cerebellum, both MCA	MEB	1/0[i]	No follow-up
Vaquero et al.	Left hemiparesis	CT	(+)	(+)	5 years	Right MCA, right P, left P, left O (3)	NS	1/2	No follow-up
Petrov	Seizure, coma	Angio	(+)	(−)	(−)	Right MCA[f]	(−)	0/0	Died
Borisenko et al.	Right hemiparesis, loss of speech	CT, MRI, US, Scint	(+)	(+)	9 months	Left MCA, left O (3)	(−)	NS	NS
Byard and Bourne	Unconsciousness, seizure	(−)	(+)	(−)	(−)	Both MCA	NS	0/0	Died
Talaslıoglu et al.	IICP	MRI	(−)	(+)	(−)	NS	NS	0/9	No recur at 2 years
Benomar et al.	Left hemiparesis, IICP, left hemihypoesthesia, fever	CT, Angio	(+)	(+)	9 months	Right MCA, brainstem	NS	0/1	Died
	Right hemiparesis, aphasia	CT, Angio	(+)	(+)	1 year	Left MCA	MEB	0/0	No change at 1 year
el Quessar et al.	Fever, urticaria, left hemiparesis, IICP	CT, MRI, Angio	(+)	(+)	A few months	Right MCA	NS	1/1[j]	Died
	Right hemiplegia, aphasia	CT, Angio	(+)	(+)	A few months	Left MCA	MEB	0/0	No follow-up
Turgut e al.	Left hemiparesis, IICP, cyanosis, double vision	CT, MRI, Angio	(−)	(+)	(−)	Both F (17), both PO (3), both P (8), right O (1)	MEB+ALB	1/8[j]	No recur at 2 years

(continued)

Table 22.2 (continued)

Author(s)	Presenting symptoms	Imaging study	Kind of cerebral lesion(s)			Location of cerebral lesion(s) (No. of cysts)[e]	Anthel treatment	No. of surgery (cardiac/cerebral)[g]	Outcome
			Infarct	Cyst	Interval				
Ugur et al.	Left hemiparesis, IICP	CT	(−)	(+)	(−)	Right F, P and both PO (7)	ALB	0/1	No follow-up
Kabbaj et al.	Left hemiplegia, facial paralysis, aphasia	CT	(+)	(−)	(−)	Right MCA	NS	1/0	No follow-up
Evliyaoglu et al.	Right hemiparesis, aphasia	CT, US	(+)	(+)	6 months	Left MCA, left F (3) right T (mult)	NS	0/2	Died
Marci et al.	Right hemiplegia	CT, MRI, US	(+)	(−)	(−)	Left MCA	ALB	1/0	No follow-up
Ulgen et al.	Vertigo, syncope, cardiac arrest	MRI	(+)	(−)	(−)	MCA	(−)	0/0[j]	Died
Maffeis et al.	Right hemiparesis	CT, MRI, Angio	(+)	(−)	(−)	Left ICA, right cerebellum	ALB	1/0	Well at 6 weeks
Kemaloglu et al.	Right hemiparesis, dysphasia, seizure, facial paresis	CT, MRI, US	(+)	(+)	6 months	Both PO (2)	MEB	1/1	Partial recovery at 3 months
Cakir et al.	Hemiparesis, speech disturbance	CT, US	(−)	(+)	(−)	Left PO (1)	MEB	1/1	No recur at 2 months
Trehan et al.	Right hemiparesis	CT, Angio, US	(+)	(−)	(−)	Left basal ganglia	ALB	1/0	Complete recovery at 1 month
Singh et al.[a]	Right hemiparesis	CT, Angio, US	(+)	(−)	(−)	Left basal ganglia	NS	NS	NS
Acarturk et al.	Right hemiparesis, seizure, aphasia	MRI, US	(+)	(−)	(−)	Left capsulostriatum	ALB	1/0[j]	Partial recovery and no recur at 6 months
Pillai et al.	Left proptosis, diplopia	CT, US	(−)	(+)	(−)	Both P (mult)	NS	0/0[j]	No follow-up
Karabay et al.	IICP	CT, MRI	(−)	(+)	(−)	Left F (1)	ALB	1/0	Well at 6 months

Yaliniz et al.	Right hemiparesis, aphasia	CT, MRI, US	(+)	(−)	(−)	Left MCA	ALB	1/0[j]	Complete recovery at 5 months
Bükte et al.[b]	Right hemiparesis, dysphasia, seizure, facial paresis	CT, MRI, US	(+)	(+)	6 months	Both PO (2)	MEB	1/1	Partial recovery at 3 months
Itumur et al.	Right hemiparesis, IICP, dysphasia	MRI	(−)	(+)	(−)	Left cerebrum (18)	ALB	1/2	No recur at 6 months
Yaliniz et al.[c]	Right hemiparesis, aphasia	CT, MRI, US	(+)	(−)	(−)	Left MCA	ALB	1/0[j]	Complete recovery at 5 months
Lotfinia et al.	IICP, coma, left hemiparesis, visual loss	CT, MRI	(+)	(+)	2 years	Left basal ganglia, left PO, right TP, right O (5)	ALB	2/2	No recur at 2 years
Aleksic-Shihabi and Vidolin	Left hemiparesis, IICP, facial paresis	CT	(−)	(+)	(−)	Right PO (1)	ALB	2/1	No follow-up
Kumar and Hasan	Right hemiplegia, fever	CT, MRI	(+)	(−)	(−)	Left basal ganglia	ALB	1/0	No follow-up
Goz et al.	Right hemiparesis	CT, MRI US	(−)	(+)	(−)	Left P, O, F and cerebellum (NS)	ALB	1/2	No recur at 15 months
Asanin et al.	Right hemiparesis, aphasia, TIA	CT, MRI	(+)	(−)	(−)	Left MCA	NS	0/0[j]	NS
Byard[d]	Unconsciousness	(−)	(+)	(−)	(−)	Both MCA	NS	0/0	Died
Kanj et al.	Right hemiparesis, IICP	CT, MRI	(+)	(+)	11 months	Left MCA, left FP (2)	NS	0/1	No follow-up
Sabouni et al.	Left hemiparesis, IICP, facial paresis	CT, US	(−)	(+)	(−)	Right T, both centrum semiovale (5)	ALB+PRAZ	1/1[j]	No follow-up
Kojundzic et al.	Left hemiparesis, IICP, facial paresis, left hemihypoesthesia	CT, MRI, US	(−)	(+)	(−)	Right T, P, O (3)	ALB	1/2[j]	No follow-up
Cansu et al.	Bilateral hemiparesis, unconsciousness, fever, seizure, ulcer of limb	CT, MRI US	(+)	(−)	(−)	Left FPO	ALB	1/0[j]	No follow-up

(continued)

Table 22.2 (continued)

Author(s)	Presenting symptoms	Imaging study	Kind of cerebral lesion(s)			Location of cerebral lesion(s) (No. of cysts)[e]	Anthel treatment	No. of surgery (cardiac/cerebral)[g]	Outcome
			Infarct	Cyst	Interval				
Potapov et al.	Left hemiparesis, IICP, right hemianopsia	CT, MRI, MR tracto	(−)	(+)	(−)	Right P, left PO (6)	NS	0/1[k]	Complete recovery at 4 months
Ekici et al.	Left hemiparesis, IICP, seizure	CT, MRI US	(−)	(+)	(−)	Right PO (3)	ALB	0/(mult)[k]	No follow-up
Fabijanić et al.	Syncope	US	NS	(+)	NS	NS (NS)	ALB+PRAZ	1/1[j]	No recur at 1 year

Abbreviations: *NS* not stated, *CT* computed tomography, *MRI* magnetic resonance imaging, *IICP* increased intracranial pressure, *TIA* transient ischemic attack, *Angio* angiography, *Scint* scintigraphy, *ICA* internal carotid artery, *MCA* middle cerebral artery, *F* frontal, *T* temporal, *P* parietal, *O* occipital, *FP* frontoparietal, *PO* parieto-occipital, *FPO* fronto-parieto-occipital, *anthel* anthelmintic, *MEB* mebendazole, *ALB* albendazole, *PRAZ*, praziquantel, *recur* recurrence, *MR tracto* MR tractography, *mult* multiple

[a]The case reported by the authors had already been described by Trehan et al. earlier

[b]The case reported by the authors had already been described by Kemaloglu et al. earlier

[c]The case reported by the authors had already been described by same authors earlier

[d]The case reported by the author had already been described by Byard & Bourne earlier

[e]No. of cysts within the brain tissue

[f]In this case, two hydatid cysts were removed from the right MCA at autopsy

[g]No. of operations include cardiac (first) and brain (second) operations

[h]In this patient, carotid sympathectomy and cervical ganglion resection were also done for occlusion of ICA

[i]In this patient, only pericardial puncture was done as a diagnostic procedure

[j]An additional surgery was done for involvement of other organs such as the lung, liver, intestine, eyeball, abdominal aorta, or femoral artery by hydatid cysts

[k]The patient was treated surgically with the aid of a neuronavigation system

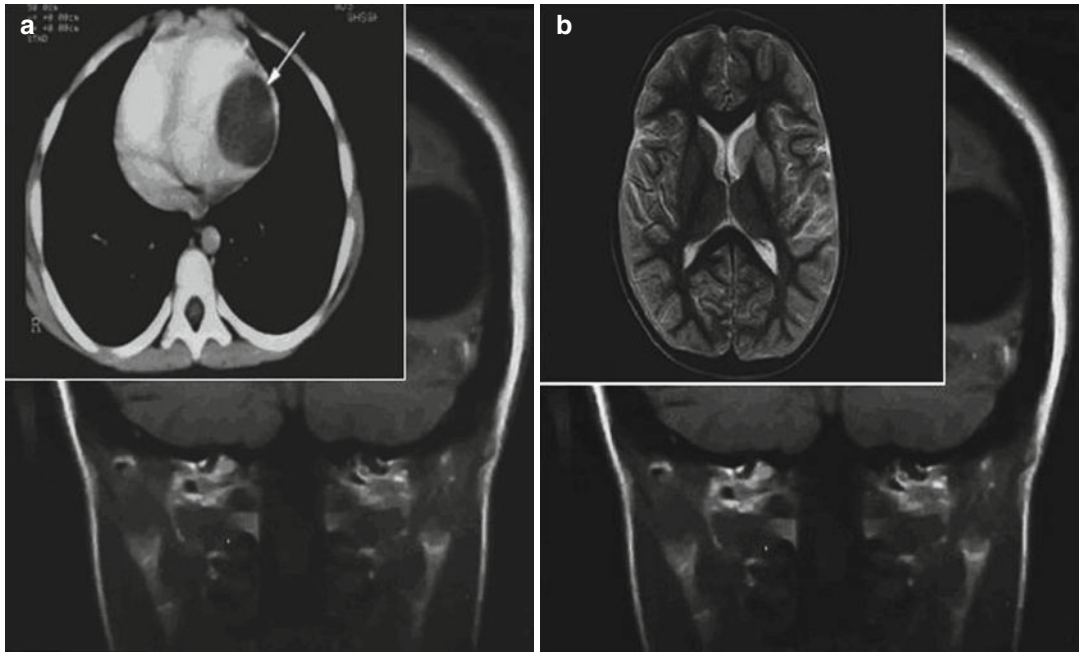

Fig. 22.5 Stroke as a complication of cardiac hydatidosis. (**a**) Axial contrast-enhanced CT of thorax shows a well-defined cystic mass (*arrow*) in the left ventricle of the heart. (**b**) Axial T2-weighted MRI shows hyperintense lesions in the left basal ganglia (From Kumar and Hasan (2008), with permission)

Interestingly, there were no EC signs of cystic formation in the heart in 10 (27 %) of 37 patients with detailed information. In addition, physical examination revealed a systolic murmur in only 8 cases with cardiac hydatidosis complicated with single/multiple hydatid cysts. Similarly, results of serologic tests for hydatid disease were negative in 4 (25 %) of 20 patients with detailed information (Table 22.1).

Imaging Findings

Radiological information for three patients was not available and data for these patients are not included. Thus, all but one were investigated by neuroimaging studies including CT, MRI, angiography, US, or MR tractography and at autopsy in five (Figs. 22.3, 22.4, 22.5, and 22.6) (Benomar et al. 1994; Turgut et al. 1997; Lotfinia et al. 2007; Kumar and Hasan 2008). In these cases, characteristic findings of cerebral hydatidosis were well-defined, smooth, thin-walled, spherical, homogeneous cystic lesions with no contrast enhancement, no calcification, and no surrounding edema. On the other hand, the diagnosis of intracardiac hydatidosis was confirmed by EC in 27 of 41 patients (Table 22.2).

Treatment

Excluding the eight cases without cardiac or intracranial surgery, 32 reported patients with detailed information had surgery ranging from one to nine operations. In cases of "stroke" with/without multiple metastatic hydatid cysts of the brain as a complication of cardiac hydatidosis, the number of cerebral cysts ranged from 1 to 29. Technically, complete removal of multiple cysts or those with atypical localization was usually difficult and radical extirpation of the cyst was not possible without rupture, although removal of a single cerebral hydatid cyst was achieved by the Dowling-Orlando technique without any difficulty. Anthelmintics such as mebendazole, albendazole, and praziquantel were administered in all but only three cases reported in the literature (Table 22.2).

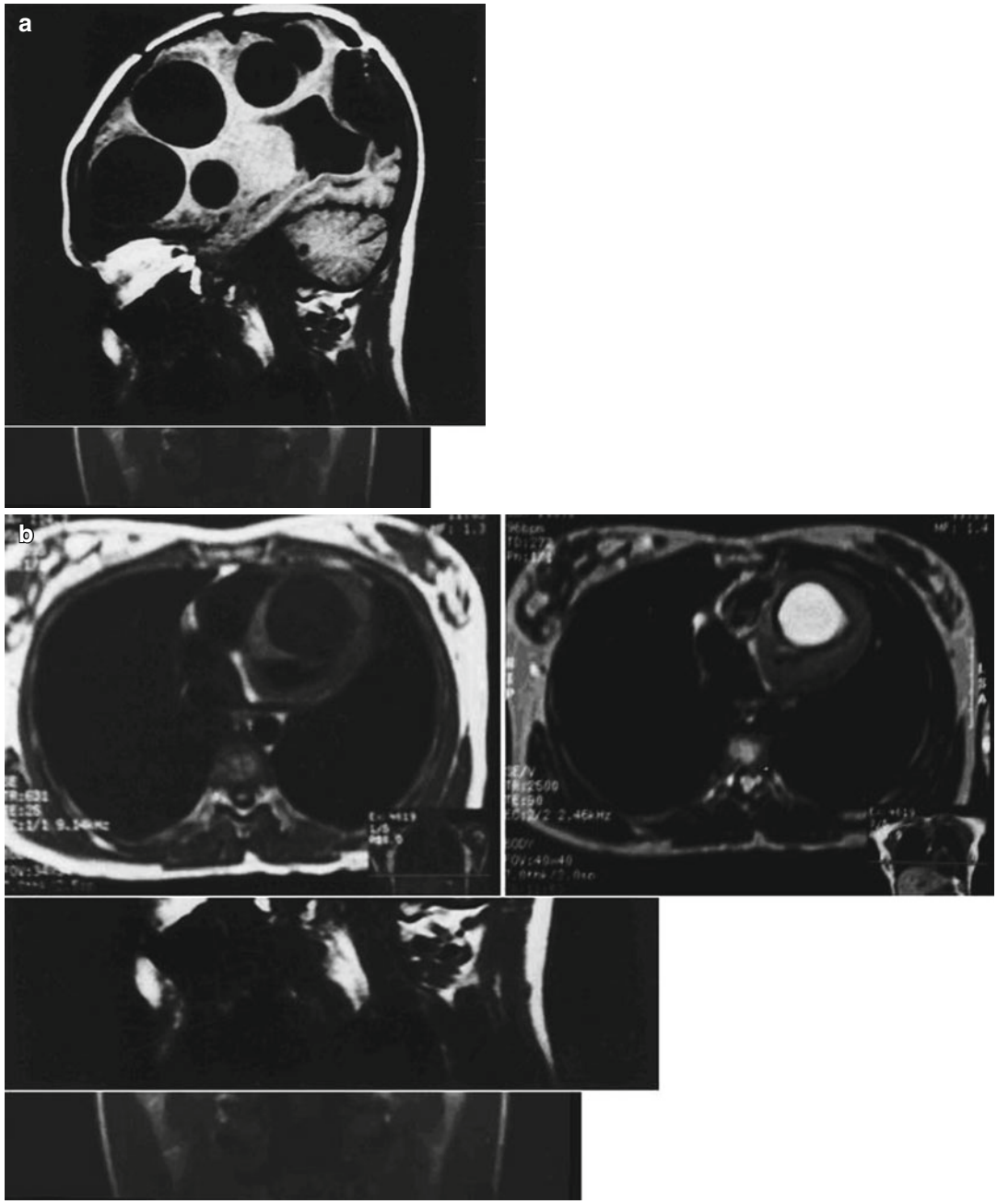

Fig. 22.6 Stroke as a complication of cardiac hydatidosis. Axial T1 (**a**) and T2 (**b**) -weighted MRI shows a giant hydatid cyst in the interventricular septum of the heart (Reproduced, with permission, from Turgut et al.: J Neurosurg 1997;86:716)

Prognosis

Some patients died preoperatively of cerebral infarction caused by embolized fragments from a ruptured cardiac hydatid cyst that was found at autopsy (Peters et al. 1945; Petrov 1987; Byard and Bourne 1991; Ulgen et al. 2000), but almost all the other patients underwent surgical intervention. We found that, in a review of the literature, outcome information for 14 patients was not

available and there were a total of 10 (24 %) deaths (Table 22.2).

Conclusion

The following conclusions may be gleaned from the present chapter and the review of the series of cardiac hydatidosis as a source of cerebral embolism from the published literature:

1. In most cases, the diagnosis is difficult in cardiac hydatidosis, owing to the presence of long latency period and nonspecific findings, but early diagnosis and treatment are important.
2. As a rule, the hydatid cyst embolism is an infrequent but serious complication of cardiac hydatidosis in geographic locations where the disease is endemic, because it remains a possible cause of sudden death.
3. In cases with cerebral hydatidosis presenting as "stroke," a persistent investigation is required to detect new hydatid cyst formation in the heart as a source of embolism, as demonstrated by some authors (Turgut et al. 1997; Evliyaoglu et al. 1998; Itumur et al. 2006; Goz et al. 2008; Kojundzic et al. 2010; Ekici et al. 2011).
4. Importantly, the neurosurgeon must always remember that all of multiple secondary cerebral cysts can seldom be removed without rupture, but there is no risk of rupture in the infertile secondary cerebral cysts.
5. Finally, as a rule, especially in pediatric and young patients with otherwise unexplained cerebral embolism, a careful search for the possibility of cardiac cyst as a source of embolism should be undertaken in patients with multiple intracranial hydatid cysts because the combined therapy with surgical treatment and chemotherapy would not be successful without removal of the intracardiac hydatid cyst.

Acknowledgments Thanks to Dimitar Vuchev and Stefan Sivkov, who translated some texts from Bulgarian and Russian to English, and Bülent Bozdoğan for having translated some texts from French and Spanish to English. We especially would like to thank Fuad Sami Haddad for having reviewed the text in English.

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Hydatidosis of the Orbit

23

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Contents

Introduction

Hydatidosis of the orbit is of rare occurrence, and very few, if any, have a wide experience of this disease in this location. We shall endeavor to use the experience of many other authors to present an as accurate as possible picture of this clinical presentation and its management.

Incidence

Hydatid disease of the orbit is rare, even in endemic areas, and accounts for less than 1 % of all hydatid cysts (Gomez Morales et al. 1988; Betharia et al. 2002). To our knowledge orbital hydatid cyst has never been described bilaterally. It commonly occurs as a primary cyst or may be associated with cysts in other locations (Sami et al. 1995; Jimenenez-Mejias et al. 2000). An orbital cyst is located in the retrobulbar space either within the muscle cone or outside, especially in the superolateral or superomedial aspect of the orbit (Alparslan et al. 1990; Guerinel et al. 1991; Gomez Morales et al. 1988). In an exceptional case the cyst was located in the medial rectus muscle (Kiratli et al. 2003). Hydatid cyst is the second most common parasitic cystic lesion in the orbit, after cysticercosis. Hydatid cysts account for 0.3–5 % of all orbital diseases (Xiao and Xueyi 1999; Subrahmanyam et al. 2008). In our series of 1,700 cases of proptosis, in only seven patients was it due to a hydatid cyst.

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Hydatidosis usually affects children and young adults. In a review article of 35 cases by Gomez Morales et al. (1988) the age range was 2–57 years, with a mean age of 16 years (Gomez Morales et al. 1988). Most of the patients are in the second decade of life below the age of 16 years. Elders are rarely affected. Xiao and Xueyi (1999) reviewed their hospital records and issues of Chinese medical journals between 1956 and 1994 and found 18 cases of orbital hydatid cyst, including ten cases from their hospital. Among the 18 cases, 7 were males and 11 were females, with an age range of 3–55 years; 15 cases were below the age of 16. However, orbital hydatidosis can occur in older people and was reported in five patients between the ages of 70 and 74 years (Sangawe et al. 1982; Lerner et al. 1991; Abbassi et al. 2007; Jeblaoui et al. 2008; Limaiem et al. 2010) (see Table 23.1).

Clinical Features

Unilateral, progressive, axial or non-axial, non-tender, non-pulsatile proptosis is the most common presentation of orbital hydatidosis and was present in almost all reported cases (Turgut et al. 2004; Garrity and Henderson 2007; Subrahmanyam et al. 2008). This proptosis is irreducible. Usually, the proptosis is of a few months' duration up to 2 years and may be associated with mild pain or discomfort. In our experience, hydatid cysts are the most common intraconal cystic lesions that occur in young patients. As the mass increases in size, it can cause relative afferent pupillary defect, choroidal folds, edema of the optic disc, limitation in ocular motility, and visual impairment (Turgut et al. 2004; Garrity and Henderson 2007; Subrahmanyam et al. 2008). In a meta-analysis, conducted in Turkey (Turgut et al. 2004), slow progressive unilateral proptosis, with or without pain, was the most frequent clinical manifestation (80 %). The other presenting symptoms were visual loss (48 %), periorbital pain (24 %), chemosis (16 %), and headache (12 %). Refractive errors, corneal complications due to exposure, decrease vision due to keratitis and optic nerve compression. Diplopia due to ocular motility restriction can be a rare symptom (Crompton et al. 1985; Kiratli et al. 2003). If they are non-axial, they may be palpable and may even present under the conjunctiva (Mehta et al. 2010). It may be associated with chemosis of the conjunctiva (Talib 1972b; Hanioglu et al. 1997; Betharia et al. 2002).

In long-standing cases, the cyst can grow to a very large size, deforming the globe (Akhan et al. 1998; Subrahmanyam et al. 2008). In a child, the course can be more rapid and may suggest an orbital sarcoma. Orbital hydatid cysts associated with exudative retinal detachment which settled after a total excision of the cyst were reported (Gelisken et al. 1994). Other unusual presentations would include spontaneous rupture of the mother cyst as in the case reported by Ozek et al (1993). A 52-year-old female presented with a 6-month history of painless proptosis of the right eye and a 4-day history of total visual loss associated with severe orbital pain. She had very gross proptosis (28 mm). Intraoperatively a ruptured mother cyst was found with 3 daughter cysts which were removed. The patient was managed successfully with irrigation of the orbital cavity with 3 % sodium chloride solution and oral mebendazole.

Orbital cysts are most often isolated but can be associated with hydatidosis elsewhere in the body, like the lung, liver, and brain (Betharia et al. 2002; Papathanassiou et al. 2008; Siddiqui et al. 2010). Hence, in orbital hydatid disease cases, a whole-body computed tomography (CT) scan and a head magnetic resonance imaging (MRI) scan are mandatory to insure that no other dissemination exists.

Diagnostic Procedures

The plain X-ray, a long forgotten diagnostic procedure, shows thinning and at times erosion of one of the walls of the orbit, the nearest to the cyst. In western countries MRI scan of the orbit is the gold standard imaging technique. However, in endemic countries, the more economic CT scans show a well-encapsulated cys-

Table 23.1 Summary of the 234 reported cases with orbital hydatidosis published in the world literature to date

Author(s)	Country	Year of publication	No. of cases and sex	Age (in years) and side	Proptosis	Visual loss	Location[a]	Surgery[a]	Cyst rupture[a]	Remarks[a]
Wood	South Africa	1925	2F, 1NS	16L, 25R, 3L	3+	2+	Intracon (3)	Operated (3)	Ruptured (3)	Pain in orbit (2)
Seale	South Africa	1926	1F	8R	+	+	Sup-med	Curetting	+	
Handousa	Egypt	1951	2F, 1M	12, 12R, 1L	3+	NS	Intracon (2)	NS (2), 1+	1=0;1=; NS (1)	Palpable (3)
Mazhar	Aden	1954	2F	35L, 35R	2+	2+	Sup-lat	Ant approach	Ruptured (2)	Both were palpable
Lidgett	Australia	1955	1M	55L	NS	NS	Upper med	Orbitonasal	NS	Hypophoria
Tonjum	Sweden	1963	1F	55R	+	+	Sup-lat	Krönlein	+	No systemic HC found
Van Selm	South Africa	1964	5	5<10	5+		Muscle cone (4)	Lat (4), sup (1) orbito	Aspirated	Review of patients below 13
Mehra et al.	India	1965	1M	30R	+	+	Sup-med	Trans-sup lid	Ruptured	
Reddy et al.	India	1970	1M	13L	+	+	Intraorbital	Lat orbito	Ruptured	5×5 cm
Baghdassarian and Zakharia	Lebanon	1971	2M, 1F	31M, 6M, 7F	3+	3+	Med (3), sup (2), inf (1)	Krönlein (1), lid incision (2)	3+	Negative follow-up at 6 months, 18 yrs, and 13 yrs
Talib	Iraq	1972a, b	11M, 11F	11<20 L/R=2/1	18+	NS	Sup-lat or sup-med	Dickson Wrght	NS	Ten years experience left/right=2/1
Zakharia et al.	Lebanon	1972	3	2<15						Unilateral exophthal (85)
Sevel and Sapeika	South Africa	1977	6M, 5F	11 below 17	11+	7+	Retrobulb (11)	Transcutaneous (5), lat orbito (6)	Ruptured (11)	
Amaya et al.	Bolivia	1980	3							
Apple et al.	Cameroun	1980	1NS	6R	+	–	NS	Orbital exploration	–	Pallor of fundus
Danziger and Price	South Africa	1980	1F	9L	+		Med	Done	Biopsy	Papilledema
Okelo et al.	Kenya	1980	1M	17R	+	+	Floor of orbit	NS	NS	
Toledo and Szelagowski	Argentina	1980	1M	18R	+	+	Muscle cone	Operated	NS	
Agarwal et al.	India	1982	1M	38	+	None	Left orbit	Mebendazole	None	HC in spleen
Hamza et al.	Tunisia	1982	9	NS	+	NS	NS	NS	NS	Study of 55 cases
Kars et al.	Turkey	1982	1M, 1F	7L, 11R	2+	+, +	Retrobulb	Cranio (2)		1st case reoperated

(continued)

Table 23.1 (continued)

Author(s)	Country	Year of publication	No. of cases and sex	Age (in years) and side	Proptosis	Visual loss	Location[a]	Surgery[a]	Cyst rupture[a]	Remarks[a]
Sangawe et al.	India	1982	1M	70R	+	+	Intraorbital	Enucl	Aspirated	Chemosis
Klaus and Chana	Kenya	1983	2M, 7F	6–25	9+					Average age 18.8
Lamba et al.	India	1983	1M	Young R	+	+	Upper med	Ant orbito	None	Restriction all eye mov
Bassiri and Jabi	Lebanon	1984	1F	56	+	NS	Intraorbital	Cranio	NS	Chest cyst, ptosis
Crompton et al.	Australia	1985	1M	59	NS	NS	Infraorbital	Sinusecto	NS	Diplopia
Staindl and Krenkel	Germany	1985	1F	5	NS	NS	Orbit	NS	NS	Liver cyst
Chana et al.	Kenya	1986	5F, 2M	5<15, 5L–2R	7+	7+	Intraorbital (7)	NS	3	
Khalili	Iraq	1987	5M, 10F	10–50	15+	11+	NS	Done	NS	
Gomez et al.	Argentina	1988	35	26<16	25+	7+	Orbital	Orbito (28)	NS	41 yrs experience
Lopera et al.	Venezuela	1989	1F	61L	+	NS	Sup nasal	Cranio	+	*E. oligarthrus*
Alparslan et al.	Turkey	1990	1M, 1F	11L, 6R	2+	+, +	Upper med	Orbito	None, +	
Lerner et al.	Argentina	1991	1F	73L	+	+	Inf lat orbit	Krönlein	+	
Nahri	Egypt	1991	1M, 1F	6L, 4L	2+	0	Intarcon (1)	Orbito (2)	Aspirated (2)	No recurrence in 24 and 18 months
Turgut et al.	Turkey	1992	1M	5L	+	+	Muscle cone	Cranio	Ruptured	Chest HC
Diren et al.	Turkey	1993	1F	10R	+	NS	Retrobulb	Cysts removed in one stage (3)	NS	HC in right frontal lobe and left ventricle
Malde et al.	USA	1993	1M	33L	+		Sup orbital	Orbito	None	
Ozek et al.	Turkey	1993	1F	52R	+	+	Sup orbital	Kronlein	Ruptured	
Mohammad et al.	Egypt	1994	1F	15R	+	None	Intracon	Anteromedial	Ruptured	Neck and liver cysts
Sperryn and Corr	South Africa	1994	10	Mean age 16 (3–41)	10+	4+	Intracon (5)	NS	NS	Ten-year review
Fink et al.	Canada	1995	1M	4 1/2 R	+	NS	Lat upper	NS	NS	Liver HC
Saenz-Santamaria et al.	Spain	1995	1M	8	NS	NS	NS	Aspiration	Aspirated	1 of 15 cases
Sami et al.	Morocco	1995	5M, 5F	Mean 25	10+	7+	Intraorbital	Cranio (9)	None	Frontotemporal (1)
Sharma et al.	India	1995	1M, 1F	18L–25L	2+	+, +	Orbito, NS	Rupture, NS	+, NS	
Sodhani et al.	India	1996	1F	25R	+	None	Intraorbital	Lat orbito	Aspirated	
D'Alessandro	Columbia	1997		NS	NS	NS	Intraorbital	NS	NS	*E. oligarthrus* (2)
Ergün et al.	Turkey	1997	1F, 3M	3<15	+	2+	Intraorbital	Cranio (4)	4, PAIR	
Gokcek et al.	Turkey	1997	1F	60L	+	+			+	
Hanioglu et al.	Turkey	1997	1M	4L	+	+	Inf-med	Exploration	Aspirated	Infiltrated maxillary sinus

Karakas et al.	Turkey	1997	2M	54R–6L	+	+	Intraorbital	Cranio		Papilledema
Saygi et al.	Turkey	1997	1M	4L	+	+	Med orbital	NS	Aspirated	Partial removal of cyst
Akhan et al.	Turkey	1998	1M	21R	+	NS	Retrobulb	PAIR	Aspirated	Diplopia
Basset et al.	Suriname	1998	1M	6L	+	+	Intraorbital	Cranio	Ruptured	*E. oligarthrus*
Rastogi et al.	India	1998	1M	25R	+	+	Retrobulb	Enucl	Ruptured	Multiple daughter cysts
Belmekki et al.	Morocco	1999	8	1–15	NS	NS	NS	NS		Out of 54 children
Chaabouni et al.	Tunis	1999	1M	5L	+	None	Inf lat orbit	Cranio	None	No systemic disease
Xiao and Xueyi	China	1999	7M, 11F	15<16	14+	6+	Intracon (11)	Orbito (13)	PAIR	38-year review. 8116 cases of HC
Zahawi et al.	Iraq	1999	1M, 3F	Mean 21.3						4 out of 92 HC cases
Zaidi	Libya	1999	1M	19		+		+		
Zaidi	Austria	1999	1		+	+			None	Systemic hydatidosis
Jimenenez -Mejias et al.	Spain	2000	1M	22L	+	+	Sup-lat	Lat orbito	+	No recurrence in 7 yrs
Kargi and Kargi	Egypt	2000	1M	4L	+	+	Inf-med	Subtotal excision	Aspirated	No recurrence in 3 yrs
Sihota and Sharma	India	2000	1M	14L	+	+	Entire orbit	Albendazole	None	2 previous surgeries
Aksoy et al.	Turkey	2001	1M	4R	+	NS	Intracon	Lat orbito	None	Cysts in liver and lungs
Gokcek et al.	Turkey	2001	1M	4	+	+	Intraorbital	Lat orbito	Intact	Papilledema
Betharia et al.	India	2002	1F	35L	+	+	Sup-med	Cryoextract	Aspirated	Systemic disease
Kaymaz et al.	Turkey	2002	1F	8R	+	NS	Intraorbital	Lat orbito	None	
Betharia et al.	India	2003	9	NS	NS	NS	NS	Surgery (9)	NS	Double wall sign
Kiratli et al.	Turkish	2003	1F	20R	NS	None	Med rectus	+		Pain on eye mov
Souhail et al.	Morocco	2003	2	NS	2+	NS	NS	NS	NS	
Cooney et al.	Kenya	2004	NS	NS	NS	NS	Retro-orbital	NS	NS	710 cases reviewed
Turgut et al.	Turkey	2004	25	18<20; 11R, 13L	20+	11+	Intracon (9)	Enucl (4); orbito (10)	9	Review of 30 yrs
Diatchuk et al.	Israel	2005	1M	14R	+	NS	Extraconal	PAIR	1	
Murthy et al.	India	2005	1F	14R	+	+	30 cysts	Enucl		*E. oligarthrus*
Ciurea et al.	Hungary	2006	1M, 1F	15L, 4L	2+	2+	Intracon	Cranio (2)	1	
Ryou et al.	Korea	2002	1F	33R	+	+	Intracon	Lat orbito	+	Pain in affected eye

(continued)

Table 23.1 (continued)

Author(s)	Country	Year of publication	No. of cases and sex	Age (in years) and side	Proptosis	Visual loss	Location[a]	Surgery[a]	Cyst rupture[a]	Remarks[a]
Abbassi et al.	Morocco	2007	1M	70L	NS	+	Multiple	Medical	None	Headache and neck mass
Sanli et al.	Turkey	2007	1F	22R	+	+	NS	Cranio	None	
Ali et al.	Pakistan	2008	2	NS	NS	NS	NS	Lat orbito (2)	NS	Over a period of 7 yrs
Jeblaoui et al.	Tunisia	2008	1M	72L	+	+	Postero-lat	Lat orbito	None	
Papathanassiou et al.	Greece	2008	1	Child				Albendazole	None	Lung and liver
Groves et al.	Kenya	2009	1F	25R	+	None	Postero-med	Aspiration	+	Into nose and fronto-ethmoid sinus
Bagheri et al.	Iran	2010	1M, 1F	11L, 8R	2+	1+, 1−	Intracon (2)	Lat orbito (2)	1+ and 1−	A case had 2 previous surgeries and one *E. alveolaris*
Benazzou et al.	Morocco	2010	6M, 4F	7 below 12	10+	8+	Retrobulb (10)	Cranioto (10)	Ruptured (9)	CNS HC 135 cases
Limaiem et al.	Tunisia	2010	1M	74L	+	+	Retrobulb	Cranioto	Rupture	
Mehta et al.	Turkey	2010	1F	35L	+	+		Trans conjunctiva	+	Double wall sign
Siddiqui et al.	India	2010	1M	7L	+	+	Thru roof	Aspirat	Punctured	Extension of epidural
Yazdani et al.	Iran	2010	1F	14R	+	+	Subtemporal	Caldwell-Luc	None	Multiple brain HC
Bhaduri et al.	India	2011	1F	40L	+	+	Intracon	Enucl	NS	
Menghi and Gatta	Argentina	2011	1F	41R	+	NS	Orbit	Surgery	Ruptured	
Sharma et al.	India	2011	1M	6L	+	+	Outside muscle cone	Extended lat orbito	Aspirated	Eye pushdown and lat. bilobed cyst
Yurt et al.	Turkey	2011	1M	3L	+		Retro-orbital	Lat orbito	None	Adherent to lat rectus
Holland	India	2012	8		8+	6+	Upper med	Conjunctiva	Aspirated (8)	Formalin injection
Kahveci	Turkey	2012	1F	6L	+	+	Inf lat orbit	Cranioto	PAIR	
Somay et al.	Turkey	2012	1M	10	NS	NS	Intracon	Cranio	None	

Abbreviations: *NS* not stated, *ant* anterior, *lat* lateral, *med* medial, *sup* superior, *inf* inferior, *F* female, *M* male, *R* right, *L* left, *CNS* central nervous system, *exophthal* exophthalmos, *HC* hydatid cyst, *intracon* intraconal, *mov* movement, *cranio* craniotomy, *cryoextrat* cryoextraction, *Enucl* enucleation, *orbito* orbitotomy, *PAIR* puncture-aspiration-injection of scolicidal fluid-reaspiration, *retrobulb* retrobulbar, *sinusecto* sinusectomy, *yr(s)* year(s)

[a]Numbers within the brackets show no. of cases for each entity

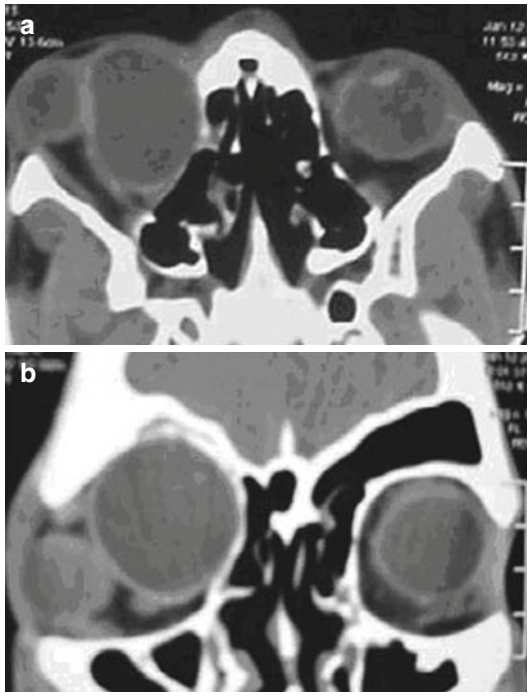

Fig. 23.1 (**a**) Axial section of CT scan of orbit showing a very large, thin-walled hydatid cyst displacing the globe laterally. The size of the cyst is larger than the eyeball. Look at the bony "excavation" with very smooth margins of the medial wall which denotes a "chronic course" of a "benign lesion." (**b**) Coronal section of CT scan of the orbit showing a very large, isodense cystic lesion displacing the globe inferolaterally and it dwarfs the globe

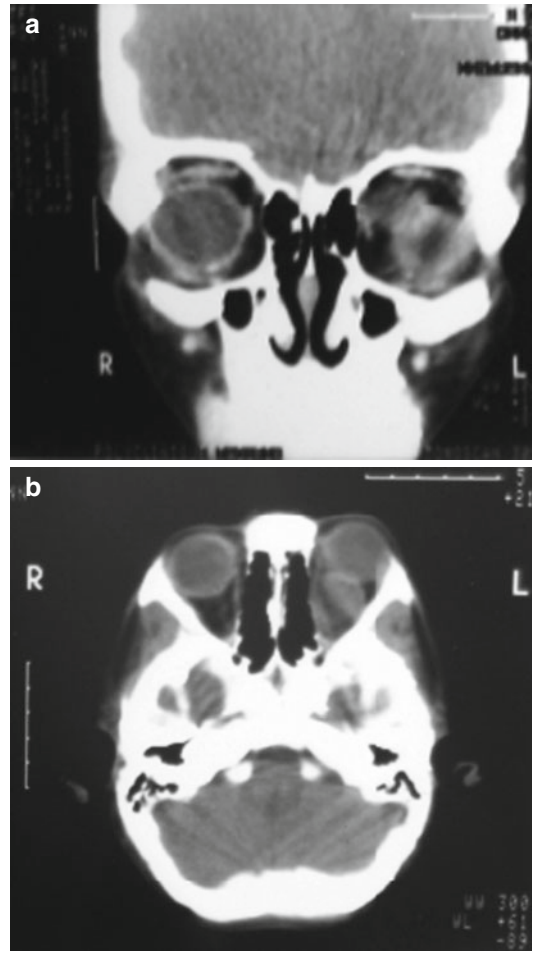

Fig. 23.2 (**a**) Coronal view and (**b**) axial view. A 28-year-old male patient; CT scan of the orbit shows hydatidosis of the orbit (Courtesy of F. Limaiem)

tic mass with cyst fluid showing attenuation values of 3–30 HU (Figs. 23.1, 23.2, and 23.3). The mass can indent and deform the globe. Calcification of the internal septa may be seen. MRI is the alternative choice of imaging diagnostic techniques. MRI shows a low-intensity signal on T_1-weighted images and a high-intensity signal on T_2-weighted images (Diren et al. 1993; Gokcek et al. 1997).

B-scan ultrasound of the orbit shows confirmatory diagnostic double wall sign; spoke wheel pattern and water lily sign are seen with cyst calcification (Malde et al. 1993). The double wall sign described by Betharia et al. (2002) was considered diagnostic of hydatid disease of the orbit. However, this double wall sign was described by Kashyap et al. (2009) in a case of an orbital schwannoma with cystic degeneration.

Other investigations are as follows:

- Hemogram is usually normal.
- Stool examination does not show eggs or cysts.
- Casoni's intradermal test is positive in 75 % of the people (Subrahmanyam et al. 2008).
- Counter immunoelectrophoresis (Kiratli et al. 2003).
- Fine-needle aspiration biopsy: microscopic analysis of the cyst fluid shows scolices and hooklets (Saenz-Santamaria et al. 1995). However, this test is strongly contraindicated.
- Enzyme-linked immunosorbent assay (ELISA) and the indirect hemagglutination test are highly sensitive procedures for serum screening; sensitivity rates vary from 60 to 90 %.

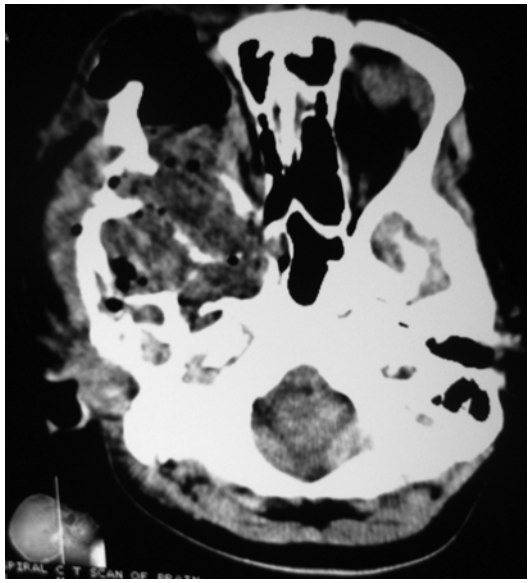

Fig. 23.3 A hydatid abscess entering into the right orbit from the surrounding anatomic structures (Courtesy of M.Z. Hossain)

Pathology

The cyst is pearly white and has a wall consisting of three layers. Unlike in brain cysts, where the pericyst is so thin that it may go unnoticed, the pericyst in retro-orbital cysts may be well formed. This is due to the proximity of fibrous tissue in the orbit. The ectocyst is a structureless, acellular, laminated, homogeneously basophilic material. The ectocyst cyst is laminated and has the characteristic "coats of an onion" appearance (Garrity and Henderson 2007). The endocyst may show overgrowth and is the germinative layer. The clear fluid filling the cyst may show hooklets and scoleces if the cyst is intact and productive. In long-standing cysts, specks of calcium may be present. Some may contain daughter cysts.

Management

Surgery

The aim of surgery is to deliver the entire cyst intact and not to spill any of its content in the orbit or the adjoining tissues. We feel it is best achieved through a subfrontal approach. We believe surgery of orbital hydatid cysts is a neurosurgical procedure and not an ophthalmological one. The essence is to deliver the cyst intact, without rupturing it, a result which is seldom achieved through an ophthalmological approach especially in those cysts located in the medial aspect of the orbit.

The eyelids should be closed with a scotch tape or a tarsorrhaphy to protect the cornea. The draping is an essential part of this procedure. The drapes should be laid loose over the affected eye to allow an eventual Credè procedure. The incision is a regular bifrontal incision, behind the hair line, if possible going way down to below the zygoma on the affected side sparing the seventh nerve on that side. The soft tissues are reflected over the eyes. They should be held high up away from the forehead and eyes, to allow for the surgeon's hand to reach the affected eye from over the drapes during surgery. A frontal free bone flap is raised as close to the supracillary ridge as possible, possibly including it. In case the frontal sinus is in the way, it should be opened, exenterated, and its inner wall completely removed. The basal frontal dura is peeled off the base of the skull until the anterior clinoid process, covered with a 0.1 % cetrimide-wetted gauze, and retracted up and back with a self-retaining retractor. The orbital roof is nibbled away carefully with a small bone rongeur and the entire roof as well as part of its lateral orbital wall is removed. The bony edges are smoothened all around the bony resection and covered with gauze imbibed in cetrimide. A thick thread or fine tape is passed under the levator palpebrae superioris, the rectus oculi superioris, and the superior oblique muscles. These are retracted in a direction not to hinder the delivery of the cyst and would depend on the position of the cyst. The periorbita is opened and the orbital fat dissected with care with a blunt instrument. Once the cyst is seen, it should be carefully uncovered from fat until the pericyst is seen. The pericyst should be dissected carefully and excised over as large an area as possible. There is no need to resect the entire pericyst. When the cyst comes clearly into view and is uncovered as far and as well as possible, the

surgeon places two fingers over the drape covering the closed eyelids and presses on the eyeball, through the drapes, using the Credè method to deliver the cyst. In case it does not come out easily, a blunt instrument is passed under the cyst and cetrimide solution is injected behind the cyst through a fine flexible rubber catheter. This maneuver is repeated until the cyst is delivered in the field; it is then scooped with a small tablespoon and placed in a basin.

In case the cyst is inadvertently ruptured, the fluid should be immediately aspirated and the entire operative area washed thoroughly with cetrimide. Then the gauze in the field should be carefully removed after sucking the excess fluid to avoid any fluid dripping from it and the field is again washed with cetrimide. The wound is then closed in the usual manner.

The wall of the cyst is very thin and may rupture very easily during surgery. To prevent rupture of the cyst, after exposing it, its contents are aspirated to shrink it in size (Fig. 23.4). Then, it can be easily removed with the help of cryo (Subrahmanyam et al. 2008) (Fig. 23.5). These two procedures should be reserved for cases which cannot be removed otherwise and only in extreme need.

Previously, the aspiration of the cyst, establishment of the diagnosis, reinflation of the mass with some agent (e.g., hypertonic saline, alcohol, formalin) to detach the scolices from the inner germinal wall, a second aspiration to empty the cyst, and followed by extirpation of the endocyst with or without the overlying ectocyst were done by many surgeons, the so-called PAIR procedure (Chana et al. 1986).

Nahri (1991) first used the cataract cryoprobe in two cases. An initial aspiration helps the cyst to collapse so that the outer fibrous wall is easily tented and grasped with nontoothed forceps and the needle puncture site is snipped open. The endocyst is attached to the cryoprobe and completely extracted. There were no recurrences during 18–24 months of follow-up, but we prefer the delivery of the intact cyst as described above.

Gokcek et al. (1997) recommends total removal of the cyst by means of a microdissection technique. Afterwards, Akhan et al. (1998) proposed a percutaneous treatment as an alternative approach to conventional surgery. Under ultrasonographic guidance, the cyst was aspirated with 15 % hypertonic saline and then reaspirated without complication. Twenty-one months later,

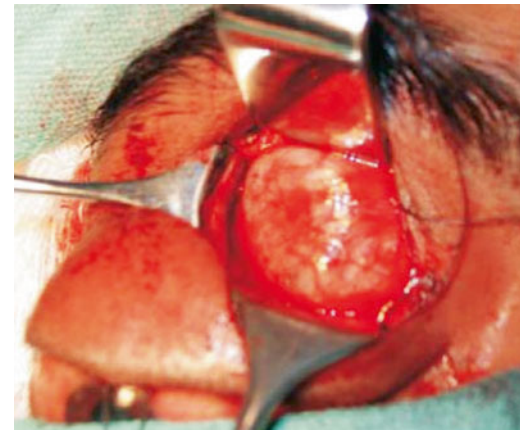

Fig. 23.4 After exposing the cyst, the contents are aspirated to shrink the cyst and facilitate its removal without rupturing the cyst wall

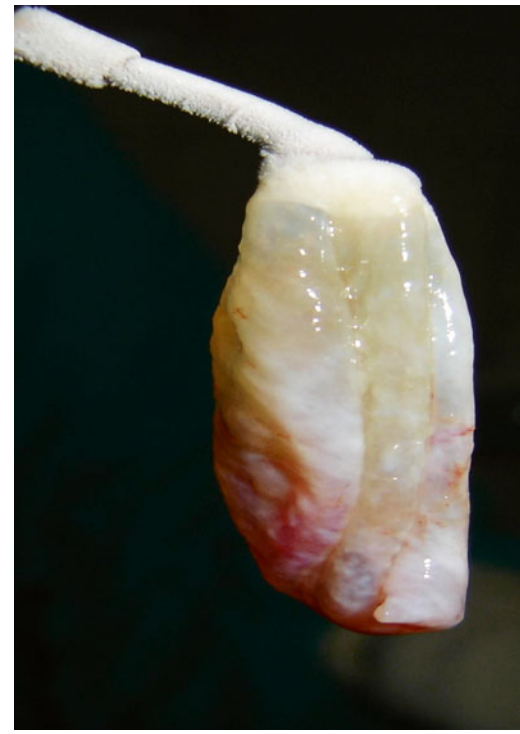

Fig. 23.5 The shrunken cyst was removed with the help of a cryo

imaging of the shrunken mass showed a volume of only 0.5 ml, and the patient was asymptomatic. Recently, Jimenenez-Mejias et al. (2000) described a case wherein the cyst ruptured during surgical removal. The surgical field was irrigated with hypertonic saline solution, and the remnants of the cyst were excised.

Anaphylaxis is a complication that the surgeon is worried about which can occur due to the rupture of the cyst during surgery. The incidence was about 2.25 % and no mortality was reported due to anaphylactic shock (Li et al. 2011).

Medical

Medical management with oral albendazole at a dose of 400 mg/day for 3 months in combination with praziquantel at a dose of 1,200 mg, every 8 hours, has been tried for primary as well as for recurrent cases of orbital hydatidosis with some success (Chana et al. 1986; Sihota and Sharma 2000). Oral albendazole is continued for 3 months after surgery. In another comparative study on hydatidosis of the liver, it was found that in the patients who received preoperative albendazole for 12 weeks prior to surgery, there were no viable cysts at the time of surgery compared to 95 % of those who did not receive albendazole prior to surgery. There was no recurrence in the first group, whereas in the second group, the recurrence rate was about 17 % (Chana et al. 1986). Hence, there is a definite role for pharmaceutical management and all the patients in whom the cyst ruptures during surgery should receive oral albendazole. It would also be recommended that, whenever possible, this drug should be used preoperatively.

Conclusion

This rare condition, orbital hydatid cyst, is an important part of the study of human echinococcosis. It can be the sole body cyst or it may be associated with cyst elsewhere in the body such as the liver, spleen, etc. Its surgical delivery is the treatment of choice. It is recommended that the patient receive medicinal treatment preoperatively and that this treatment be continued in case of cyst puncture or rupture for a period of at least 3 months. A combination of albendazole and praziquantel is recommended.

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Alveolar Hydatidosis of the Central Nervous System

24

Sikó Barabási Sándor

Contents

Introduction

Alveolar echinococcosis (AE) is caused by the larval stage of the fox tapeworm *Echinococcus multilocularis*. This cestode has a sylvatic life cycle in foxes (as the definitive hosts) and in arvicolid rodents (voles), which represent the larval metacestode stage (as intermediate hosts). Foci of human AE also occur where foxes or domestic dogs are fed on infected rodents and where there is accidental ingestion of *E. multilocularis* eggs from canine fecal matter (McManus et al. 2011; Sikó 2011a).

Alveolar hydatid disease (AHD) occurs in at least 42 countries of the Northern Hemisphere. Recent studies in Europe and Asia have shown that the endemic area of *E. multilocularis* is larger than previously known, and the parasite has regionally expanded from rural to urban areas. In addition, increasing fox populations may be associated with higher infection risk in humans with a phase lag of 10–20 years in Europe.

AHD is an aggressive and a highly lethal parasitic infection caused by the larval stage of *E. multilocularis*. It is characterized by the appearance of a tumor with extensive character, primarily in the liver of intermediate hosts including humans. The tumor has a pronounced pseudomalignant growth and can induce metastasis to different organs (Sikó 2011b). The diagnosis and the treatment are difficult. AHD is a life-threatening parasitosis. Mortality rate is 94–100 % in patients diagnosed late or undiagnosed and untreated. Long incubation period (10–15 years), considerable hospital costs

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(17,800 USD/patient/year), low survival rate, expansive character of the area of distribution, increase in human cases from year to year, and persistence of the parasite in nature are sufficient arguments for AHD caused by the larval form of *E. multilocularis* to be considered as a first emergency parasitic disease in Europe.

Cerebral hydatid disease is very rare, representing only 2 % of all cerebral space-occupying lesions even in the countries where the disease is endemic (Bükte et al. 2004). Alveolar hydatid cysts constitute 3 % of cerebral hydatid cyst cases (Senturk et al. 2006; Ozdol et al. 2011). Intracranial AE accounts for about 1 % of all cases of AE and is generally considered to be fatal (Yang et al. 2005).

The first AE lesion in the brain was reported in 1884 (Devé 1946). A European study of 600 cases of AE collected up to the year 1932 showed that in only 31 cases was the brain involved (WHO 1996). Altinors et al. (2000) found a total of 219 cases of intracranial echinococcosis in the 5-year period 1994–1999 in Turkey. Of these 16 were AE. Two of them were AE with no extra central nervous system (CNS) involvement. The proportion of CE:AE cases in various studies from Turkey was 1,109:169 (Torgerson et al. 2010). A large study in China suggested that 4 % of AE cases had neurological involvement (Jiang et al. 2005). Likewise, a large European study found 17 of 559 (3 %) cases of AE had brain involvement (Kern et al. 2003).

Table 24.1 Cases of the *Echinococcus multilocularis* infection in definitive hosts, in intermediate hosts, or in humans reported in central and eastern parts of Europe and in Turkey

Country	Year	Host
Poland	1995–2006	Fox
	1955–2007	Human
Slovenia	2006–2007	Human
Hungary	1988	Human
	2003, 2008–2009	Fox
Slovakia	1999, 2001	Fox
	2009	Dog
	2000–2008	Human
Bulgaria	1980	Rodents
Turkey	1934, 1939	Human
	1965	Fox
Greece	1978	Human
Moldavia	1961	House mouse
	1971	Fox, raccoon dog, human
Ukraine	1957, 2006–2008	Fox
Romania	2009, 2011	Fox, voles, human
Armenia	1958	Human
Belarus	1957, 1958	Rodents
	2001, 2003	Fox
Lithuania	2003, 2009	Beaver
	2005–2006	Dog, pig
	1997–2006	Human
	2001–2004	Fox
Latvia	2008	Fox
Estonia	2005	Fox
Russia	1957	Fox
	1966	Wild cat
	1970, 1972, 1998	Fox, human
Kyrgyzstan	2010	Fox

Adapted from Sikó (2011a)

Epidemiology

In 1980 in Europe the *E. multilocularis* was known and described in only four countries (Austria, France, Germany, and Switzerland). In 1996 the number of these countries has reached 9. The presence of the parasite is reported more frequently in Eastern Europe (Slovakia, Hungary, Ukraine, Bulgaria, and Romania), Turkey, Asia (Russia, Kazakhstan, and China), North America (Dakota), and Japan (Table 24.1). In most countries AE has already an endemic character and is still expanding with alarming rapidity. Epidemiology of alveolar hydatidosis is discussed in Chap. 4.

The main source of infection and life cycle in Europe is forestry including mainly the European red fox (*Vulpes vulpes*) and several species of rodents as intermediate hosts: water mouse (*Arvicola terrestris*), field mouse (*Microtus arvalis*), forest mouse (*Clethrionomys glareolus*), and other species. Foxes can spread oncospheres of tapeworm in an area over 18 ha and at distances over 15–16 km. Also, from a single stool containing oncospheres, in 10 days they can disperse distances of over 80 m from the excrement in question. Increasing fox populations and extending their life by urban territories is an increased risk factor for humans, and this is all the more so as these animals, the definitive hosts, show no clinical signs to a massive 100,000 tapeworm infection.

The *E. multilocularis* oncospheres are viable outdoors 3–8 months during summer and autumn and in cold temperatures in winter up to 8 months.

Foxes and small rodents represent the natural hosts of parasite. Naturally the parasite transmits between foxes or dogs and small mammals, while humans are aberrant intermediate hosts. Transmission of AE to humans is by consumption of parasite eggs which are excreted in the feces of the definitive hosts: foxes and, increasingly, dogs (Sikó 2011a). Human infection can be through direct contact with the definitive host or indirectly through contamination of food and contaminated green vegetables and fruits or possibly water with parasite eggs.

The incubation period is long (5–15 years); the parasitic tissue grows slowly and is of the infiltrating type. The liver is the organ primarily involved. Metastasis may occur and can involve virtually any organ. In systematic surveys, metastasis to the brain was reported in only 1–3 % of patients with AE (Bresson-Hadni et al. 2000; Kern et al. 2003). Among possible metastases of hepatic AE, locations to the brain are rare, usually fatal, and they have especially been assigned to concomitant immune suppression (Yang et al. 2005; Tappe et al. 2008). Brain metastasis is considered a sign of the terminal phase of the disease (Barjhoux et al. 1970; Bresson-Hadni et al. 2000). Few reports on the rare primary infections of the brain have been published (Aydin et al. 1986; Qiu et al. 1986). Pregnancy has been proposed to play a role as a predisposing factor for cerebral metastasis in AE (Yang et al. 2005).

Pathophysiology and Pathogenesis

AHD is very aggressive. Lesions develop rapidly in the liver where an invasive pseudomalignant (paraneoplastic) mass may be produced. This may spread locally to adjacent organs such as the lung or metastasize to distant structures (Sikó 2011b).

According to the results of animal experiment in Japan, the mechanism of metastasis was due to the detached proliferated bud, even very small or only a few nuclei entering the blood vessels (Matsuhisa et al. 1996). Nevertheless, it was incapable of causing metastasis if protoscoleces were injected into the vessels.

In the European registry 34 % of patients who have metacestode lesions in the liver have simultaneously a lesion in one or more extrahepatic organs, at the time when the patients reach medical attention (Kern et al. 2003).

The metacestode was characterized by internally protrusive hyperplasia from the mother alveolar wall into the alveolar cavity and then proliferation extending continuously to reach the opposite wall of the cavity. So, septum-like budding was formed. Sometimes two or more proliferative sites on the alveolar wall propagated simultaneously into the cavity in opposite directions and mingled with each other to form a septum dividing the mother cyst to form two or more small alveoli (Jiang et al. 2005).

After ingestion of contaminated foods and/or water, embryos of *E. multilocularis* migrate through the portal system to the liver where vesicular masses are formed. The disease may extend gradually to adjacent organs or spread via the bloodstream (hematogenous metastasis) to distant areas such as the brain. Primary affected is usually the liver, and then the secondary localization by metastasis is in the lung. Bensaid et al. (1994) report a patient with right frontal lobe and palpebral lesions secondary to a primary hepatic focus with secondary lesion in the lung. The intracerebral, frontal lobe, palpebral lobe, disseminated, or other CNS localizations appeared usually after the lung metastasis due to an immunosuppressive effect of parasite.

Sato et al. (1998) made an experimental infection of larval *E. multilocularis* in the rodent brain attempting to establish a murine model for cerebral AE. Mice and jirds (*Meriones* genus) were injected intracranially with 10 % of a homogenated hydatid cyst mass. Small cystic larvae were observed macroscopically in the cranial cavity 1, 2, and 5 months post infection in both mice and jirds. Some larval cysts from both rodents contained mature or immature protoscoleces. In mice, the laminated layer was found in the lateral ventricle 2 months post infection but without protoscoleces. At 5 months post infection, larger larval cysts were found in the cranial cavity of a mouse, which also demonstrated partial palsy of the legs. A laminated layer with mature protoscoleces was observed in the third ventricle, and the mouse also harbored, in the left lung, a larval cyst containing

protoscoleces surrounded by lymphocytes. Jirds were also found to be infected with metacestodes in the cranial cavity, but neither unusual behavior nor establishment of cysts inside the brain was observed in jirds during the course of infection.

Clinical Features

In the cerebral AE the lesions may remain asymptomatic until they are quite large. The clinical presentation usually includes symptoms of increased intracranial pressure, progressive and severe headaches (vomiting, motor weakness, etc.), seizures, cranial nerve findings, and visual disturbances (Takci et al. 2008). Ozdol et al. (2011) present a case of a 23-year-old man with nausea, imbalance, occasional urinary and fecal incontinence, and a severe headache for 1 month. These symptoms were caused by multiple calcified mass lesions in the right upper lobe of the lung and right liver and another solid tumor between the right kidney and liver. Other symptoms such as hemiparesis, seizures, visual field alteration, and gait disorders may vary with the location of the metacestode. Cerebral AHD can also cause intracranial hypertension, seizures, and focal neurological deficits. However, the clinical course is usually more rapid and more severe than in cystic hydatid disease. AE cases are usually present in adults. The average age of patients with cerebral AE is significantly higher than the age of those with cystic echinococcosis (Ammann and Eckert 1996).

Types of Lesions

The infiltrating growth of *E. multilocularis* metacestode is particularly significant because it may resemble a neoplasm, the so-called malignant hydatid disease. It is especially serious when the *E. multilocularis* lesions involve the brain, termed a "fatal disease" (Qiu et al. 1986). Cerebral metastasis of primary hepatic AE is often multifocal (Tappe et al. 2008). The cerebral AE is present like multiple intracranial masses which show cauliflower-like contrast enhancement pattern on magnetic resonance imaging (MRI) (Tunaci et al. 1999).

Based on imaging characteristics the AE lesions are divided into three types: (1) solid type (a solid lesion without liquid necrosis or only small patches of necrosis), (2) mixed type (solid component surrounding large and/or irregular liquid necrosis area), and (3) pseudocystic type (large cyst without visible solid component).

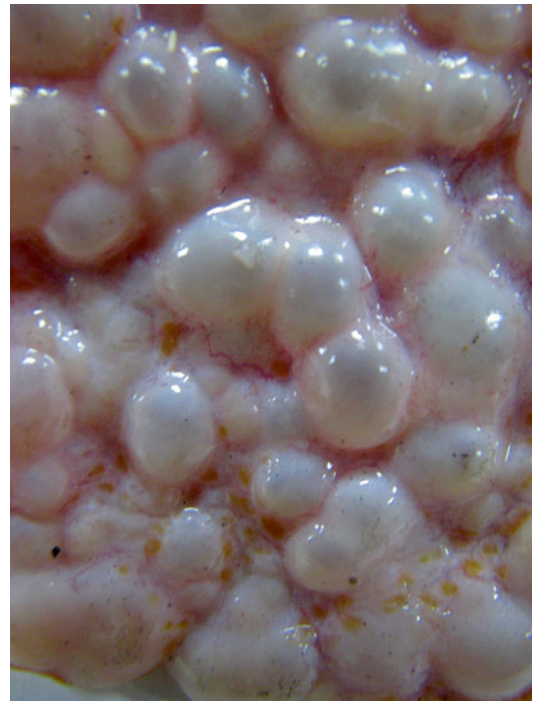

Fig. 24.1 Alveolar echinococcosis an expansive tumoral formation

Calcification in alveolar echinococcosis may be categorized into three patterns: (1) mild calcification (inconspicuous calcification or punctuate scattered calcification), (2) moderate calcification (coastline calcification located at the periphery of the lesion, with or without the central dot-calcification), and (3) abundant calcification (large calcified deposits) (Wang et al. 2011).

According to the Chinese records, intracranial AE can be subdivided into three types: (a) monomassive type, (b) multifocal type, and (c) extracerebral type (Qiu et al. 1986). The volumes of the lesions are variable, between $6.0 \times 4.5 \times 3.5\,cm^3$ and $9.0 \times 6.5 \times 8.5\,cm^3$ (Qiu et al. 1986).

The most frequent morphological profile of AE is represented by a heterogeneous, infiltrative, and destructive mass (Fig. 24.1), with irregular outlines and a nonvascular and necrotic center. The cyst it appears as a spongy structure, resembling a crumb

Fig. 24.2 The internal spongy structure of the tumoral formation

of cheese, with empty cavities or with a gray jelly content (Fig. 24.2). Most of the cavities do not have a well-defined content. In other samples, the formation had mainly a cystic structure, without a divided multivesicular character. In the intracerebellar tissues the metacestode showed a pale yellow mass. Calcification and perilesional edema are prominent (Algros et al. 2003).

In contrast with *E. granulosus*, the *E. multilocularis* cysts are small, group in clusters, elicit a severe inflammatory reaction from the host, and tend to metastasize both locally and distantly. Within the CNS, they usually are located within the brain parenchyma. Intracranial AE is thought to be rare with CNS involvement usually a manifestation of metastases from a primary lesion.

AHD is a biologically aggressive infestation mimicking a malignant neoplasm as assessed radiologically and macroscopically (Ozdol et al. 2011). AE develops within the liver as a rapid invasive pseudomalignant growth and may metastasize to different organs. AE involvement of the brain and liver is similar to an infiltrative tumor (Sikó 2011a, b).

Cerebral cystic echinococcosis lesions are usually single. The cerebral alveolar echinococcosis lesions may be single (and multiseptated) or multiple (Tunaci et al. 1999). Piotin et al. (1997) reported a disseminated intracerebral AE case, secondary to primary hepatic infection. Oktar et al. (1999) described a brain computed tomography (CT) which showed multiple intracranial lesions with remarkable peritumoral cerebral edema. Hakan and Aker (2001) describe a 53-year-old man who presented with headache and right-sided seizures, and on MRI multiple cranial lesions were seen (Figs. 24.3 and 24.4). There were three multiloculated cystic lesions, in the left cerebellum, in the right occipital and left frontal lobes, and two solitary lesions, in the left frontal and left parietal lobes. CT showed multiple masses in the liver and lung. Aydinli et al. (2008) reported a 62-year-old man who had liver AHD with simultaneous lung and brain metastases. Other intracranial localizations were reported in the right frontal lobe and palpebral lesions secondary to a primary hepatic focus with secondary lesion in the lung (Bensaid et al. 1994).

The histopathological examination reveals a diffuse growth composed of compartments that are filled with a gelatinous matrix and many brood capsules and protoscoleces filled with necrotic tissue (Sikó 2011a, b). The larval cestodes of *E. multilocularis* produce a typical infiltration and induce destruction of the organ. The human organism responds with a granulomatous inflammatory reaction and peripheral formation of granulation tissue. In centripetal direction, the adventitial layer's components are formed by the fibroconjunctive reaction; inflammatory cells are

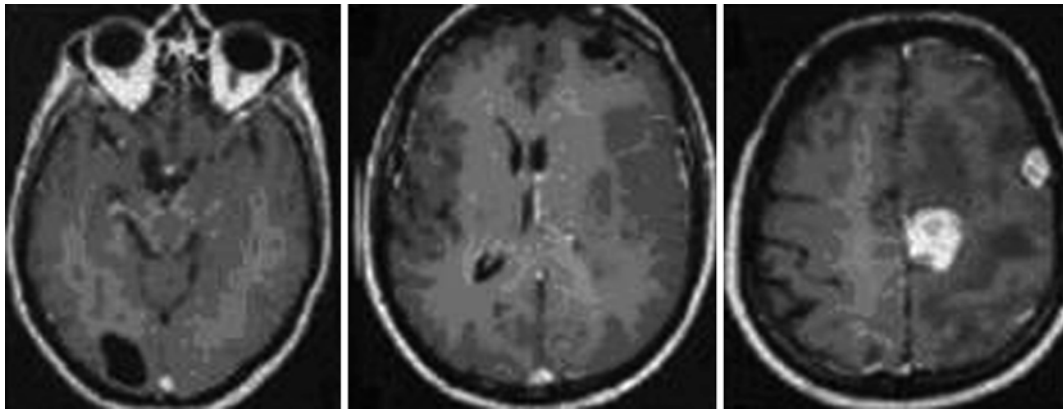

Fig. 24.3 Sagittal T1-weighted MRIs with a subcortical, solitary multilocular cystic lesion (From Hakan and Aker (2001), with permission)

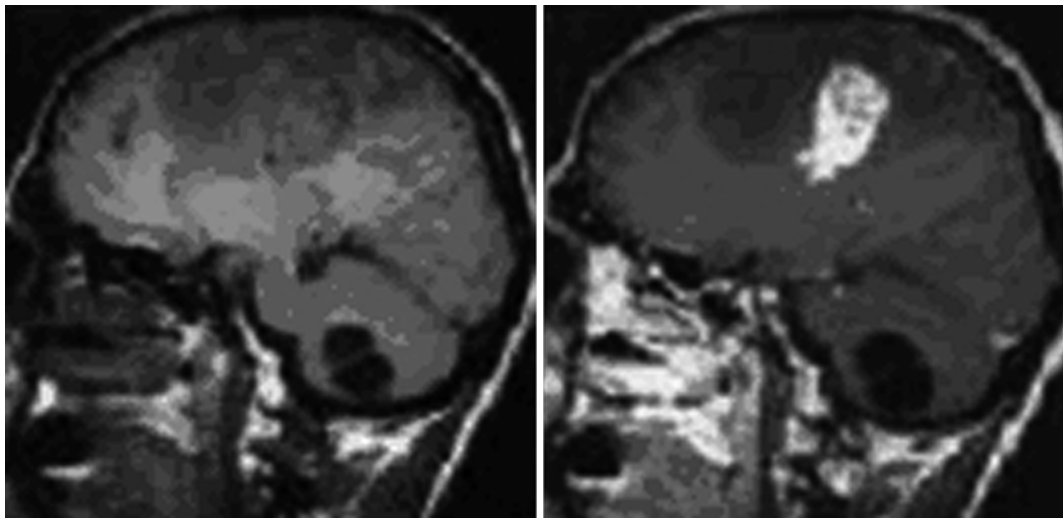

Fig. 24.4 Axial CT of the head after contrast administration. The multiloculated cystic lesions in right occipital, in left frontal lobe, and solitary lesions, one in left frontal and the other one in left parietal lobe (From Hakan and Aker (2001), with permission)

present. In the peripheral areas lymphocytes and monocytes dominate. They are followed by a rich infiltration of the giant cells and a decrease of the inflammatory local reaction (Fig. 24.5). These structures were gradually replaced by a fibroconjunctive reaction. The surrounding brain tissues show edema, degeneration of neurons, proliferation of gliocytes, and an increase in the number of vessels with distension of lumen by engorgement and complicated by focal necrosis (Qiu et al. 1986; Sikó 2011a, b).

Poorly hyalinized cuticle and more cellular reaction, especially with multinucleated giant cells, could be seen in the dense fibrous tissue infiltrated by an inflammatory cell layer. The cuticular layer is mono- or multistratified, formed by concentric conjunctival tissue layers, which penetrate in the cystic cavity and develop many anastomoses conferring it a multivesicular aspect. In the spaces between these blade cells similar to giant cells, we could also notice rare histiocytes and eosinophils. Due to the multitude of anasto-

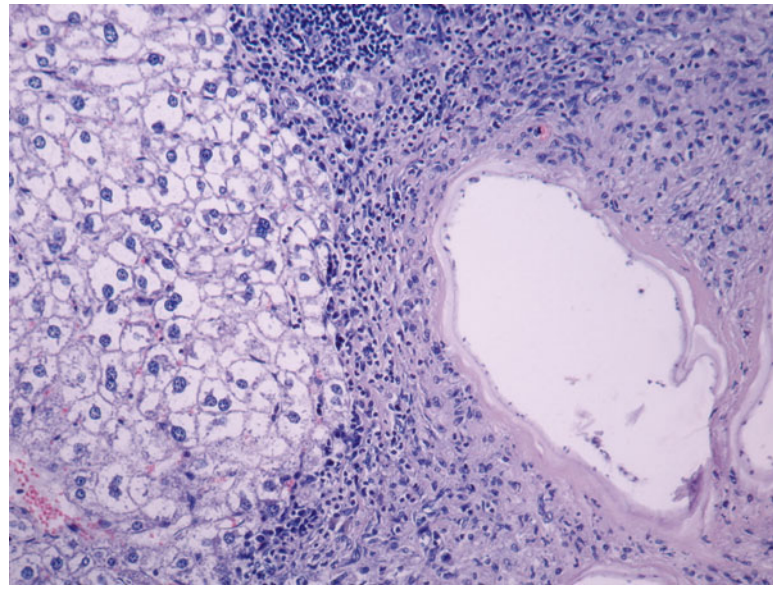

Fig. 24.5 Inflammatory local reaction with multinucleate giant cells, lymphocytes, plasmocytes, and macrophages. Hematoxylin-eosin stain, ×200

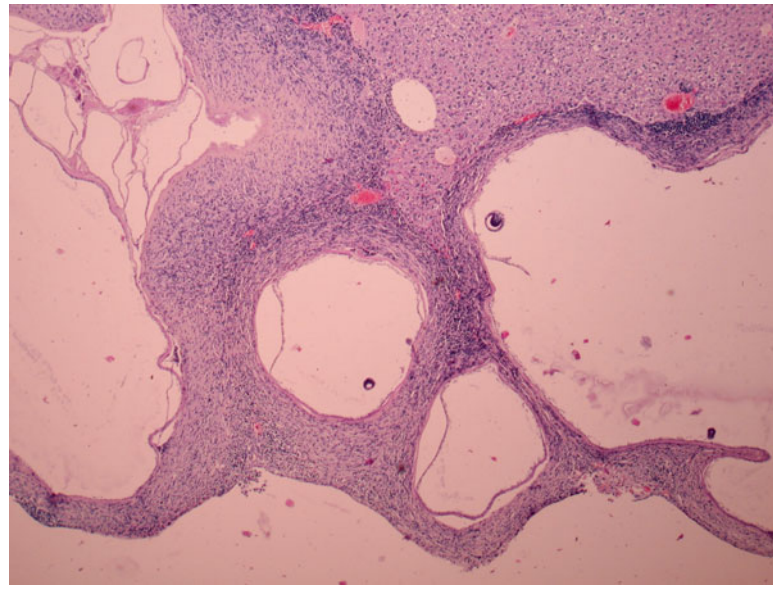

Fig. 24.6 Anastomosis with an invasive character. Pappenheim's stain, ×40

moses, the cyst is a structure with an invasive character (Fig. 24.6). In most cases there were collapsed cysts characterized by a fragmented or folded laminar layer and massive necrosis.

The germinative layer which lines the new formed cavities has a plasmatic structure with rare multinucleate cells. This layer has many young cells and gives a rhizoid aspect characteristic of malignant tissues. Some cysts contained remnants of a single germinative layer.

Studies aiming at the histological aspects have suggested that *E. multilocularis* produces multilocular alveolar cysts (1–10 mm in diameter) that resemble alveoli. They grow by means of exogenous proliferation with cysts that progressively invade the tissue by means of peripheral extension

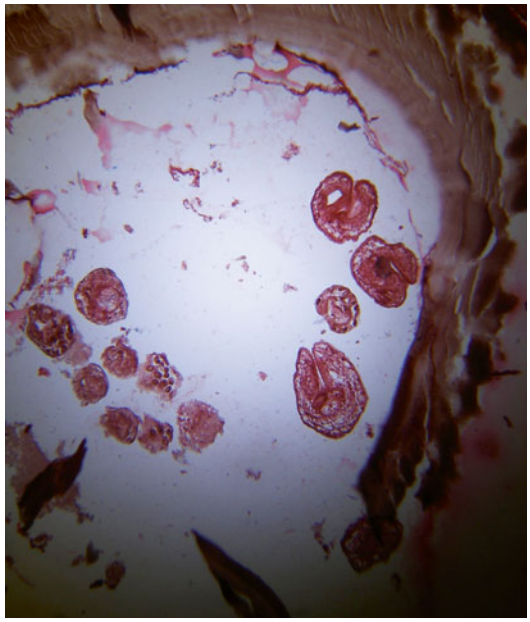

Fig. 24.7 Protoscoleces in the cyst of alveolar echinococcosis. Hematoxylin-eosin stain, ×40

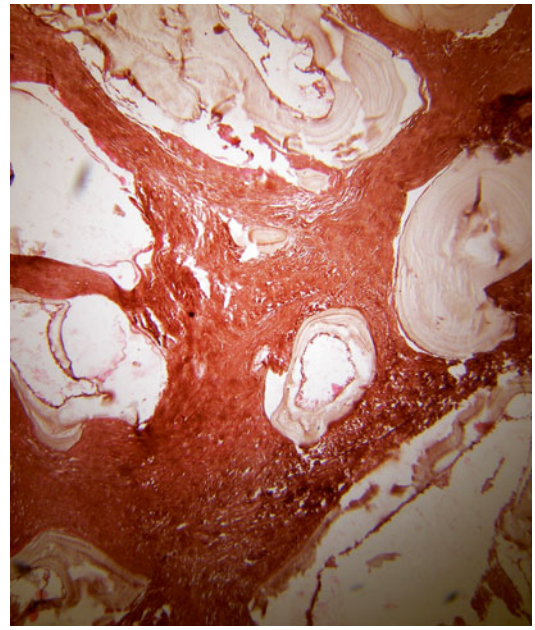

Fig. 24.8 Infiltrative and invadant character of alveolar echinococcosis. Hematoxylin-eosin stain, ×40

of the processes originating in the germinal layer. The larvae cause invasive and destructive changes in the tissue. This area is separated from the parenchyma by inflammatory cells.

The lesions are characterized by many alveoli with different sizes and shapes. Observation of the alveolar wall shows that the thick, noncellular, laminated outer layer looks bank-like, sometimes folding within the alveolar cavity. The thin, germinal inner membrane lined by a single layer cell is usually deficient due to detachment. Brood capsule or protoscoleces were occasionally seen (Fig. 24.7). The lesion may be complicated by central necrosis, producing a cavity or pseudocyst after liquefaction. In the periphery of alveoli group, there is hyperplasia of fibroconnective tissue and cellular infiltration of eosinocytes, lymphocytes, plasma cells, and giant cells, forming a typical alveococcus nodule (Fig. 24.8).

Histopathological examination reveals a periodic acid-Schiff (+) cuticular membrane with wide areas of necrosis and inflammation which are typical for AE. They are usually supratentorial and within the watershed zone of the middle cerebral artery; however, infratentorial AE is extremely rare.

Diagnosis

The diagnosis of AE is based on case history, clinical findings, morphological lesions identified by imaging techniques, the polymerase chain reaction (PCR), or immunofluorescence/immunohistochemistry and immunodiagnosis.

Early diagnosis of AE can result in significant improvements in the quality of the management and treatment. In most cases, the early stages of infection are asymptomatic, so that methods that are inexpensive and relatively easy to use are required for large-scale screening of populations at high risk (Zhang et al. 2003; Zhang and McManus 2006).

The diagnosis of AE has improved due to the use of new or more optimal methods for purification of *Echinococcus* antigens from somatic materials, by the application of molecular tools for parasite identification and the synthesis of recombinant diagnostic antigens and immunogenic peptides (Zhang et al. 2003).

Any person with the following findings might be diagnosed with alveolar echinococcosis: a slowly growing tumor – signs and symptoms vary with tumor location, size, and type (solid,

partly multivesicular, centrally necrotic), visualized by imaging techniques (Kern 2010).

A case is verified if at least two of the following four parameters are fulfilled: (1) typical organ lesions detected by imaging techniques such as abdominal ultrasound, CT, and MRI; (2) detection of *Echinococcus* sp.-specific serum antibodies by tests of high sensitivity and confirmed by assays with high specificity; (3) histopathology compatible with a metacestode of *E. multilocularis*; and (4) detection of *E. multilocularis* nucleic acid in a clinical specimen.

AHD causes different neuroimaging findings, on the CT scan or MRI, because the lesions are multiple and surrounded by edema and show ringlike enhancement. The CT and MRI appearances of cerebral alveolar echinococcosis have rarely been reported. On CT and MRI, cerebral AE lesion appears as a solid, semisolid, or multilocular cystic mass with definite margins and surrounding contrast enhancement. Calcification and surrounding edema are common (Algros et al. 2003). Contrast enhancement occurs within the region of inflammatory reaction around the cysts (Bensaid et al. 1994; Reittner et al. 1996). Bükte et al. (2004) described a case where the CT and MRI showed a well-defined, multicystic appearance with a central solid component and calcifications. In the cerebral AE, CT showed a well-defined, multiseptated mass consisting of hyperdense solid and hypodense cystic components and hyperdense calcifications (Bükte et al. 2004).

On MRI the metacestode mass showed a multicystic appearance with a central solid component and punctate calcifications with contrast enhancement of the wall, and solid components. The solid components were iso-/hyperintense. The cystic components were hypointense. The lesion presented as an intracranial mass which is slightly hyperdense on CT scans and very hypointense with central hyperintensity on T2-weighted MRIs. The hypointensity on T2-weighted MRIs appears to be characteristic of lesions of cerebral alveolar echinococcosis. The lesion exhibited marked contrast enhancement on both CT and MRIs and is accompanied by extensive white matter edema (Wada et al. 1996).

The alveolar hydatidosis of the spinal canal may be visualized by MRI, although the findings are nonspecific. Usually the CT scan is better than MRI to demonstrate bone erosion in vertebral bodies. The CT is a superior method in detecting calcification of the cyst wall or septa. The MRI method is the better method in detecting multiplicity and defining the anatomic relationship of the lesion with the adjacent structures and helps in surgical planning (Bükte et al. 2004).

Asanuma et al. (2003) had intracranially injected 36 female Wistar rats (6–8 weeks old) with a 10 % homogenate of echinococcal larval tissues. They observe a neoplastic fine structure of the rat brain. The T2-weighted MRIs revealed a hyperintense region in the cerebral cortex at 2 weeks after injection. At 3 weeks after injection, this region was found to have cysts on the basis of results of histological examination. Unmarked areas corresponding to hyperplasia and the subsequent calcification of the cuticular layer, at 6 and 13 weeks after injection, respectively, were observed in T2-weighted and proton density MRIs. Using this secondary cerebral AE animal model, it was concluded that the MRI method was suitable for early detection of secondary cerebral AE (Sato et al. 1998).

Immunodiagnosis provides such an approach and can also confirm clinical findings. The immunologic diagnosis is not accurate due to cross-reaction with other parasitic diseases or false-negative results in patients with intact cystic hydatid lesions. Immunofluorescence, indirect hemagglutination tests, enzyme-linked immunosorbent assay (ELISA), and immunoelectrophoresis with antigenic extracts of *E. multilocularis* are usually supportive laboratory tests for a diagnostic accuracy. However, the serological cross-reactions between various cestodes and between cestodes and the phylogenetically related trematodes may occur.

The serodiagnosis of AE provides a complementary role to other procedures in early detection of the infection. The methods are similar to those used for CE, but serological tests for antibody detection are generally more reliable. The Em2, a species-specific native antigen isolated from the metacestode of *E. multilocularis*, has

been used for immunodiagnosis of human AE with encouraging results. The sensitivities of Em2 in ELISA varied depending on the geographic origin of the patient. They ranged between 77 and 92 %. The Em2^{plus} ELISA, a combination of Em2 with a recombinant protein designated II/3–10, increased the sensitivity to 97 % (Zhang et al. 2003; Zhang and McManus 2006; Brunetti et al. 2010).

DNA probes and PCR may be applied to differentiate between *Echinococcus* spp. In order to confirm the assumed echinococcal etiology of these lesions, Georges et al. (2004) and Tappe et al. (2008) used a specialized PCR with primers directed against the spliced leader RNA gene in chromosomal echinococcal DNA on a cerebrospinal fluid sample of the patient. PCR has been used to confirm the echinococcal etiology of lesions in unusual locations. Diverse protocols have been developed to detect echinococcal nucleic acids in biological samples, and PCR is increasingly being accepted as a complementary diagnostic tool for echinococcosis.

Differential Diagnosis

The differential diagnosis of cerebral AE includes the following: cystic echinococcosis, tuberculosis, bacterial abscesses, fungal infections, glial tumor, invasive brain tumors, and metastases (Isik et al. 2007). The differential diagnosis encompasses coenurosis (a single, large grapelike mass in the brain without other organ involvement), cysticercosis (small cysts in multiple brain locations and in the muscles, the grapelike racemose type in the cisternae), brain paragonimiasis, toxoplasmosis, glioma, and cerebral metastasis of malignant neoplasias. In the case presented, the cerebral lesions were not biopsied due to their location (Tappe et al. 2008).

McManus et al. (2011) described a case in China, when in a patient the primary diagnosis was of undifferentiated metastatic cancer in the liver and brain, with current pulmonary bacterial infection. After a systematic review of her clinical records, it was suspected that the patient had hepatic AE which had metastasized to the brain and lungs. This case demonstrated that differential diagnosis for AE should generally include assessment for the presence of tumors and other lesions such as abscesses caused by tuberculosis, which may require specific pathological examination or molecular analysis of biopsy material to provide a definitive diagnosis.

Epidemiologically, the infection of *E. multilocularis* is endemic in high-altitude zones and areas of cold climate; *E. granulosus* infection is mostly seen in areas of moderate climate. Both may however be seen outside endemic areas due to migration from endemic areas or due to tourism. Infestation with *E. multilocularis* is a more malignant disease, referred to as AE. In AE the latter lacks limiting membrane thus can grow aggressively.

Radiological differentiation from brain tumor is difficult. The diagnosis should be suggested by evidence of a primary hepatic focus, appropriate clinical history, high prevalence of the infection in the host's geographic location, and laboratory findings (Reittner et al. 1996; Piotin et al. 1997; Tunaci et al. 1999). The clinical manifestations of alveolar hydatidosis are nonspecific and similar to those caused by primary or metastatic brain tumors. The cyst of AE differs from that of cystic echinococcosis in that it grows by external budding of the germinal membrane with progressive infiltration of the surrounding tissue (Kammerer 1993; Bükte et al. 2004).

Histopathological examination is necessary for a definite and certain diagnosis.

Immunofluorescence, passive hemagglutination tests, ELISA, and immunoelectrophoresis with antigenic extracts of *E. multilocularis* may provide a diagnosis. Serological testing can be positive, but this does not always help make a definite differentiation between the infections of *E. granulosus* or *E. multilocularis*.

Imaging techniques may be more sensitive than serodiagnosis.

Basically, in an immunodiagnostic process, an 18-kDa antigen (Em18) from PSC of AE was reported as being a highly species-specific (96.8 %) and sensitive (97 %) antigen with potential not only for differentiation of AE from either CE or other helminth infections but also for

differentiation of active from inactive AE. Subsequently, Em18 was shown to be a fragment of the C-terminal of Em10, and the recombinant protein was recognized by 87.1 and 90.3 % of 31 serum samples from AE patients in ELISA and immunoblotting, respectively. Recombinant Em18-ELISA and Em18-immunoblot assays have proved invaluable for differentiating AE from CE infection, the former also being useful for evaluating the efficacy of treatment in patients with AE (Zhang et al. 2003; Zhang and McManus 2006; Brunetti et al. 2010).

Prognosis

The cerebral AE has a poor prognosis. Locations to the brain are usually fatal (Yang et al. 2005)

Treatment

AHD is a life-threatening parasitosis (Wang et al. 2009). The first attempt of medical treatment of AE was by Hanstein (1957). The initial start of chemotherapy dates to 1974 when benzimidazole compounds were demonstrated to be effective against larval *Echinococcus*. The first agents used were mebendazole and its fluorine analogue flubendazole. Doses of mebendazole ranging from 15 to 60 mg/kg/day have been administered to human subjects. Duration of therapy is not exactly known; it may be continued for months or in some cases for years. Another benzimidazole compound, albendazole, is better absorbed and diffusion of its metabolites into tissues and cysts is far higher than with mebendazole. Dosage of albendazole is 10–15 mg/kg/day.

Mebendazole and albendazole are the drugs of choice for the long-term treatment of AE. The mebendazole or albendazole treatment followed up for an average of 42 months had a success rate in 80–97 % and was defined as non-progression for more than 1 year (Reuter et al. 1998).

Radical resection is generally considered as the only method of surgical treatment. The standard treatment of cerebral AHD consists of open brain surgery and systemic albendazole therapy postoperatively (Wang et al. 2009). Surgical excision of solitary lesions of *E. multilocularis* has been described. However, cyst rupture during removal may lead to dissemination and/or chemical meningitis. Fatal anaphylactic shock has also been described (Hakan and Aker 2001). Radical excision should be performed for all accessible surgical lesions. The surgical treatment for multiple cerebral lesions is usually palliative with alternative chemotherapeutics for at least 2 years.

Several cycles of postoperative albendazole chemotherapy are almost always required (Ozdol et al. 2011). Gamma knife radiosurgery may be an alternative to surgery for patients with inoperable alveolar hydatid cysts or with a high risk of surgery and anesthesia (Schmid et al. 1998; Yamamoto 1999).

The decision making to choose between the surgery and medical treatment with albendazole or mebendazole must take into account the surgical mortality (≥2 %), postoperative complications (8–25 %), recurrence rate after surgery (2–25 %), and cure rate with medical treatment (30–40 %). Definitive treatment still consists of surgical removal. Takci et al. (2008) showed that radical surgery combined with antihelmintic therapy of sufficient duration is mandatory to prevent the progression of symptoms, but the disease continues to be difficult to cure. Surgical removal of alveolar cysts usually requires resection of adjacent tissue, and this may cause neurological deficits if the lesion is located in an eloquent cerebral area.

In the encephalic localizations, Weber et al. (1988) suggest the treatment with flubendazole, with a 4-year follow-up. Albendazole administration should follow or even precede the surgical procedure or may be used as primary therapy for patients with inoperable alveolar hydatid disease. The drug is given 10 mg/kg body weight per day for lifetime. Using this approach, 90 % of lesions regress or remain static, and only 10 % continue to grow. Isik et al. (2007) suggested a postoperative treatment started on albendazole at a daily dosage of 800 mg for 3 months. The patient has remained free of any mass lesion for 5 years. Albendazole (800 mg, 3 × 28-day treatment cycle, followed by a 14-day albendazole-free interval)

and cefotaxime were prescribed for postoperative treatment (Ozdol et al. 2011). A further operation was performed to resect the lesion in the lung a month after intracranial surgery. Postoperative early CT examination and MRI performed 6 months after surgery showed no recurrence. However, Li et al. (2010) reviewed by a follow-up of 1–7 years 17 cases of complicated AE in multiorgans (liver, lung, and brain). They concluded when more than two organs are involved by AE lesion, it was rather difficult to diagnose and cure. Thus the life quality and long-term survival of patients were seriously endangered.

It is concluded that cerebral *E. multilocularis* lesions are amenable to surgery and that their removal provides useful prolongation of life despite the presence of hepatic or pulmonary disease. In any case long-term chemotherapy may be indicated as a life-saving measure for patients with severe liver dysfunction but is associated with a relatively high risk of proliferation of intraoperatively undetected parasite remnants.

For AE, early diagnosis and radical (tumor-like) surgery followed by anti-infective prophylaxis with albendazole remain the key elements. However, most patients with AE are diagnosed at a later stage, when radical surgery (distance of larval to liver tissue of >2 cm) cannot be achieved. The backbone of AE treatment remains the continuous medical treatment with albendazole and, if necessary, individualized interventional measures (Brunetti et al. 2010).

Prevention

AHD may be prevented by reducing human contact with definitive host feces. Any person who lives in an area where *E. multilocularis* is found in rodents and wild canines should take the following precautions to avoid infection:

- Do not touch a fox or other wild canines, dead or alive, unless you are wearing gloves. Hunters and trappers should use plastic gloves to avoid exposure.
- Do not keep wild animals, especially wild canines, as pets or encourage them to come close to your home.
- Do not allow your dogs and cats to wander freely or to capture and eat rodents.
- If you think that your pet may have eaten rodents, consult your veterinarian about the possible need for preventive treatments.
- Wash your hands with soap and warm water after handling dogs or cats and before handling food.
- Teach children the importance of washing hands to prevent infection.
- Do not collect or eat wild fruits or vegetables picked directly from the ground. All wild-picked foods should be washed carefully or cooked before eating.
- AE can be effectively controlled and prevented when care is taken to avoid exposure and contact with wild animals such as foxes, coyotes, and dogs and by limiting the interactions between dogs and rodent populations.
- Do not allow dogs to feed on rodents and other wild animals.

Conclusion

Hepatic failure, local extension, or metastases to the vital organs lead to mortality. In untreated patients the mortality may reach 90 %. In the present case, there were multifocal brain lesions, hepatic failure, and superimposed secondary infection. In patients with multiple cerebral lesions who live in or have visited an endemic area and especially if there has been contact with foxes, dogs, or rodents, *E. multilocularis* should be remembered in the differential diagnosis. AE remains today a very lethal disease. The cerebral lesions may be multiloculated, solid, solitary, or multiple and may involve the infra- or supratentorial areas.

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Control and Prevention of Hydatidosis

25

Jorge A. Guisantes

Contents

Introduction

The control of the parasitic zoonoses is encompassed by a complex group of actions because of its existence in the life cycle of animal hosts (domestic and wild) as well as humans. This complexity is the reason why – despite knowing thoroughly the life cycle of *Echinococcus granulosus* and their mechanisms of transmission – hydatidosis continues to be an important zoonosis in many regions of the world.

This chapter aims at describing the main methods recommended and employed to control cystic hydatidosis or cystic echinococcosis (CE) in control programs in several countries. Additionally, standards and recommendations for prevention are also described.

Biology and Life Cycle

Cystic hydatid disease in man is a parasitic zoonosis; men can be infected during the metacestode stage of the tapeworm *E. granulosus*. The adult worm lives in the small intestine of dogs and other canids; the parasite eggs are excreted in the feces of these animals, which may thus contaminate soil, grass, and water. The transmission of *E. granulosus* usually occurs through domestic livestock and dogs and other canids (Fig. 25.1). Man is an aberrant intermediate host of *E. granulosus* because the parasite cannot complete its development in humans. Ten strains or genotypes are described in *E. granulosus* using mitochondrial gene analysis and are numbered

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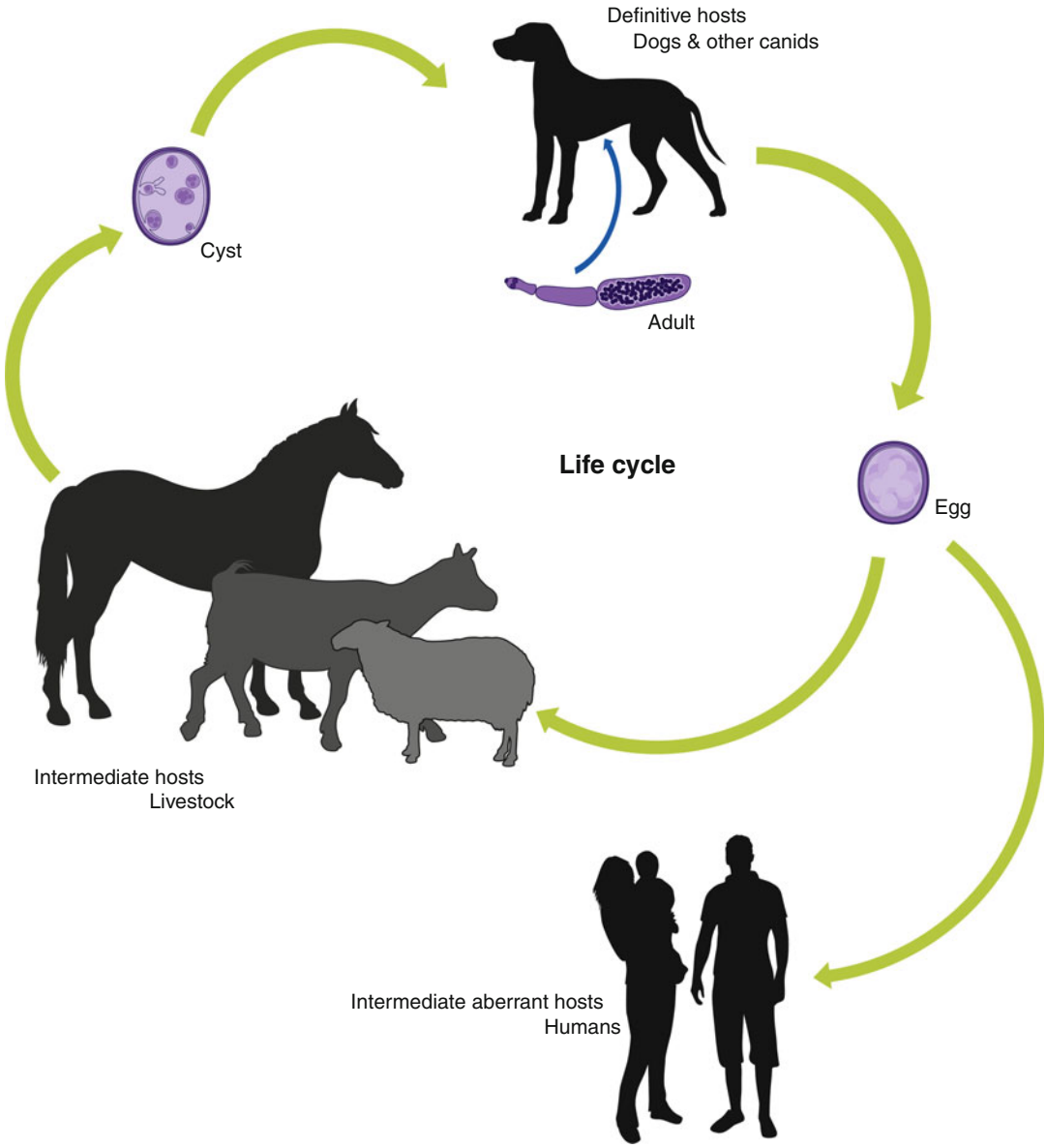

Fig. 25.1 Life cycle of *Echinococcus granulosus*

G1 to G10 (Kamenetzky et al. 2002; Lavikainen et al. 2006; McManus and Thompson 2003). The preponderant strain is the sheep-dog strain or G1 genotype, but other genotypes include horses, cattle, camels, pigs, and cervids as intermediate hosts. The existence of these strains currently leads to consider the existence of an *E. granulosus* complex or new species in relation to these strains. In this regard, have been elevated to species *E. granulosus sensu stricto* (G1, G2 and G3), *E. equinus* (G4), *E. ortleppi* (G5) and *E. canadensis* (G6, G7,G8, G9, G10) have been elevated to species *E. granulosus* sensu stricto (G1, G2, and G3). Recently the lion strain has been proposed as a new species: *E. felidis* (McManus 2011). The knowledge about the predominant strain in a particular country or region is important for the design of more efficient control programs (Pearson et al. 2002).

The eggs passed in the feces of dogs are the infective stage for the intermediate host like domestic livestock, wild intermediate hosts, and humans, where the oncospheres develop into hydatid cysts (Fig. 25.1). The number of eggs produced varies between 100 and 1,500 per proglottid (Thompson 1995), and a dog may have hundreds of adult cestodes. Therefore, an infected dog can spread thousands of fertile eggs of *Echinococcus* that may remain viable for months in the environment.

Each hydatid cyst may have thousands of protoscolices in brood capsules. When dogs ingest raw offal containing hydatid cysts from intermediate hosts, each evaginated protoscolex attaches between the villi of the small intestine and, in about 40 days, develops a mature adult tapeworm. An interesting fact is that the protoscolices of *E. granulosus* have a double biotic potential: if ingested by dogs, they result in adult worms, but if they fall into serous cavities (e.g., pleural or peritoneal cavities) of an intermediate host, including man, they can redevelop into a new cyst (secondary hydatidosis).

Control

Approaches and Options

According to Gemmell and Schantz (1997), control may be defined as an active implementation of a program to limit the prevalence of a specific disease by a recognized authority on an instruction from the legislature. It is different from eradication that Gemmell and Schantz (1997) defined as the purposeful reduction of specific disease prevalence to the point of continued absence of transmission within a specific area by means of a time-limited campaign.

The preventive and control programs require interrupting the life cycle of the parasite acting on the epidemiological chain. For this it is necessary to act on the following: (a) the definitive hosts (dogs and other canids); (b) the herbivorous intermediate hosts such as sheep, cattle, and goats and a rather large number of other suitable hosts such as camels, pigs, horses, etc.; (c) the human population; and (d) other stages of the life cycle.

Since 1863 several programs of control have been employed in many countries. Several of them have been employed in islands such as Iceland (1863–1960), New Zealand (1938–2002), Tasmania (1964–1996), Falkland Islands (1965–1997), Cyprus (1971–1985), and Sardinia (1960–1997), with different efficacy reviewed by Craig and Larrieu (2007).

From the analysis of the control programs developed in continental and insular countries, it is apparent that two main approaches were employed (Gemmell and Schantz 1997; Gemmell 2001): (a) a "horizontal" approach based on health education, sanitation improvement, meat inspection and slaughterhouses facilities, and developing safe water supplies and (b) "vertical" approach that targets the parasite by testing dogs, regular dosing of dogs with praziquantel, and massive reduction of dog populations, including baseline surveys and continuing surveillance of livestock and human infections. These approaches are not mutually exclusive (Gemmell and Schantz 1997; Gemmell et al. 2001). Certainly, the "horizontal approach" is cheaper than the "vertical" approach.

According to Gemmell and Schantz (1997) and Gemmell et al. (2001) and based on previous experiences, the control programs can be divided into four phases: (a) planning phase, (b) attack phase, (c) consolidation phase, and (d) maintenance of eradication phase. During the planning phase, the support of the control authority must be obtained, and the plan should establish methods of control, cost-benefit ratios, and the extent and duration of the program.

In the attack phase, the control measures to be applied must be targeted to the parasite and its definitive hosts; this includes dog-dosing campaigns with praziquantel, massive reduction of dog populations, regulation on dog feeding practice, ruling the keeping of dogs, and introducing an obligatory dog license fee that allows to create a record of rural and urban dogs. This is a costly phase.

In the consolidation phase, the campaign must be focused on at-risk areas as farms are identified using trace-back of the livestock through slaughterhouses surveillance. A trace-forward of the

livestock of these farms must be also implemented. During this phase the quarantine of infected farms is important and the dog registration should continue.

The maintenance of eradication phase can begin once the parasite has been potentially eliminated. During this phase, specific activities of previous phases cease, and vigilance activities are employed (e.g., trace-back from slaughterhouses). It is important that the dog registration still takes place during this phase (Gemmell and Schantz 1997; Gemmell et al. 2001). During the planning or preparatory phase taking into account the cost-benefit ratios, five options can be discerned (Gemmell and Schantz 1997; Gemmell et al. 2001):

Option 1: No control, for a variety of reasons such as lack of resources.

Option 2: Implement a horizontal approach.

Option 3: A slow attack option oriented toward preventing the dog's infection from raw offals by testing dogs and creating legislation for quarantining farms still harboring infected animals. This slow attack option may last for more than 30 years.

Option 4: A fast attack option A, which includes an educational approach, legislation, and surveillance of the human and animal population, as in option 3, but in addition the dog population must be drastically reduced. This attack phase can last more than 30 years.

Option 5: A fast attack option B, where all dogs are treated with praziquantel at predetermined intervals. The duration of this attack phase may be as short as 10–15 years. According to Gemmell and Schantz (1997), options 3, 4, and 5 are "vertical" approaches.

Craig and Larrieu (2007) summarize and simplify the approaches to control in slow track and fast track. The slow-track relies on specific health education, meat inspection, and upgrading of slaughterhouses. This approach was the only one employed in the Iceland program for many years and was successful (Craig and Larrieu 2007); however, most authors consider that the use of slow track as the sole tool of control does not lead to a significant reduction in transmission (Gemmell and Schantz 1997; Lloyd et al. 1998; Craig and Larrieu 2007). On the other hand, Wales' experience showed that although the unique use of education failed to reduce the transmission of echinococcosis, it had a positive effect on the praziquantel dosing of dogs by the farmers (Lloyd et al. 1998). The fast-track option leads to a shorter time to control the transmission of echinococcosis.

Based on the proposal of Gemmell et al. (2001), Craig and Larrieu (2007) described better the options for control of echinococcosis, which are as follows:

Option 1: Decision not to proceed because CE is not a public health problem, funding is not available, socio-economics features, and other reasons.

Option 2: Implementation of a long-term (slow-track) approach. Experience in some countries indicates that it would require 30–100 years to be fully implemented.

Option 3: Vertical slow-track approach incorporating at least annual testing of dogs together with on-site education of owners and quarantine of positive dogs.

Option 4: Vertical fast-track approach with elimination of stray dogs and euthanasia of positive dogs. Employed in Cyprus, this approach was effective after 10–15 years.

Option 5: Vertical fast-track approach including regular treatment of all registered dogs with praziquantel. Employed in New Zealand after 1990, it was effective after 10–15 years.

Health Education

Health education, as mentioned, is one of the tools for the control and prevention of echinococcosis, both in slow-track and fast-track approaches. Even in some control programs, such as Iceland (1863–1960), it was the only action taken during many years, and it recorded good results. Health education is a multidisciplinary activity, which requires knowledge of medical sciences, teaching, and communication methods. For the purposes of this paper, health education is defined as a specialty that uses educational principles to promote changes in behavior with regard to health in the individual and the community.

According to Parodi et al. (2001), health education includes three types of activities that tend to be dependent on one another:

1. Information: It involves the transfer of expert knowledge to the group targeted. This activity aims to highlight certain points to get the community to actively participate in preventive actions.
2. Health education sensu strictu: It is aimed to target groups who are not professionally concerned about the problem, such as schoolchildren or the public at large.
3. Occupational training: It targets those who must implement health standards in their professional activities (e.g., farmers and butchers).

The objectives of health education are for the community to support the programs and to be able to influence the importance of health priorities (Parodi et al. 2001). Therefore, health education must be included in all control programs previously defined. It is necessary to enhance the use of new technologies of communication and the spread of knowledge.

Costs and Benefits

The cost-effectiveness analysis and cost-benefit analysis are important tools to compare alternative echinococcosis control programs. For an economic evaluation it will be necessary to estimate the costs of the control program and losses produced by the disease (Nonnemaker and Schantz 1997). There are three types of costs to evaluate: (a) costs of CE in humans, (b) costs of the disease in animals, and (c) costs of the control program.

The cost of control programs must be evaluated realistically, taking into account that there are programs that will be necessary to implement over many years, supported by government budgets. Per Nonnemaker and Schantz (1997), the cost-benefit analysis is more comprehensive than cost-effectiveness analysis, and it determines if the net benefits of a control program outweigh the net cost to society. Whenever possible, the interruption of a control program for lack of funds should be avoided; sufficient funding from the legislature to complete this period of the program should always be in place. Loss of confidence by the government, resulting from inadequate data about evidence of success in the program, may result in a premature withdrawal of funding (Gemmell et al. 2001). To obtain sufficient funds in the budget, it is necessary to make a good analysis of the costs and benefits of the program because an economic evaluation of the effect of the disease should be an integral part of any control program. Therefore, it is necessary to sustain with data that CE has an important economic impact on human health and livestock production (Torgerson 2003a). Human health costs include human morbidity and mortality cost. Morbidity costs should include costs of diagnosis, surgical and medical treatments, nursing care, and paid sick leaves. It must also be considered that hydatidosis is a long-term disease that affects the quality of life both in undiagnosed individuals and in surgically treated individuals (Torgerson and Dowling 2001). The burden of CE may be also estimated using nonfinancial metrics such as the disability-adjusted life year (DALY) defined as a measure of overall disease burden and expressed as the number of years lost due to ill-health, disability, or early death, as proposed by Torgerson (2011). As Torgerson (2003b) said, the mortality costs are difficult to calculate because the value of life is a controversial subject and has been calculated in a number of ways. Because of these difficulties many economists prefer to use the concept of DALYs. It should be noted that the costs of human health are very different in poor countries as compared to the rich developed countries.

The cost estimates for livestock production are based on prevalence of CE in livestock, the value of livestock-related products, and an evaluation of likely production losses. It is accepted that infected animals have a reduction in the growth, milk production, and fecundity. Moreover, after inspection at slaughterhouses, the infected viscera (mainly the liver and lungs) are confiscated and destroyed. Because of all these factors, CE has important costs in livestock.

In a study made in Jordan, a country of lower-middle income with a population of 5,100,981,

Torgerson et al. (2001) estimates annual economic loss attributable to hydatidosis in animals and humans from US$ 2,602,215 to 6,533,661 with a median of US$ 3,874,070. In another study made in Wales, an endemic region of the United Kingdom, a wealthy and industrialized economy, Torgerson and Dowling (2001) estimate an annual human cost of hydatidosis of US$ 1million and perhaps as much as US$ 7.9 million. In Spain, a European country with 47,021,031 inhabitants, a study made by Benner et al. (2010) estimates the overall economic loss attributable to CE in animals and humans in 2005 at 148,964,534 euros. In China, in the province of Sichuan, with 84 million inhabitants, a study made by Budke et al. (2005) quantified the annual combined human and animal economic losses by CE at US$ 218,676 if only liver-related losses in sheep, goats, and yaks are taken into account. However, total annual losses can be nearly US$ 1 million if additional livestock production losses are assumed. Data such as those presented above serve as examples of arguments that must be handled with the government authorities to justify the cost of control programs.

Pharmacological Treatment of Dogs

The antihelminthic treatment of dogs is included in all programs of control. The drug of choice is praziquantel (5 mg/kg/bw) administered orally at intervals of 6 weeks. This interval was based on the prepatent period of infection with *E. granulosus* and has proven to be effective in preventing transmission Cabrera PA et al. (2002). Depending on the program of different countries, the praziquantel dosing is done by the owners of the dogs or by technicians in charge of the program, and the drug may be free or payable by owners.

Reduction of Dog Population

The reduction of dog population was implemented in some programs. A massive reduction of dog population was employed in the control program of Cyprus between 1970 and 1985. The drastic measure taken was the elimination of stray and unattended dogs. During the first year of the campaign, more than 18,000 stray and unattended dogs were killed. All dogs that tested positive for *E. granulosus* were also killed, and a dog registration fee was introduced (Craig and Larrieu 2007). This massive killing of dogs is not currently accepted.

In the current Control Program of Echinococcosis in Uruguay, since 2007, they have introduced a voluntary and free surgical castration of owned dogs. The spaying of stray dogs is also performed. The spaying is performed in dogs of both sexes by veterinarians in mobile units throughout the country. From January 2007 to October 2011, 100,440 dogs have been spayed. This action has the approval of the Society for the Protection of Animals of Uruguay and is made together with a campaign on responsible dog ownership (Ferreira and Irabedra 2007; Guisantes 2009; Purpura 2011).

Controlled Slaughter of Cattle

Measures must be taken to prevent that raw offal is eaten by dogs. Safe slaughtering includes veterinary inspection and improving facilities of abattoirs. The adoption of laws that forbid illegal killing is very important. The measures on home slaughter should be based on health education, especially in rural areas.

Vaccination

The vaccination against CE in livestock may be an important tool of control. The preparation of a vaccine (EG95) to protect sheep, goats, and bovines against hydatidosis is an important advance in this field (Lightowlers et al. 1996; Heath et al. 2003; Zhang and McManus 2008; Jensen and Thevenet 2011). The large-scale trials made in China and Argentina confirmed the efficacy of the dog vaccine developed by Lightowlers et al. (1996), and leads to their incorporation into future control options. The vaccine is a recombinant protein cloned from the oncosphere, which is injected together with Quil A subcutaneously on two occasions 1 month or more apart and induces

protection against *E. granulosus* which lasts for at least 12 months. A trial of vaccination of bovines with EG95 (5 doses) was also successful (Heath et al. 2011). However, operational difficulties and problems in field applications may limit the application in some countries (Mujica et al. 2011).

Surveillance

Epidemiological surveillance is defined as the ongoing and systematic collection, analysis, and interpretation of health data in the process of describing and monitoring a health event. This information is used for planning, implementing, and evaluating public health interventions and programs. Surveillance data are used both to determine the need for public health action and to assess the effectiveness of programs.

As recommended by Schantz (1997), the epidemiological surveillance applied to CE requires the measurement of infection in dogs and intermediate hosts (including humans) and the description of those factors relating to the hosts, the agent, and the environment pattern of distribution and transmission. Therefore, there is a significant relationship between surveillance and control because surveillance provides the baseline data necessary for any control program.

The surveys enable establishing the importance of CE in a country or region, obtaining baseline data and an insight into the process of transmission, and providing baseline information for formulating effective control policies for some or all the affected areas and information against which to monitor the progress of control (Gemmell et al. 2001). All this information should be obtained in the planning phase of the control program. The surveillance surveys must include data on human hydatidosis, data on canine echinococcosis, and data on prevalence of CE in livestock.

Data on Human Hydatidosis

These data are very important and may be obtained from different sources described in the following sections as annual surgical and treatment incidence, ultrasonographic (US) surveys, and serologic surveys.

Annual Surgical and Treatment Incidence

This data is the gold standard (Craig and Larrieu 2007). It must be expressed in total patients per 100,000 rural and/or total/rural population. These rates should be classified by age, sex, ethnic group, residence, occupation, etc. The incidence in children is important because it gives data on recent transmission. This data is of great value for monitoring the success of the control program.

Ultrasonographic Surveys

US is an excellent screening technique which has been employed in several control programs (Schantz 1997; Cohen et al. 1998; Larrieu et al. 2000; Frider et al. 2001; Wen et al. 2002; Macpherson et al. 2003; Guisantes 2009). US is a technique with good sensitivity, specificity, and clinical correlation. Its use in surveys has high acceptability to the population, and it can explore the abdominal organs, provide immediate results, has low cost, and can be used under field conditions (Gemmell 2001).

Serologic Surveys

Immunodiagnostic tests may be employed to evaluate the prevalence of hydatidosis. To be applied in seroepidemiologic studies, these tests must have good sensitivity, specificity, and predictive values. As part of this approach, a screening test of high sensitivity as the enzyme-linked immunosorbent assay must be employed, as well as a confirmatory test with high specificity as immunoblot. However, the immunodiagnostic tests have certain limitations: a) a variable proportion of persons with CE do not have detectable antibodies; b) the presence of antibodies not give information on the location, size and other data of the cyst; and c) the existence of cross-reactivity with other parasitic diseases (Gemmell et al. 2001). Currently it is accepted that a mass screening by US with confirmatory serologic testing is a good approach to surveillance of hydatidosis (Cohen et al. 1998).

Data on Canine Echinococcosis

The detection of *E. granulosus* in the definitive host plays a pivotal role in the transmission dynamics of CE. It represents a crucial milestone in the development of epidemiological studies and implementation of control programs in endemic areas (WHO/OIE 2001). Therefore, it is crucial to determine the prevalence of this zoonosis to have reliable methods of diagnosis in dogs and to develop appropriate control programs (Guisantes 2011). The methods in the following sections have been employed for the premortem and postmortem (necropsy) diagnosis in dogs.

Postmortem Diagnosis: Necropsy

The study of the small intestine during necropsy is the most reliable indicator of the prevalence and changes in patterns of infection of dogs with *E. granulosus* (WHO/OIE 2001). The parasitological examination by necropsy was the recommended method for the diagnosis in feral and unwanted dogs (Gemmell et al. 2001). Given its diagnostic accuracy, it is critical to include in all programs for the control of echinococcosis and other parasitic zoonoses, at least, a study based on necropsy. Nevertheless, this is a laborious and ethically questionable procedure, which is not suitable for mass screening.

Premortem Diagnosis in Dogs

This diagnosis includes the following: arecoline purging method, serologic diagnosis, coproantigen detection, and detection of copro-DNA.

Arecoline Purging Method

Identifying *E. granulosus* in feces after treatment with arecoline hydrobromide was discontinued in many control programs due to the many drawbacks.

Serologic Diagnosis

Since its proposal by Gasser et al. (1988), the detection of parasite-specific antibodies in serum has been used in several studies like Benito et al. (2006) in many countries and continents. However, this method has several drawbacks, which include the following: (a) variable informed diagnostic sensitivity (35–90 %), depending on the antigens, countries, and regions studied; (b) false-positives because some studies in endemic areas have found high positivity in noninfected dogs (diagnosed by arecoline); (c) it does not always indicate current infection; and (d) there is no correlation between the number of parasites and the serologic response.

Coproantigen Detection

Since the reports of Allan et al. (1992) and Deplazes et al. (1992), the method has been used worldwide in many studies (Jenkins et al. 2000; Benito et al. 2006) and control programs (Craig and Larrieu 2007; Ferreira and Irabedra 2007; Guisantes 2009). At present, the main advantages may be summarized (Guisantes 2011) as follows: (a) it is positive in the prepatent period; (b) it is an indicator of current infection; (c) it has a good sensitivity and specificity with some antigens and methods; (d) improves the results obtained by arecoline; (e) it can be applied to the analysis of individual cases or in larger studies; and (f) a properly treated sample can be stored and shipped at room temperature. The advantages of this method are the reason why the study of *Echinococcus* coproantigens is the recommended procedure by most authors nowadays. Presently, it is the most suitable method for the diagnosis of *E. granulosus* in dogs applicable to control programs, and its use in many countries has given good results.

Detection of Copro-DNA

The introduction of molecular methods based on polymerase chain reaction (PCR) should provide the required specificity and sensitivity for the detection of *E. granulosus* in dogs. This methodology is reported in many interesting papers, such as Cabrera M et al. (2002a), Abbasi et al. (2003), Dinkel et al. (2004), Stefanic et al. (2004), Varcasia et al. (2006), Naidich et al. (2006), Boufana et al. (2008), and Armua-Fernandez et al. (2011). Copro-PCR methods could be used for confirmation of coproantigen-positive stool samples. Naidich et al. (2006) propose that in areas where control programs and surveillance for canine echinococcosis are undertaken, the

copro-PCR could be used to verify that dogs are not longer infected with *E. granulosus* due to its high sensitivity and specificity. Whenever technological and economic conditions allow it, the detection of copro-DNA in feces is another good option for diagnosis in dogs. Its application in control programs worldwide will lead to a better large-scale evaluation of this methodology.

Data on Prevalence of Cystic Echinococcosis in Livestock

These data are very important to know the prevalence in a country or region before beginning a control program and to track its success. A proper inspection of meat in slaughterhouses is essential for a good surveillance. The prevalence data on livestock is usually supplied by the control authorities from slaughterhouses data. It is also important to trace back infected animals arriving to abattoirs to identify the infected farms and regions. In summary, an adequate surveillance system is very important to develop an efficient control program with a good cost-benefit relation.

Prevention

All control measures discussed above are directed toward prevention of infection. In relation to such measures, the prevention of human infection by *E. granulosus* eggs is based primarily on health education. It is important to determine the personal, socioeconomic, and environmental risk factors involved in the transmission of human hydatidosis in each country or region (Carmona et al. 1998; WHO/OIE 2001; Larrieu et al. 2000). One risk is the lack of potable water and the use of rural water tanks that collect rainwater from the ground surface and roofs (Carmona et al. 1998). All personnel handling dogs in endemic areas should be aware of the health risk of acquiring hydatidosis and must take safety precautions.

At a personal level, the prevention is mainly based on simple rules of personal hygiene, such as avoiding contact with unknown dogs that may be infected, washing hands before eating, and washing vegetables before eating them raw. Dog owners should treat the dogs regularly with praziquantel and avoid feeding them with raw offal potentially infected with cysts. The analysis of dog feces through the study of coproantigens is also a measure of safety at the household level.

Conclusion

The following concepts may be gleaned from this chapter:

1. Despite knowing thoroughly the life cycle of *E. granulosus* and their mechanisms of transmission, CE continues to be an important zoonosis in many regions of the world.
2. The control of CE includes a complex group of actions, due to the existence of human and animal hosts in the life cycle of *E. granulosus*.
3. A varied number of approaches and options to control CE have been employed in several countries, with different results.
4. The approaches to control CE have been well summarized by Craig and Larrieu (2007), both for slow-track and fast-track implementations. The slow-track is a long-term implementation that relies on specific health education, meat inspection, and upgrading of slaughterhouses. The slow-track implementation includes a vertical slow-track approach, which incorporates at least annual testing of dogs together with on-site education of owners and quarantine of positive dogs. The vertical fast-track approach also includes elimination of stray dogs and euthanasia of positive dogs and may add a regular treatment of all registered dogs with praziquantel.
5. Health education is a key tool for the control and prevention of CE, both in slow-track and fast-track approaches.
6. The cost-effectiveness analysis and cost-benefit analysis are important tools to compare alternative echinococcosis control programs.
7. The control measures of CE include pharmacological treatment of dogs, reduction of dog population, controlled slaughter of cattle, and vaccination.

8. The surveillance data is crucial to determine the need for public health action and to assess the effectiveness of the programs. The surveillance surveys must include data on human hydatidosis, data on canine echinococcosis, and data on prevalence of CE in livestock.
9. The control measures described are aimed to prevent CE in animals and in men, but of all these control measures, the prevention of human infection by *E. granulosus* eggs is based primarily on health education. Additionally, prior to taking any preventative measures, it is important to determine the personal, socioeconomic, and environmental risk factors involved in the transmission of human hydatidosis in each country or region.

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