7 The Skull, Brain and Associated Structures: Part II The Patient with a Headache

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Headaches are defined as the symptom of pain anywhere in the region of the head or neck. Like dizziness, they are one of the most common neurological problems which present to general practitioners and neurologists. They may also attend the emergency department. For many patients headaches can be painful and debilitating and are important cause of absence from work or school. It is important to appreciate that headache is only a symptom, and therefore it is not a diagnosis. Pain can arise from of a wide number of differing conditions involving the head, neck, eyes, face and beyond. Untreated hypertensive crisis, a systemic disorder, can result in severe pain. The brain itself is not sensitive to pain, as it lacks pain receptors. The sensation of pain is instead caused by the pain-sensitive structures sited around the brain. These include the periosteum of the skull, the meninges, muscles, nerves, arteries and veins, subcutaneous tissues, eyes, ears, sinuses and mucous membranes. Each of these structures can become irritated, diseased or deformed by a wide variety pathologies, resulting in a wide range of symptoms and underlying diagnoses. Pain can not only arise as a result of local pathology but can also be referred. This can make the diagnosis of headaches difficult.

A number of different classification systems exists, mostly based on the underlying pathology. A commonly used classification is taken from the International Headache Society, in which 'headache disorders' are classified as primary or secondary. The aetiology of primary headaches is not well understood and they are therefore classified according to their clinical pattern. The most common primary headache disorders are tension-type headache, migraine and cluster headaches. Secondary headaches are due to an underlying disorder (such as raised intracranial pressure and infection). For this reason, the symptom of a headache must always be taken seriously, especially if it is unusual for the patient, or its usual characteristics

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have changed. Although most cases of headaches are benign and self-limiting, there are a few which are due to serious pathology, and which may prove fatal or result in significant disability without prompt diagnosis and treatment. Successful management therefore is awareness of important causes and their key symptoms, or worrying features that can indicate serious pathology. In many cases diagnosis is made by eliminating known causes from the differential diagnosis clinically and when necessary by further investigation.

7.1 Classification of Headaches: Separating Benign from Serious Causes

The International Classification of Headache Disorders (ICHD) is a useful guide to the causes of headache and is accepted by the WHO. It is a detailed hierarchical classification of all headache-related disorders published by the International Headache Society and is considered the official classification of headaches by the World Health Organization. In addition to pain, the classification also contains diagnostic criteria. To receive a particular headache diagnosis the patient must, in many cases, experience a minimum number of attacks of (or days with) that headache and must fulfil a number of other requirements described within that headache's criteria. Below is a simplified and truncated version. The complete version can be found online and is far more comprehensive.

7.1.1 Primary Headaches

These are the most common types and include (i) migraine, (ii) tension-type headache and (iii) trigeminal autonomic cephalalgias (TACs). These usually have typical features. By definition, clinical examination is normal, including the neurological examination. Rarer types include cluster headache (severe pain that occurs in periodic episodes), primary cough headache, primary exercise headache, cold stimulus headache, and primary headache associated with sexual activity. Hemicrania continua is headache of unknown cause in which there is continuous pain on one side of the head. Hypnic headaches are benign primary headaches that affect the elderly. Patients describe moderate, throbbing, bilateral or unilateral headaches that wakes the sufferer from sleep once or multiple times a night, often at the same time. Patients whose history is typical of one of the primary headache syndromes and who have a normal neurological examination, are likely to have normal laboratory tests and imaging studies.

7.1.2 Secondary Headaches

These are defined as headaches that occurs in a close temporal relation to another disorder, or whenever there is evidence of a causal relationship (for example raised

intracranial pressure or following trauma). At the same time the headache is also significantly improved or resolves (usually within 3 months or less) following successful treatment or remission of the underlying cause (e.g. hypertension or medication overuse). These headaches are generally classified based on their aetiology and not symptoms. For most secondary headaches the characteristics of the headache will not necessarily indicate the cause. There are more than 200 types. Causes include

- Head or neck trauma
- Cranial or cervical vascular disorders
- Vertebrobasilar artery dissection
- Intracranial haemorrhage (ICH)
  - Subarachnoid haemorrhage (SAH)
- Post—craniotomy
- Ischaemic stroke or transient ischaemic attack
- Pituitary apoplexy
- Vascular malformations
- Arteritis
  - Temporal arteritis

Cervical carotid or vertebral artery disorders

- Cerebral venous thrombosis
  - Cavernous sinus or Sagittal sinus thrombosis
- Low or high pressures of the cerebrospinal fluid pressure
  - Hydrocephalus
  - Benign /Idiopathic intracranial hypertension
  - Post—LP headache
- Non-infectious inflammatory disease
- Intracranial neoplasm
- Dural puncture
- Chiari malformation (Fig. 7.1)
- Substance ingestion or its withdrawal
- Medication overuse
- HIV/AIDS
- Intracranial infections
  - Meningitis, Brain abscess, Subdural empyema
- Systemic infections
- Dialysis
- High blood pressure
- Hypothyroidism
- Cardiac cephalagia
- Fasting
- Injury to facial structures including the teeth, jaws or temporomandibular joint.
- Psychiatric disorders

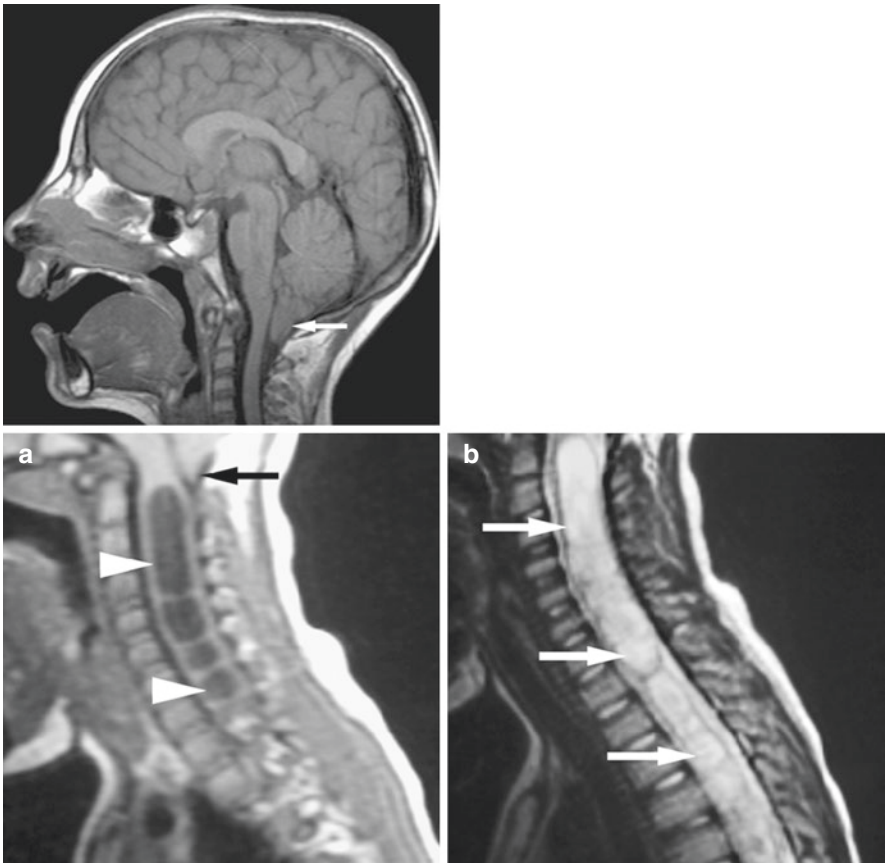

Fig. 7.1 (I) Chiari malformation type I: 7-year-old female with Noonan syndrome presents with neck pain. Mid-sagittal T1-weighted MRI shows descent of point of tonsils through foramen magnum (*arrow*) and absence of CSF in cisterna magna. (II) Chiari malformation Type I; 5-year-old asymptomatic male. (**a**) Mid-sagittal T1-weighted MRI demonstrates caudal displacement of cerebellar tonsils (*arrow*). Dark signal in center of cervical cord represents syringo- or hydromyelia with multiple locations (*arrowheads*). (**b**) Sagittal T2-weighied MRI reveals associated hydromyelia with multiple locations of fluid in center of cord. These are sequelae of decreased CSF dynamics through foramen magnum (*arrows*)

This list is by no means complete. Nevertheless, it illustrates the diverse nature and potential significance of any patient who presents to the emergency department with a headache. In the absence of identifiable pathology, management usually involves analgesia.

7.2 Assessing a Patient with a Headache

Most headaches can be diagnosed by a detailed clinical history alone. If the symptoms sound dangerous, further testing with neuroimaging or lumbar puncture may then be necessary. Electroencephalography (EEG) is generally regarded as not

useful in the diagnosis of headache. The first step to diagnosing a headache is to determine if the headache is old or new, or if it has changed its usual characteristics. Any significant change to the pattern or site of a headache should raise suspicion of serious pathology. Questions may include

1. Where the pain is
2. Its character and severity and any regularity (diurnal rhythm)
3. Its duration
4. If there is an aura (changes in vision, blind spots, or bright lights) before the headache
5. What other symptoms or warning signs occur (weakness, nausea, sensitivity to light or noise, appetite changes, changes in attitude or behaviour)
6. Age of onset
7. How long the patient has been experiencing them
8. Is each headache identical or do they vary
9. How often they occur
10. Any symptoms that occurred between headaches
11. Any known causes (For example, certain situations, foods, or medicines)
12. If physical activity makes the pain worse
13. Any family history

The key elements in a headache history include the following

7.2.1 Date of Onset, Age at Onset, and Frequency of Symptoms

The length of time that a patient has suffered from headaches is important in differentiating benign headaches from those arising from progressive or severe neurological disorders or systemic disease. Headaches that are worst first thing on wakening are typical of a raised ICP. They can also occur with caffeine withdrawal. Early morning headache in the elderly is also often the result of contracture in upper cervical ligaments. Headache from temporal arteritis also occurs late in life.

Long-standing, intermittent headaches with pain-free intervals occurring over months or years are rarely due to serious intracranial or systemic pathology. Most patients with these symptoms have stress-tension headaches. However, the sudden onset of severe and persistent headaches in someone who has never been troubled by them, especially if accompanied by focal neurological signs or symptoms, warrants urgent investigation. Sudden onset of a headache is often referred to as a 'thunderclap' headache. The most concerning cause of this is a subarachnoid haemorrhage (Fig. 7.2). In this regard migraine may initially cause concern in a patient who has never previously experienced it. This is often accompanied by visual deficits (e.g. hemianopia).

Headaches which develop or progress, over weeks to months, also need urgent investigation. Although most headaches in this category have a benign cause, intracranial or systemic pathology should be carefully considered. Headaches arising

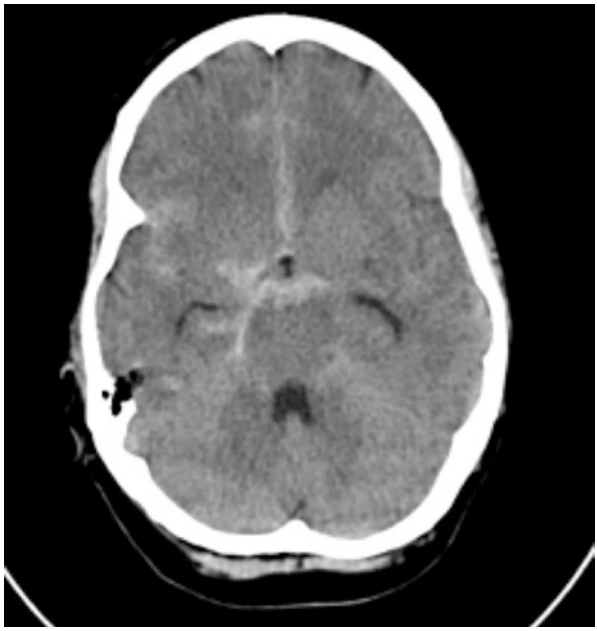

Fig. 7.2 Subarachnoid haemorrhage—typically there is sudden onset of severe headache

from intracranial mass lesions or increased intracranial pressure rarely have headache-free intervals.

7.2.2 Location

Stress-tension headaches tend to occur in the occipital region and radiate into the neck and shoulders. However, posterior fossa tumours can also cause similar symptoms. A band-like distribution of discomfort is also common in stress-tension headache. Hemicranial headaches that spread across the head are generally vascular (e.g. migrainous). Disorders involving the joints between occiput and C1, or between C1 and C2, can give rise to pain both in the upper neck and/or head. Cervical spine disease is therefore part of the differential diagnosis of the patient with a headache.

7.2.3 Duration

Persistent and uneasing pain that lasts for days at a time should arouse suspicion of intracranial or sinus disease, cranial arteritis, or carotid dissection. Headaches that occur at night for weeks can be a feature of cluster headaches.

7.2.4 Predisposing Factors

In some patients who have vascular headache syndromes, certain foods and other substances are known to precipitate headaches. Examples include chocolate, red

wine and fatty foods. Other triggers include bright lights, exercise, sexual intercourse, stress and alcohol. Hormonal status (pre-menstrual, OCP), emotions, and barometric changes can be associated with migraine. Straining, coughing or sneezing can worsen headaches associated with raised intracranial pressure. A cough impulse headache is common in Chiari malformation. Caffeine withdrawal can cause severe symptoms, which are quickly relieved by ingestion of caffeine.

7.2.5 Preceding Symptoms

Many patients with vascular type headaches often have some form of autonomic disturbance that precedes the headache, sometimes by up to 24 h. Visual hallucinations occur in 10–15% of migraine sufferers. These usually last about half an hour and are followed almost immediately by the headache. Any visual symptoms must be carefully evaluated as these can also occur in epilepsy, ocular and other intracranial disease.

7.2.6 Quality and Severity of Pain

Pain from a vascular headache usually starts as a dull ache, which then becomes throbbing in nature. It usually made worse by physical activity and can be alleviated by massage of the external carotid artery. Cluster headaches and headaches from intracranial haemorrhage are usually severe, the latter is often accompanied by neurological signs.

7.3 Other Associated Factors

A family history may suggest migraine—patients with family members who suffer from migraines are far more likely to also have migraines themselves. Familial hemiplegic migraine has been shown to be related to an inherited gene. This form of migraine has been subdivided into 4 categories. With some types of headache, age of onset is a useful indicator. Temporal arteritis is most commonly seen in patients over 60 and should not be diagnosed in young patients on clinical grounds alone. Migraine is often seen in puberty. Children commonly suffer from benign headaches, but if headache is acute in onset of headache it is important to consider meningitis. Females are more likely to have SAH, migraine (which can be menstrual related), venous sinus thrombosis and tension headache. Men tend to get cluster headaches. Associated medical problems include depression and anxiety. In some cases, headache occurring exclusively during psychiatric disorders (major depressive disorder, panic disorder, generalised anxiety disorder and undifferentiated somatoform disorder) may best be considered as attributed to these. They can be associated with tension-type headache. If a patient wears spectacles, eyestrain should be considered. Smoking and hypertension are well known risk factors for subarachnoid haemorrhage and stroke. Pregnancy predisposes to thrombosis or pre-eclampsia.

7.4 Associated Symptoms

Nausea, photophobia and drowsiness frequently occur during migraine headaches. These typically do not indicate serious pathology and normally resolve following the migraine episode. However these same symptoms can also occur in association with acute intracranial pathology. As such, if these are not symptoms commonly experienced by patient, they should therefore always be treated with suspicion. If the patient with a headache appears increasingly drowsy, and it is not possible to fully rouse them, it is important to consider the possibility of raised ICP. Fundoscopy may reveal papilloedema. If this is suspected urgent CT is required. Subarachnoid haemorrhage (SAH), malignant hypertension, intracerebral haematomas (ICH), tumour or intracranial infection are all possible causes. Nausea and vomiting are also commonly seen with raised ICP.

Visual disturbances are commonly seen with a number of headache disorders. These can take the form of visual hallucinations (auras, such as flashing lights, are a feature of classic migraine), loss of part of the visual fields, blurred vision, double vision and in extreme cases, loss of sight. In migraine more than 90% of auras are visual, consisting of either positive phenomena (flicker, "fortification figures") or of negative phenomena (such as hemianopsia). These generally occur before the headache and last no longer than 60 min. Auras with different features (longer duration, nonvisual, arising after the headache) are so rare, that they should always be suspected of indicating another problem. Conditions that can mimic a migraine aura include strokes, TIAs, seizure disorders, tumours, venous thrombosis, arteriovenous malformations and carotid dissections. A useful feature to differentiate an aura from ischaemia is spreading—auras expand gradually to cover an increasingly larger area, while ischaemic symptoms usually present suddenly, in their full extent. Sudden loss of sight may occur during or following headaches due to temporal arteritis. Recent repeated attacks of amaurosis fugax associated with headache are very suggestive of this. It is also known as giant cell arteritis (GCA). Any recent persisting headache in a patient over 60 years of age should suggest GCA and be investigated. This is discussed further in a chapter on the eye. For this reason, diagnosis of temporal arthritis and treatment with high-dose steroids needs to be made as soon as possible. In many cases patients present with a visual field disturbance, which progressively deteriorates. This may be accompanied by unilateral headache and tenderness over the temple. The underlying pathology is a pan arteritis, blindness is thought to occur as a result of ischaemia of the optic nerve secondary to arteritis of the ophthalmic arteries. Both eyes can be affected by this. The time interval between visual loss in one eye and in the other is usually less than 1 week. Cavernous sinus thrombosis (discussed elsewhere) can also cause loss of vision. Loss of visual acuity and visual field constriction can be a feature of raised ICP in hydrocephalus and benign/idiopathic intracranial hypertension. Ophthalmoplegia can occur in pituitary apoplexy, cavernous sinus thrombosis or in cavernous carotid fistula.

Autonomic features such as rhinorrhoea, unilateral nasal obstruction and lacrimation are usually seen in trigeminal autonomic cephalalgias. Ask if the pupil becomes small (ptosis) or if the eye becomes red or swollen. These are features of

Horner's syndrome and indicate the possibility of TACs. Hypersensitivity phenomena such as photophobia, phonophobia or osmophobia are often seen only with migraine. Photophobia is often seen in classic migraine but if seen with thunderclap headache, SAH must be considered. It also occurs in meningitis along with neck stiffness. Syncope in a headache patient may occur in migraine or more rarely a colloid cyst of the third ventricle. Dysphasia, hemiparesis or sensory disturbance occurring in association with a headache is a concerning finding—brain tumour, SAH or a stroke should be considered. However, some migraines can also cause temporary hemiparesis or hemisensory loss. Irritability and confusion with a headache should suggest migraine and restlessness or pacing up and down is common with cluster headache. Jaw claudication is pain on chewing, and may be seen occasionally in temporal arteritis when the facial artery is involved.

Worsening of a headache with a Valsalva manoeuvre or when coughing or sneezing suggests temporary elevations in intracranial pressure. This can arise from a posterior fossa or cranio-verteberal junctional anomaly, such as a Chiari I malformation. If this is ruled out, then a primary cough headache is diagnosed. If a headache worsens on exertion, consider cardiac cephalalgia, phaeochromocytoma, dissection or primary exertional headache. If the headache begins or worsens with sexual activity, suspect a sub-arachnoid haemorrhage, or dissection, or primary sexual headache. Some patients can experience more than one type of headache—this implies there are distinctive types of headache and not just headaches of differing severity. Migraine and cluster headache can coexist, cluster headache can be associated with trigeminal neuralgia (cluster–tic syndrome) or migraine patients may have acute sinusitis. Therefore, it is important to recognise different headaches when they coexist. When there is more than one type of headache, it helps to have the details of each type of headache. Weight loss, arthralgia and fever can occur in temporal arteritis. Seizures may occur in brain tumours, subarachnoid haemorrhage or intracranial infection. Headaches persisting for longer than 6 weeks or those with abnormal physical signs should be investigated. Initial tests include FBC, ESR (to exclude temporal arteritis) and CT or MRI brain to exclude intracranial pathology.

7.4.1 Worrying Features of a Headache

It is important to consider and enquire about these in all headaches. If present they should prompt further investigations.

1. Onset after age 50
2. worsening headache with fever
3. sudden-onset headache reaching maximum intensity within 5 min
4. new-onset neurological deficit
5. new-onset cognitive dysfunction
6. change in personality
7. impaired level of consciousness
8. recent (within the past 3 months) head trauma

9. headache triggered by a cough, valsalva manoeuvre (trying to breathe out with nose and mouth blocked) or a sneeze
10. headache triggered by exercise
11. orthostatic headache (headache that changes with posture)
12. symptoms suggestive of temporal arteritis
13. symptoms and signs of acute narrow-angle glaucoma
14. a substantial change in the characteristics of their headache.

Also, consider further investigations and/or referral for people who present with a new-onset headache plus any of the following

1. compromised immunity, caused for example, by HIV or immunosuppressive drugs usage
2. a history of malignancy known to metastasise to the brain
3. vomiting without other obvious cause.

7.4.2 Ictal Headaches

These are headaches associated with a seizure. They can occur either before, during or after the seizure occurs. Patients may be misdiagnosed as having migraine with aura, or cluster headache. However, ictal headache often involve the entire head. Severity can vary widely from a mild to being so severe that (like cluster headache) it is sometimes referred to as "suicide headache". Temporary blindness has also been reported. Treatment involves anticonvulsants.

7.5 Primary Headaches

These are not emergency conditions. However they are included as they commonly fall within the differential diagnosis of headache. The dura is sensitive to pain, especially where it is related to the dural venous sinuses and meningeal arteries. Consequently, stretching of arteries at the cranial base or veins near the vertex, where they pierce the dura, causes pain. Distension of the scalp or meningeal vessels (or both) is believed to be one cause of headache.

7.5.1 Migraine

Migraine is a severe form of primary headache that may present acutely as a recurrent unilateral throbbing headache, or as facial pain affecting the cheek, orbit or forehead. In severe cases it can last for days and be associated with nausea and vomiting. Classical migraine has a preceding visual disturbance, an 'aura'. Migraine is a frequent cause of headache in children. Classical migraine features

are rare before the age of 6 years, but some migraine-related syndromes have been described. Many childhood episodic syndromes have been described as common precursors of migraine. A strong association between infantile colic and migraine has also recently been reported. Migraines are believed to be due to a combination of genetic and environmental factors. It can run in families and there is some evidence to suggest hormone levels may play an important part. However the underlying mechanisms are still not fully understood. Current opinion suggests a complex process, in which vascular and neurologic events combine in the pathogenesis of an attack. It is believed this involves activation and sensitisation of trigeminovascular pathways, as well as brain stem and diencephalic nuclei. All nociceptive information from craniovascular structures is relayed through the trigeminocervical complex (TCC), and via ascending connections to other areas of the brain stem and diencephalon. These key sites are thought to be involved in the processing of pain and other sensory information. Several complicated theories have thus been proposed.

1. The Neurovascular theory—migraine is primarily a neurogenic process with secondary changes are occurring in the cerebral perfusion. Some reports suggest there is a heightened state of neuronal hyperexcitability in the cerebral cortex, in some sense, similar to patients with epilepsy.
2. Cortical spreading depression theory—migraine occurs secondary to cellular depolarisation which spreads across the cerebral cortex like a slow-moving wave, resulting in changes in blood flow, activation of the trigeminovascular system and other complex cellular processes.
3. Vasoactive substance and neurotransmitter theory—release of various chemicals, such as substance P and nitric oxide produces vasodilation and local irritation of the cerebral cortex
4. Migraine centre theory- a potential ‘migraine centre’ has been proposed in the brainstem.
5. Brainstem activation theory—PET scans in patients during a migraine headache has shown foci of activation. This spreads to involve the trigeminovascular complex with secondary vessel dilation.

Other theories have been proposed (cutaneous theory, dopamine theory, endothelial dysfunction theory, serotonin theory etc.) making this a very complex disorder which is still not fully understood. Several risk factors have been identified including obesity, hypertension, hypercholesterolaemia, disturbed sleep, stress, hormonal changes and high homocysteine levels. Overuse of medication to treat migraine can also predispose patients to chronic headaches.

Migraine typically presents with recurrent severe unilateral headache, associated with nausea and vomiting. Patients are almost always awake, although occasionally pain may develop during the waiting period. Approximately one third of patients will experience an aura. Four stages have been described

1. The prodrome. This may precede the headache phase by up to 72 h and can include a variety of symptoms, such as altered mood, depression, fatigue, or other non-specific symptoms. Prodromal symptoms occur in around two thirds of migraine patients. Although they vary in their nature, they tend to remain consistent within any given patient, such that many patients know in advance a migrainous attack is coming.
2. The aura. This is a transient and focal neurological symptom that can occur before or during the headache. It usually develops over 10–15 min and last around 1 h. Symptoms can be visual, sensory or even motor in nature. Most commonly they are visual such as an alteration in the visual field ('halo' or 'tunnel vision'), flashing lights, even temporary loss of vision. In other patients 'pins-and-needles' or numbness can develop in the upper limb or face. Other neurological symptoms include hemiparesis, aphasia and confusion. Not surprisingly therefore, migraine can easily be confused with other disorders such as subarachnoid haemorrhage, transient ischaemic attack and stroke.
3. The headache. In classic migraine this is unilateral, throbbing and moderate to severe in intensity. It usually comes on gradually and can be aggravated by physical activity. The headache is initially unilateral and often localised to the forehead and periorbital region. It is usually built up over a period of several hours, spreading posteriorly. However in some patients the pain can involve both sides and can even spread into the neck. In adults the pain can last only a few hours or it can persist for up to 72 h. Its intensity varies from moderate to severe and is usually made worse by movements or physical activity. During this time patients may also experience unpleasant autonomic symptoms. Many patients therefore prefer to find somewhere quiet and dark where they can rest during the attack.
4. The postdrome. These symptoms develop following the acute headache and can vary in their nature. Most patients report feeling tired and weak. Nausea and vomiting can occur and occasionally patients can develop photophobia and lightheadedness.

Several variants have been described including hemiplegic migraine (described below) and vestibular migraine (pain associated with tinnitus, aural fullness, dizziness and hearing loss). Trigger factors include stress, diet (chocolate, cheese, red wine), hormonal state (pre-menstrual, OCP), emotions (anger, excitement), and barometric changes.

Diagnosis of a migraine is usually made on clinical grounds. However imaging may be required, particularly if symptoms are not typical for migraine. During an attack patients may develop focal neurological signs, which can result in diagnostic confusion. Headache, neck pain and meningism, may suggest subarachnoid haemorrhage or meningitis. Headache, drowsiness and alternate mental state may suggest raised intracranial pressure. Aphasia, unilateral paralysis and third nerve palsy with a headache, may suggest an intracerebral bleed. Since headaches and neurological/visual symptoms can also be caused by other serious intracranial pathology patients presenting with migraine for the first time often require investigation. Current

guidelines indicate that known migraine patients do not need to be investigated with every episode, however if their pattern of migraine changes significantly (in site, severity or distribution), if they develop a fever, or if they develop migraine for the first time over the age of 50, CT or MRI is indicated. In view of the widespread nature of the symptoms, the differential diagnosis is wide and includes temporal arteritis, cluster headaches, acute glaucoma, meningitis and subarachnoid haemorrhage. It is therefore important to take a thorough history and detailed examination, looking particularly for evidence of papilloedema. This would not be present in migraine. It is important to remember that some migraines can cause temporary hemiparesis (Hemiplegic Migraine) or hemisensory loss.

Management involves recognising and removing any precipitating causes and simple analgesics in the first instance. In many cases simple analgesia alone can provide relief in most patients with mild to moderate severe pain. Simple analgesics include paracetamol and non-steroidal analgesia. Anti-emetics may also be used to treat nausea and vomiting. If attacks are frequent and affect routine daily life then prophylactic treatment can be considered. Medications include oral Pizotifen at night, or daily beta blockers. In severe cases patients may be prescribed Triptans (e.g. Sumatriptan), Ergotamines and intravenous metoclopramide. Occasionally surgery may be indicated to deactivate "trigger sites". Botulinum toxin A (Botox) has been reported to be of some benefit in patients with chronic migraine that has failed to respond to other measures. However this requires careful case selection and should not be given simply to patients with a bad headache. Transcutaneous electrical nerve stimulation (TENS) has also been reported to provide some benefit.

7.5.2 Cluster Headaches

Cluster headaches are a primary headache disorder affecting up to 0.1% of the population. They are often classified as trigeminal autonomic cephalalgias (TACs). Attacks are characterised by severe unilateral pain mainly in the first division of the trigeminal nerve, with associated prominent unilateral cranial autonomic symptoms and a sense of agitation and restlessness during the attacks. The pathophysiology of cluster headache is complex and the underlying mechanisms are not fully known. It is currently thought to be a neurovascular rather than a vascular headache, with vascular cerebral changes being driven by the effects of trigeminocervical complex (TCC) and trigeminal-autonomic reflex activation.

Attacks can be triggered by various substances. These include alcohol and strong smells such as petroleum and nail varnish. Pain generally occurs in clusters, usually at night for 1–3 weeks, every 12–18 months, lasting between 15 min to several hours. They are more common in men between 20 and 40 years and may be precipitated by alcohol. The headaches are characteristically excruciating, unilateral, and commonly involves the first division of the trigeminal nerve, around and behind the eye and in the temple. Typically the patient is woken at night by severe unilateral, stabbing or burning pain. Pain may also be perceived to have arisen from the sinuses

or from the dentition, and patients may therefore initially attend their dentist or be referred to an ENT surgeon. In some patients pain is so severe that this condition is also known as "suicide headache." Pain generally builds up quickly in intensity resulting in a severe discomfort, which dissipates in a similar timeframe, with a clear onset and resolution. Attacks are strictly unilateral, however, on occasion they can switch sides within or between episodes. There may also be accompanying autonomic symptoms such as lacrimation, unilateral nasal congestion, conjunctival injection and swelling around the eye. These cranial autonomic symptoms occur on the same side as the pain and are thought to be due to parasympathetic activation. Sympathetic impairment can also present as miosis and Horner syndrome. Unlike migraine, nausea is not a common feature.

One prominent feature during attacks is a sense of restlessness and agitation. This is a useful feature that can help in distinguishing cluster headache from migraine—the latter patients prefer to lie still. Cluster headache patients tend to pace back and forth or 'rock' during attacks and attempt to lessen the intensity of the pain by applying pressure to the affected area. In some cases headaches occur with remarkable diurnal regularity, with attacks occurring at a precise time of the day. This has resulted in its alternate name—"alarm clock headache". Such observations have prompted researchers to speculate that this is in some way relating to dysfunction of the hypothalamus. Otherwise the cause of this condition is unknown, although it has been reported to run in families, suggesting a genetic basis. The nature of the symptoms has resulted in the suggestion that this is a vascular disorder.

Cluster headaches often respond to Ergotamine, although there is no known cure. Triptans have shown a very beneficial and rapid effect; they can be administered subcutaneously (sumatriptan 6 mg) or intranasally (zolmitriptan 5 mg or sumatriptan 20 mg). Other medications include verapamil, topiramate, and lithium. Verapamil is the drug of choice for preventative treatment of cluster headache. Because of its effects on cardiac conduction, control ECGs are essential before and during therapy. Corticoids are highly effective in brief cluster episodes, or as temporary treatment until verapamil or lithium becomes effective, and for temporary treatment of a severe episode in chronic cluster headache. In the short term, prednisone can be used at higher dosages and intravenously. However because of their side effects, long-term use of steroids is contraindicated. Nerve stimulators may help in the small number of people who do not improve with medications. Occipital nerve block using a corticoid and a local anaesthetic may also provide temporary relief.

Deep brain stimulation of the posterior hypothalamus and the occipital nerve have been reported with variable success. Spinal cord stimulation (SCS), vagus nerve stimulation (VNS), and sphenopalatine ganglion (SPG) have also been reported.

7.5.3 Tension Headache

Tension-type headaches account for around 90% of all headaches and are the most common type of primary headache. Tension headaches are described as a feeling of

pressure, or a 'band-like' tightness around the head, that varies in intensity, frequency and duration. It is often felt bilaterally over the forehead or temples but can affect the vertex, occiput or eyes. It is commonest in middle aged women with associated stress or depression and it can become chronic or episodic. Various precipitating factors include stress, sleep deprivation and eye strain. Clenching of the teeth (bruxism) is another cause of pain, which is frequently associated with discomfort in the temporomandibular joints (TMJs). Hyper-excitability of the trigeminal central nociceptive neurones and complex interactions with neurotransmitters have also been suggested, based on the fact that these headaches can be treated with antidepressants such as amitriptyline. However, other mechanisms are probably also involved, making this (and other causes of facial pain) difficult to treat. Patients often describe the headache as a constant pressure, as if the head were being 'squeezed'. If symptoms do not settle with simple measures and analgesics, MRI should be considered. Ibuprofen and regular tricyclic antidepressants appear to be helpful in this condition. Preventative treatment includes amitriptyline. Botulinum toxin, acupuncture and spinal manipulation have also been suggested as potential treatments, but evidence supporting these is lacking.

7.5.4 Hemicrania Continua (Paroxysmal Hemicrania)

Paroxysmal hemicrania, also known as Sjaastad syndrome, is a persistent and sometimes debilitating headache that can be unremitting. Episodic and chronic variants exist, depending on the frequency and duration of attacks. The pain is usually severe and unilateral, affecting the area around the eye. It can present as multiple short lived but severe attacks, lasting between 5 and 30 min, or a more continuous episode, without pain-free periods. Compared to the cluster headaches these attacks are usually shorter. There may also be lacrimation, nasal congestion or ptosis, although most patients do not experience nausea or vomiting. The cause of hemicrania continua is unknown and there is no definitive diagnostic test for it. However a number of serious pathologies can produce similar symptoms, including aneurysms, AV malformations and some intracranial neoplasms. Patients presenting with these symptoms should therefore be imaged urgently, preferably with MRI. This condition generally responds to non-steroidal anti-inflammatory drugs, of which indomethacin has been found to be particularly effective. Lamotrigine and topiramate have also been reported to be effective.

7.5.5 Thunderclap Headache

This term refers to the sudden-onset of severe headache that takes only a few seconds to a minute to reach maximum intensity. Thunderclap headaches are uncommon, with an estimated incidence is about 43 per 100,000 adults per year in the developed world. But they can be a warning of potentially life-threatening conditions—usually associated with bleeding in and around the brain. It can be indication of a number of serious conditions. As such this symptom should be taken seriously

and investigated urgently. However in many cases no abnormalities are found. Causes of thunderclap headaches include.

1. Subarachnoid haemorrhage (10–25% of all cases)
2. Cerebral venous sinus thrombosis
3. Cervical artery dissection
4. Hypertensive crisis (severely raised blood pressure)
5. Spontaneous intracranial hypotension
6. Stroke
7. Pituitary apoplexy
8. Colloid cyst of the third ventricle (Fig. 7.3)
9. Primary cough headache, primary exertional headache and primary sexual headache
10. Infectious disorders (including meningitis which is rare), intracranial hypertension, and hypotension syndromes occasionally present with thunderclap headache
11. Suspect reversible cerebral vasoconstriction syndrome when thunderclap headaches recur over a few days

The most important causes to consider are subarachnoid haemorrhage, cerebral venous sinus thrombosis and carotid/vertebral artery dissection.

1. In subarachnoid haemorrhage, there may be loss of consciousness, seizures, meningism, visual symptoms, and vomiting. Headaches typically persists for several days afterwards.
2. Cerebral venous sinus thrombosis usually also causes symptoms related to raised intracranial pressure. The headache is therefore made worse by anything that increases the ICP further (such as coughing). In most cases there are other neu-

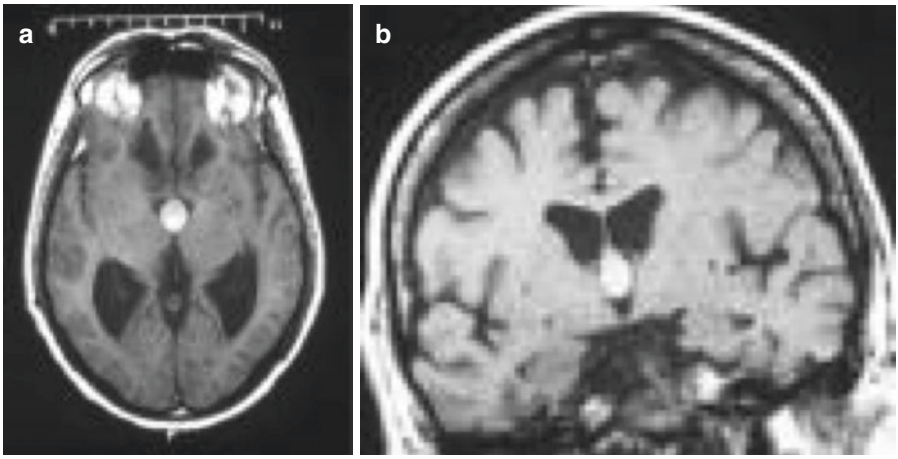

Fig. 7.3 T1 axial and coronal MRI showing colloid cyst

rological abnormalities, such as seizures and weakness, but in one third of patients the headache is the only symptom.

3. Carotid artery dissection and vertebral artery dissection often cause pain on the affected side. This may soon be followed by ischaemic symptoms such as visual disturbance and limb weakness.

The underlying pathophysiology of primary thunderclap headache (TCH) and reversible cerebral vasoconstriction syndromes (RCVS) is unclear. Excessive sympathetic activity or an abnormal vascular response to circulating catecholamines has been suggested. This would explain the occurrence of TCH during physical activity, in patients with pheochromocytoma, acute hypertensive crises and in patients who take sympathomimetic drugs or tyramine containing foods concurrently with monoamine oxidase (MAO) inhibitors. Sympathetic afferents that innervate the intracranial vasculature contain neuropeptide Y and noradrenaline, both vasoconstrictors. TCH may therefore be a result of spontaneous and abnormal central sympathetic responses.

The key feature that differentiates TCH from other headaches is the rapidity with which it develops. Severity alone is not sufficient. Symptoms are often very dramatic. Pain strikes suddenly and severely, peaking usually within 60 seconds. This may be accompanied by nausea or vomiting. In addition patients may develop an altered mental state, fever or have a seizure. The most important initial investigation is urgent CT of the brain to exclude subarachnoid haemorrhage. If this is normal, a lumbar puncture may then be performed. This is because a small proportion of SAH may not be visualised on CT, especially if there is a delay in scanning. If both investigations are normal, the description of the headache and the presence of other abnormalities may indicate further tests, such as magnetic resonance imaging (MRI). Magnetic resonance angiography (MRA) may help identifying vascular causes (such as arterial dissection). Magnetic resonance venography (MRV) may identify venous thrombosis (Fig. 7.4).

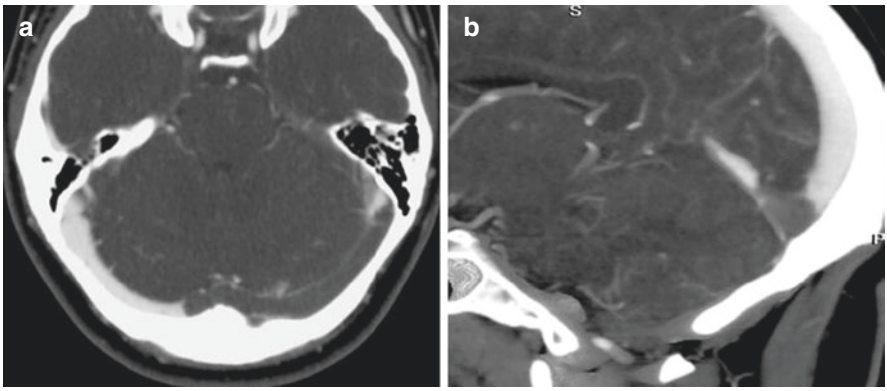

Fig. 7.4 (**a**, **b**) Venous thrombosis, (**a**) Axial image demonstrates a large filling defect of the left transverse sinus involving the torcula. This indicates acute thrombosis, (**b**) Sagittal maximum intensity projection (MIP) image demonstrates thrombus within the torcula. The posterior superior sagittal sinus and the straight sinus are widely patent and opacify with contrast

7.5.6 Reversible Cerebral Vasoconstriction Syndrome (RCVS)

This term is sometimes used to include a number of complex disorders, such as 'thunderclap' headaches with reversible vasospasm, benign angiopathy of the CNS, postpartum cerebral angiopathy, migrainous vasospasm, migraine angiitis, and drug-induced cerebral arteritis or angiopathy. The usual age of onset is around 40 years, and it affects more women than men. Reversible cerebral vasoconstriction syndrome (RCVS) is characterised by reversible multifocal narrowing of the cerebral arteries with manifestations of recurrent thunderclap headache with or without focal neurologic deficits. Around two thirds of cases occur secondary to a known underlying cause, most commonly following exposure to vasoactive substances or during the postpartum period. Trigger factors include the Valsalva manoeuvre or emotional stress, implicating a dysregulation of cerebral arterial tone with increased sympathetic stimuli. Cerebral endothelial dysfunction has been suggested as a key factor.

Patients present with recurrent sudden-onset and severe headaches over a several week period, often accompanied by nausea, vomiting, photophobia, confusion and blurred vision. This may be complicated with the development of subarachnoid haemorrhage (without an aneurysm), ischaemic stroke or intracerebral haemorrhage. RCVS may therefore be misdiagnosed as migraine, ischaemic stroke and primary CNS arteritis (PCNSA). However, the clinical course, prognosis and management are different. Diagnosis requires demonstration of the characteristic 'string of beads' on cerebral angiography with resolution within 1–3 months. Many treatments have been reported, but it is unclear whether they prevent haemorrhagic or ischaemic complications. Calcium channel blockers, such as nimodipine, nifedipine or verapamil, have been used. Other treatment modalities include steroids. In many patients this condition RCVS generally self-limited and has a low incidence of recurrence.

7.6 Extracranial Causes of Headache

Many varying disorders outwith the head can result in the symptom of headache. Some are discussed here, others are discussed in the relevant chapters throughout this book. Pathophysiologically, many of these result in dilation and distension of the extracranial arteries supplying the surface tissues of the head, or sustained contraction of the skeletal muscles of the face, scalp, and neck. Excess fatigue, neck problems, and eyestrain can all cause extracranial headaches.

7.6.1 Temporal Arteritis (Giant-Cell Arteritis)

Temporal arteritis (Giant Cell Arteritis) is a vasculitic disease which predominantly affects patients over 60 years of age. It is the most common vasculitis in Caucasians and is commonly linked with polymyalgia rheumatica (see later). Both conditions

occur in the elderly and are associated with constitutional symptoms and a systemic inflammatory response. It is therefore an important diagnosis to consider in any elderly patient who presents with severe headache. Untreated, acute visual loss in one or both eyes is by far the most feared and irreversible complication of giant cell arteritis. The main blood supply affected is to the anterior optic nerve head via the short posterior ciliary arteries and that of the retina via the central retinal artery. Choroidal ischaemia can also occur due in inflammation of the short posterior ciliary arteries which supply this region.

Despite advances in molecular medicine and immunology, the initial events triggering the cascade of immune and inflammatory reactions responsible for giant cell arteritis remain unclear. The initiating step may be a response to an infectious agent by activated dendritic cells—many experience an initial flu-like illness, leading to the suggestion that temporal arthritis may be a complication of a viral infection, although no virus has ever been identified. Histologically there is a pan-arteritis, with giant cell granuloma formation in the internal elastic lamina. Intimal thickening results in reduced vessel diameter or even obliteration of the lumen and the vessels become enlarged and nodular. Involvement of the arteries is often patchy, with the term 'skip lesions' often used—this is an important feature to remember when undertaking temporal artery biopsy for diagnostic purposes. If the length of the vessel removed is too small the lesions will be missed.

Headache is the main symptom in more than 60% of patients. This is either a generalised 'tension' type or severe and localised over the temporal arteries. This is usually a sudden-onset, severe, localised pain in the temporal region, but it may affect the occipital region and is sometimes poorly localised. Jaw claudication on chewing is considered a variant of this and is thought to be due to involvement of the facial artery. There may also be weight loss, arthralgia and fever. The importance of this condition is the risk of sudden loss of sight which may occur within weeks of the first symptoms. This begins as a visual field disturbance, which becomes progressively worse. Features predictive of permanent visual loss include a history of amaurosis fugax, jaw claudication and a painful tender temporal artery. Amaurosis fugax is an important visual symptom because it precedes permanent visual loss in almost half of patients. Transient or permanent diplopia can also occur. The exact aetiology of ophthalmoplegia in giant cell arteritis is not known, although ischaemia of the extraocular muscles or cranial nerves has been postulated. Rare ocular symptom in giant cell arteritis include (i) tonic pupil, (ii) Horner syndrome and (iii) internuclear ophthalmoplegia. Visual hallucinations has also been reported in patients with cortical blindness secondary to occipital infarction.

There appears to be a relationship between giant cell arteritis and polymyalgia rheumatica. Both conditions affect elderly people and their genetic backgrounds are often quite similar. Both conditions are generally responsive to corticosteroids. Polymyalgia rheumatica is present in approximately 50% of patients with giant cell arteritis and approximately 10% of polymyalgia rheumatica patients develop giant cell arteritis. Giant cell arteritis generally affects medium and large sized arteries. Branches of the carotid arteries are the commonest sites of involvement, but the vertebral, meningeal and intracerebral vessels can be involved leading to

hemiplegia or epilepsy. All elderly patients presenting with unilateral headaches should be suspected of having this condition. Investigations include (i) ESR—erythrocyte sedimentation rate. This is usually markedly raised in excess of 90 mm/h in these patients. (ii) Temporal artery biopsy—in patients with a raised ESR, this will help to confirm the diagnosis. A common error is to take too small a biopsy. Skip lesions are separated by histologically normal tissues. It is therefore recommended that at least 3 cm of the temporal artery is taken. This is commonly accessed through an incision just in front of the ear, extending upwards into the temporal hair bearing skin. A negative biopsy (in a setting of otherwise typical features of giant cell arteritis) does not exclude the diagnosis of giant cell arteritis. Temporal artery histology may remain positive 2–4 weeks after start of glucocorticoid therapy.

Analogous to the UK's "Time is Brain" ACT-FAST campaign for stroke, "Time is Sight" has been proposed for giant cell arteritis. The main issues in management are urgent recognition and prompt institution of corticosteroid therapy. Early high-dose steroid treatment is essential for rapid symptom control and to prevent further visual loss as far as possible. Improvement in symptoms often begins within hours to days after commencing steroids. Initial high-dose intravenous methylprednisolone may be given if patients present with threatened vision. The dose can then be titrated against the ESR, and clinical response, but in some cases it may be necessary to continue treatment several months or even years followed by a gradually reducing dose. The British Society of Rheumatology guidelines recommend the following starting doses for steroids:

1. Prednisolone 40–60 mg daily for uncomplicated giant cell arteritis (no jaw claudication or visual disturbance)
2. Intravenous methylprednisolone 500–1000 mg for 3 days before oral steroids for evolving visual loss (recent onset of visual symptoms over 6–12 h) or amaurosis fugax (complicated giant cell arteritis)
3. Prednisolone 60 mg daily for established visual loss, to protect the contralateral eye

The initial high dose of steroids should be continued for 3–4 weeks and reduced in the absence of any clinical symptoms or normal laboratory results. Unfortunately, in some patients the disease can relapse, resulting in the need for long term steroids, or oral immunosuppressive agents (methotrexate, azathioprine).

7.6.2 Polymyalgia Rheumatica (PMR)

Polymyalgia rheumatica (PMR) is one of the most common rheumatologic conditions in older adults. It is an inflammatory condition that is a form of vasculitis. This is believed to be an autoimmune illness and is three times more common than giant cell arteritis, with which it seems to be associated. It is a condition of middle-aged/elderly patients and can start at any age from 50, but mainly affects people over the age of 60. Women are affected 2–3 times as often as men and it affects about 1 in 2000 people. The condition is characterised by painful

stiffness of the joints, which is often worse in the morning. Polymyalgia rheumatica causes aching and stiffness in selected muscle groups, predominantly in the neck, shoulders, upper arms, and pelvic girdle. Imaging studies have revealed inflammation of the bursae and periarticular structures. The interstitial fluids from painful muscles have also been shown to contain high cytokine levels. Typically, these myalgias are associated with heightened systemic inflammation, accounting for their markedly elevated levels inflammatory markers.

Symmetric proximal myalgias combined with laboratory abnormalities underlie the diagnosis of polymyalgia rheumatica. It often occurs suddenly, developing over several weeks, sometimes after a flu-like illness. Other symptoms include (i) systemic upset—weight loss, fever, fatigue, (ii) Malaise, (iii) Severe arthralgia with stiffness–usually bilateral and symmetrical and (iv) Elevated ESR. No diagnostic gold standard test exists for PMR, so clinicians have to rely on existing classification criteria, laboratory findings, and response to treatment to make a diagnosis. Patients typically have a raised erythrocyte sedimentation rate or C-reactive protein, but occasionally the inflammatory markers are normal. Although interleukin-6 is typically elevated in untreated patients, no specific biomarker exists. Alternative diagnoses such as myositis, infection, malignancy and endocrinopathies should be excluded. To complicate matters, around 50% of patients with giant-cell arteritis have symptoms of PMR, whereas 10% of patients with PMR have giant cell arteritis. Like giant-cell arteritis, polymyalgia rheumatica is responsive to glucocorticoids. This response to corticosteroids is considered an important diagnostic feature of PMR. Low–moderate doses of oral corticosteroids are highly effective. Once symptoms improve they can often be gradually reduced over months, but most patients require either prolonged or continuous treatment. Unfortunately corticosteroids cause disproportionate side effects in polymyalgia rheumatica compared to other rheumatic diseases. Steroid-sparing drugs such as Methotrexate may be used for relapsing disease. Leflunomide and tocilizumab are being investigated.

7.6.3 Glaucoma

This is discussed in detail in the chapter on the eye, but is noted here as symptoms often include severe headache. Patients may complain of pain in and around the eyes. It is therefore important to consider ophthalmic conditions in any elderly patient with unilateral headache, especially glaucoma.

7.6.4 Frontal/Ethmoidal Sinusitis

These sinuses are often affected together. Infection in either is a potentially serious condition due to the risk of intracranial infection. The frontal sinuses make up one of the four paranasal sinuses. They are formed by an upwards extension of the ethmoidal air cells, into which they drain. The frontal sinuses are absent

at birth, but become well developed by the age of 7, reaching their full size after puberty. In about 4% of the population they can be absent. The right and left sinuses form a cavity within the frontal bone, which is highly variable in size and shape and is rarely symmetric. The average sinus volume is approximately 6–8 mL.

Each sinus is lined by a ciliated mucus-secreting epithelium. Mucus drains towards the middle meatus of the nose via the frontonasal ducts (or frontal sinus drainage pathways [FSDP]). These ducts pass through the ethmoid sinuses via a variable pathway. This is important to remember when managing apparently isolated nasoethmoid fractures—It is around the drainage of the frontal sinus that classification, management, and complications of these injuries are based.

If free drainage of mucus from the frontal sinus is impaired, the mucus can stagnate forming a mucocele (Fig. 7.5) or an infection may occur, resulting in frontal sinusitis. Patients complain of frontal headache, which is tender to percussion.

Ethmoid sinusitis usually occurs in association with other sinus infections. Patients complain of a deep-seated throbbing pain, deep to the bridge of the nose, between the eyes. The medial orbital walls are thin, and therefore if this is not treated quickly orbital cellulitis can rapidly develop.

Frontal and ethmoid sinusitis often occur together. They share similar symptoms which include

- Headache/facial pain
- Sensation of dull, constant pressure over the affected sinus
- Symptoms are often made worse on bending, straining or lying down
- Nasal discharge
- Halitosis
- Post-nasal drip
- Pott's Puffy tumour—a rare clinical entity characterised by subperiosteal abscess associated with osteomyelitis. It is usually seen as a complication of frontal sinusitis or trauma predominantly in the adolescent age group (Fig. 7.6)

Untreated, infection in either sinus can spread intracranially or into the orbit (resulting in orbital cellulitis). Early sinusitis can be treated with antibiotics and decongestants. Ephedrine nasal drops and menthol inhalations may help reduce congestion and improve sinus drainage. However if there is a blockage to free drainage of the sinus this will need to be relieved surgically. Drainage can now be established endoscopically, often by ENT surgeons. Acute abscesses need urgent admission and surgical drainage.

7.6.5 Drug (Medication) Induced Headache

People who use pain-relief medicine more than two or three times a week or for more than 10 days out of the month can set off a cycle called 'medication-overuse headaches' (MOH). As each dose of medicine wears off, the pain comes back,

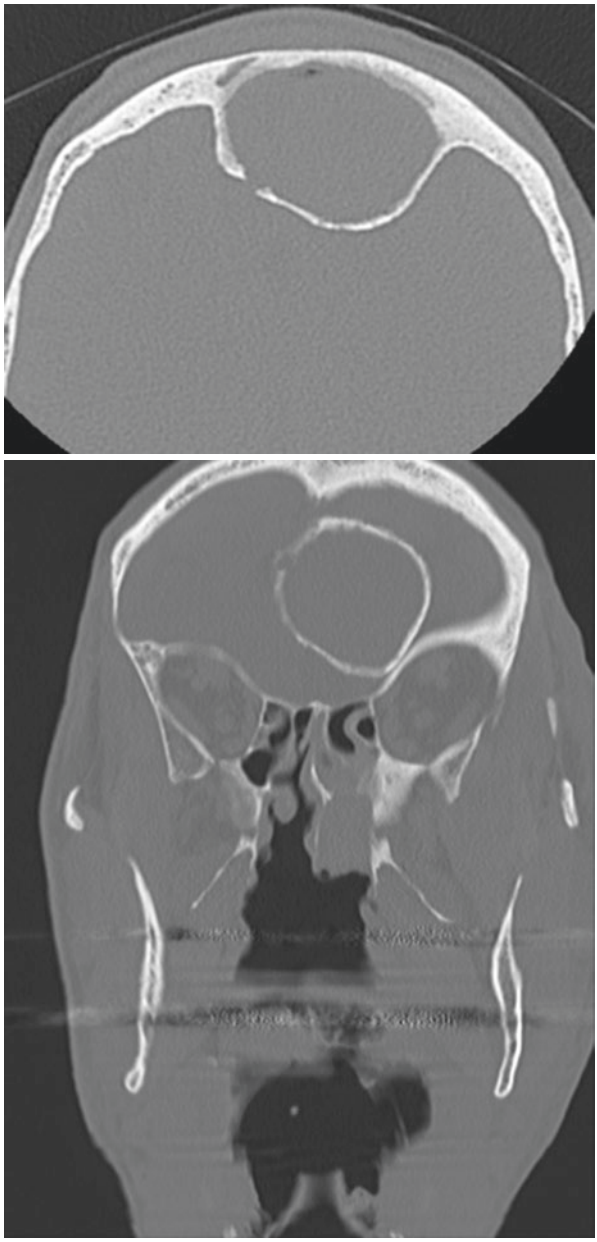

Fig. 7.5 Large frontal sinus mucocele following untreated facial trauma several years previously

leading patients to take more. MOH can occur with both over-the-counter and prescription medicines. They can occur whether used for headache or another pain. Many drugs, both prescribed and recreational can cause headaches among their side effects. Caffeine can result in severe pain, often first thing in the morning. Migraine sufferers are particularly vulnerable to a vicious cycle of pain

requiring increasing medication, which then triggers more pain. Medication should be slowly withdrawn. In some cases prednisone may help control pain during this period.

Long term codeine based analgesics can paradoxically cause headaches.

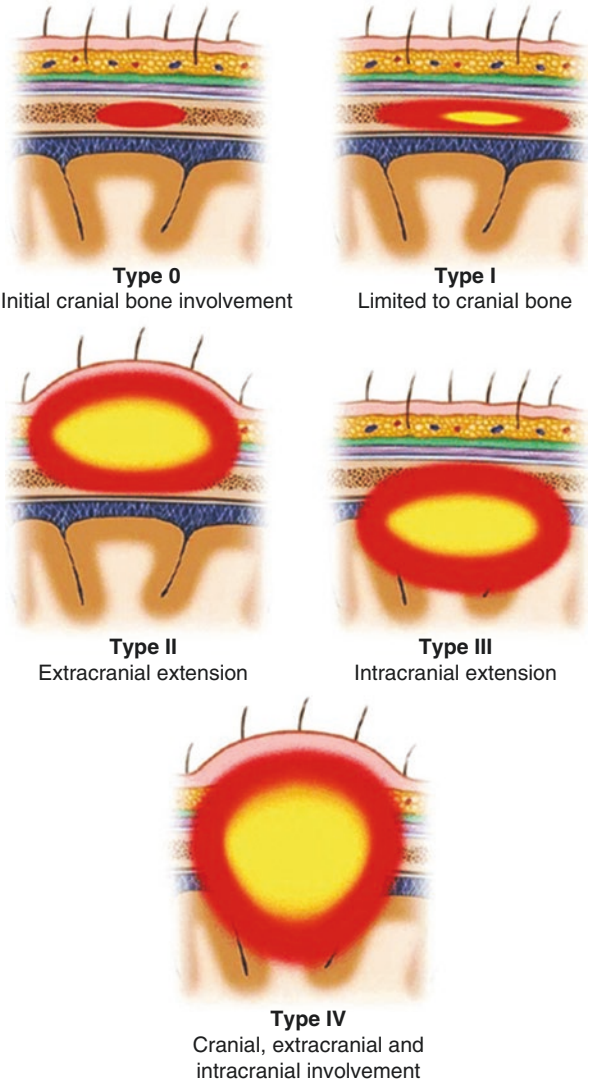

Fig. 7.6 Main topographic complications of Pott's puffy tumor, (**a**) Extracranial extension, (**b**) intracranial extension, and (**c**) orbital extension

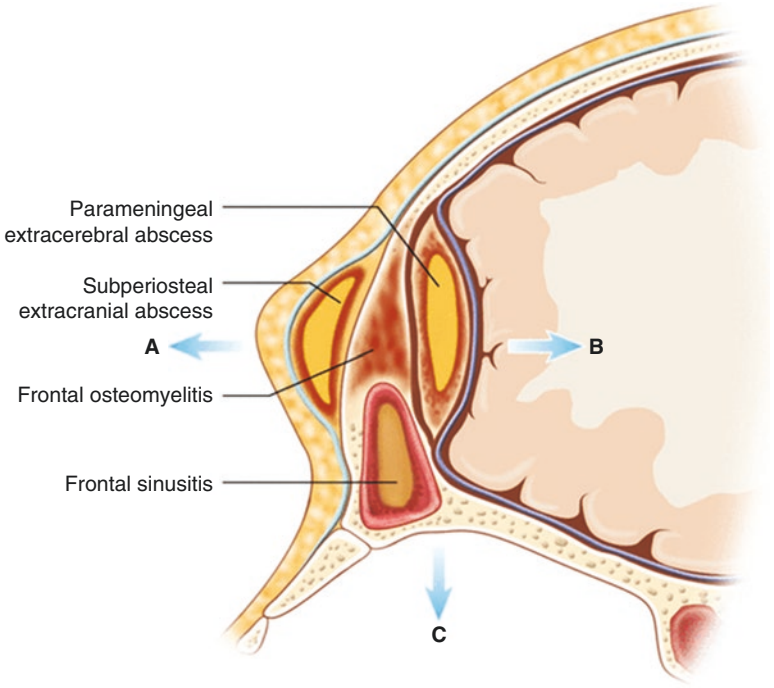

Fig 7.6 Continued

7.6.6 Ice Cream Headache

Cold stimulus headache, also known as ice cream headache, is a common problem and is reported to occur in about a third of a randomly selected population. This may be related to migraine, especially to active migraine sufferers. Patients develop sudden, sharp head pain within a few seconds of eating or drinking anything cold, which stimulates the palate. The pain usually lasts less than a minute and resolves completely. It is believed to result from either rapid constriction of the anterior cerebral arteries, or as a result of referred pain from the roof of the mouth to the head. Treatment is preventive (eat slowly).

7.6.7 Primary Sexual Headache (Coital Cephalalgia)

This is a rare type of severe headache commonly seen in young men. As the name suggests this occurs during or shortly after sexual activity. A pressor response to exercise has been suggested as a mechanism. The pattern of headaches can be variable. Typically they usually come on suddenly, with gradually worsening during

sexual intercourse, or they occur at the moment of orgasm. The headache is usually worsened by movement. It lasts for a few minutes to a few hours, although sometimes it can last up to a few days. Attacks may be mild or severe. The differential diagnosis is SAH as this can be precipitated by coitus in patients. Management includes avoiding/reducing activities which precipitate symptoms. Propranolol, Indometacin and Calcium-channel blockers (e.g. diltiazem) may help.

7.6.8 Ice-Pick Headaches (Jabs and Jolts Syndrome)

Ice-pick headache (IPH), also named as "primary stabbing headache" is characterised by a stabbing, momentary headache attack lasting seconds, being repetitive and transient. It has a female dominance. Stabbing pains are more dominant in the branches of trigeminal nerve such as orbital, temporal, and parietal regions. Although the exact mechanism in the pathophysiology of IPH is unknown, irritation of the trigeminal or other nerves has been suggested as a possible mechanism. It is often responsive to indomethacin.

7.7 Spontaneous Intracranial Bleeding

The term 'cerebrovascular disease' includes all disorders that result in damage to the blood vessels to the brain, often culminating in neurologic impairment. Many of the underlying causes are asymptomatic and can remain dormant for years. Crudely speaking either a blood vessel can rupture resulting in intracranial haemorrhage, or it can become blocked off resulting in an embolic stroke. It is important to differentiate between the two as soon as possible as treatments can differ. "Stroke" and "cerebrovascular accident" (CVA) are commonly used terms to describe any acute neurological injury resulting from a sudden and often severe interruption in the blood supply to the brain. The brain is very sensitive to hypoxia and therefore any significant interruption can result in irreversible infarction in less than 4 min. Cerebrovascular disease is the third leading cause of death in developed countries. The majority of patients are over 60 years of age. Symptoms are variable and include paralysis, sensory loss, visual difficulties, and speech impairment.

7.7.1 Subarachnoid Haemorrhage (SAH)

Subarachnoid haemorrhage following trauma is described in the section on head injuries. Most cases of SAH are due to this. Spontaneous subarachnoid haemorrhage is a separate entity, which can also occur. Approximately 80% of these are the result of bleeding from an intracranial saccular aneurysm. These are sometimes referred to as Berry aneurysms (Fig. 7.7). An aneurysm is a localised dilatation of an artery, caused by a localised weakness or defect within the vessel wall. In the case of Berry aneurysms, these typically occur on the vessels that make up the circle of Willis and their walls lack an external elastic lamina and contain a very thin adventitia. The aneurysm is thought to expand as a result of hydrostatic pressure

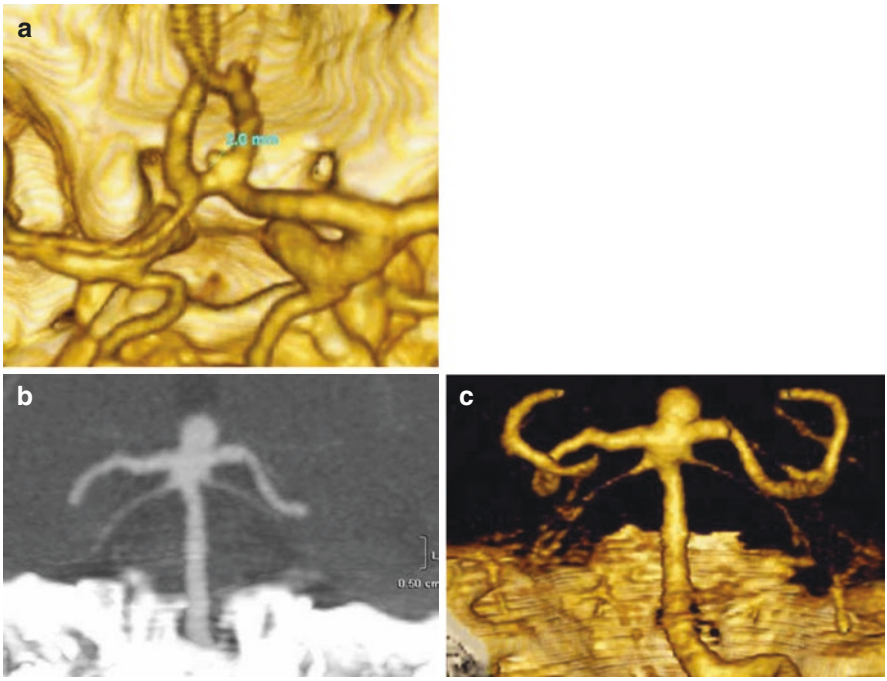

Fig. 7.7 (**a**) Anterior communicating artery aneurysm. A small, 2-mm anterior communicating artery aneurysm is well visualized in this patient with prior subarachnoid hemorrhage (SAH) and "negative" cerebral angiography. (**b**) Basilar tip aneurysm on CT angiography with reconstruction (**c**)

from the pulsatile blood flow together with turbulence, which occurs at the arterial bifurcations. A mature aneurysm has a paucity of media, replaced by connective tissue, and has diminished or absent elastic lamina.

Aneurysms are anatomically divided into a neck, body and fundus. The fundus is composed of tunica adventitia and intima only, with no tunica media or internal elastic lamina. This is where they usually rupture. Aneurysms tend to occur at branching points and along the curves of vessels. The size of the aneurysm is important in determining its likelihood of rupture. Elsewhere, so-called 'true' aneurysms may occur in arteries whose walls have been damaged by conditions such as atherosclerosis, mycotic infections and syphilis. 'False' aneurysms can occur after traumatic rupture of an artery and its subsequent repair by fibrous tissue.

Most aneurysms remain asymptomatic and are incidentally found in up to 2–3% of routine post-mortems. However aneurysmal SAH can result in major morbidity and mortality. When the cerebral aneurysm ruptures, blood leaks into the subarachnoid space, sometimes seeping into brain parenchyma and/or ventricles (Fig. 7.8). This can result in a sudden increase in intracranial pressure. This increase, plus the destructive and toxic effects of blood on brain parenchyma and the cerebral vessels, accounts for most complications. Smoking, a strong family history and hypertension are known risk factors. Some hypertensive states (such as those induced by cocaine abuse and other stimulants), promote aneurysm growth and early rupture. In around 15% of

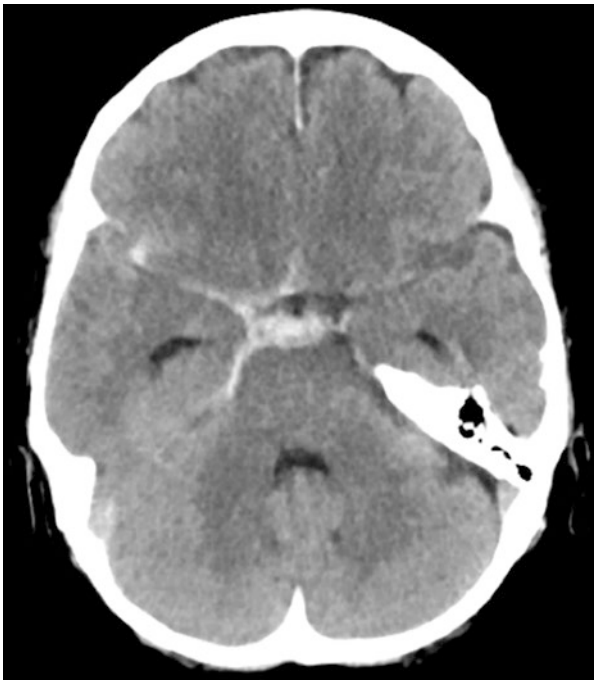

Fig. 7.8 Subarachnoid haemorrhage in basal cisterns

subarachnoid haemorrhages, no cause can be found. Cocaine abuse, sickle cell anaemia, anticoagulant therapy, clotting problems and pituitary apoplexy have all been reported to cause this. In the remaining 5%, causes include arteriovenous malformations (AVMs).

Symptoms following rupture of an aneurysm are usually sudden and severe. However in some patients Sentinel leaks or 'warning headaches' are thought to occur as a result of minor leaks of blood from the aneurysm. Patients develop similar, but less severe symptoms, commonly sudden focal or generalised pain that may still be significant. They can also complain of neck pain, nausea, vomiting and photophobia.These symptoms may precede aneurysm rupture by a few hours to a few months and are therefore important early warning signs. Without treatment rupture of an aneurysm will eventually occur. Occasionally symptoms can occur in the absence of rupture. Instead, pulsatile compressive forces can cause injury to local tissues and/or compromise of distal blood supply (mass effect). Depending on their location an expanding aneurysm can result in characteristic signs

1. Posterior communicating artery/internal carotid artery—retro-orbital pain and oculomotor nerve palsy
2. Middle cerebral artery: contralateral paresis (hand and face), aphasia, contralateral visual neglect
3. Anterior communicating artery: bilateral leg paresis and bilateral Babinski sign

4. Basilar artery: vertical gaze, paresis
5. Vertebral artery/posterior inferior cerebellar artery: vertigo

Following rupture, an estimated 10–15% of patients die before reaching the hospital, whist approximately 25% of patients die within 24 h, with or without medical attention. Historically, up to 50% of patients with aneurysmal subarachnoid haemorrhage (SAH) die within a month of the initial bleed. Current mortality is around 30%. Untreated, the re-bleed rate approaches 50% after 1 month and 80% of these patients will die or become dependent. It is therefore vital to confirm the diagnosis quickly and treat the aneurysm to prevent the risks of re-bleeding and mortality. With AVMs, the risk of re-bleeding is much less—around 6% in the first year and 3% for each subsequent year. Treatment of these, which can be complex, can therefore be delayed and planned.

Irrespective of the cause, acute bleeding into the subarachnoid space presents with the following symptoms and signs.

1. 'Thunder clap' headache—usually the patient develops a sudden severe agonising occipital headache radiating over the head and down the neck. This is often described as being similar to a sudden blow to the head, resulting in a blinding pain unlike anything experienced before
2. Impaired conscious level
3. Neck stiffness. Symptoms of meningeal irritation (nuchal rigidity, back pain, bilateral leg pain), occur in up to 80% of patients with SAH. This may take several hours to develop.
4. Photophobia
5. Nausea or Vomiting
6. Seizure. SAH in a person known to have seizures may suggest an arteriovenous malformation.
7. Focal neurologic deficits. In addition to parenchymal haemorrhage (middle cerebral artery aneurysm), emboli originating from the thrombus can cause transient ischaemic attacks.
8. Cranial nerve palsies occur in 25% of patients. The most frequent is oculomotor nerve palsy (affected eye looking downward and outward with inability to lift the eyelid) which may indicate bleeding from the posterior communicating artery. Abducens nerve palsy may indicate increased ICP. Rarely, loss of vision can be caused by an ophthalmic artery aneurysm compressing the ipsilateral optic nerve.
9. Visual loss (rare)
10. Retinal haemorrhages (Terson Syndrome) and papilloedema may be seen on fundoscopy

All patients presenting with a sudden-onset headache should be investigated for SAH, even if the headache has improved. Unfortunately, 'thunderclap' headaches are non-specific and less than 25% of patients presenting with this symptom in isolation will actually have a SAH. Diagnosis thus requires a high index of suspicion

and radiologic confirmation (urgent non-contrast CT). A negative CT scan must be followed by a lumbar puncture if concerns remain regarding diagnosis. CSF is analysed by spectrophotometry. Timing is important. If samples are taken too soon, the CSF can be normal. This is because bilirubin will not have been produced from the dissolution of the blood. LP should therefore **not** be performed within 12 h of the onset of headache.

Today, CT can rule out SAH with reported sensitivity of around 99%. CT scan should be undertaken as soon as possible. Any delay reduces the diagnostic rate as the blood lyses. Once SAH has been confirmed, CT angiography or cerebral catheter angiography is performed to determine the cause. Often CT angiography is the first line investigation to look at the intracranial vessels (Fig. 7.9).

Laboratory studies include:

1. FBC—to assess for possible infection or haematological abnormality
2. Serum biochemistry—a baseline to detect ongoing complications
3. Clotting studies (Prothrombin time (PT) and activated partial thromboplastin time (aPTT))—to assess for possible coagulopathy
4. Blood typing
5. Arterial blood gas (ABG)
6. MRI has been reported as a useful modality in the diagnosis of AVMs or cavernomas that have not been identified on cerebral angiography. It can also be used to diagnose and monitoring unruptured cerebral aneurysms. MRI can detect aneurysms 5 mm or larger and may be used to follow up small, unruptured aneurysms

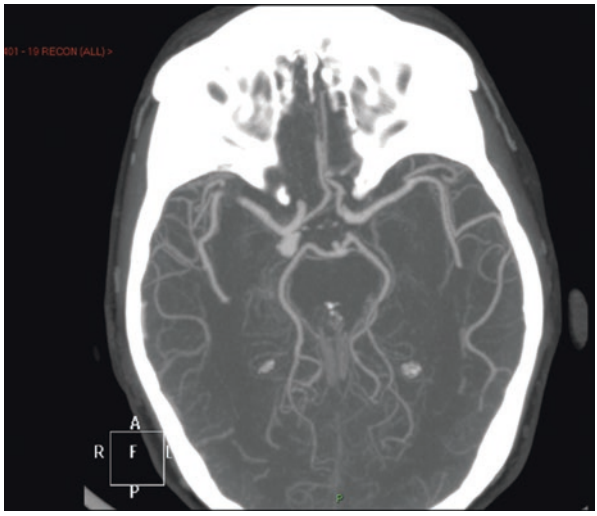

Fig. 7.9 Internal carotid artery bifurcation aneurysm

Modified World Federation of Neurological Surgeons (WFNS) Grading System for SAH

Grade	Clinical condition
1	GCS 15
2	GCS 14
3	GCS 13
4	GCS 7–12
5	GCS 3–6

This is an important grading system. Generally speaking the prognosis for recovery is poorer with increasing grade.

The Fisher scale (CT scan appearance) is another useful grading system:

Group 1—No blood detected

Group 2—Diffuse deposition of subarachnoid blood, no clots, and no layers of blood greater than 1 mm

Group 3—Localised clots and/or vertical layers of blood 1 mm or greater in thickness

Group 4—Diffuse or no subarachnoid blood, but intracerebral or intraventricular clots are present.

Management of subarachnoid haemorrhage varies, depending on the underlying cause of the bleeding and the extent of damage to the brain. Treatment may involve initial lifesaving measures, symptom relief, repair of the bleeding vessel and treatments of complications. For the first 10–14 days following SAH, patients may be managed in a specialist ward, or ideally a stroke unit or intensive care unit. Treatment involves.

1. Resuscitation with IV fluids. Euvolemia should be maintained and carefully managed, without over hydrating. Whilst it is important that the tissues are optimally perfused for recovery, at the same time hypertension must be avoided. If the mean arterial pressure rises above 130 mm Hg, there is a significant increased risk of further bleeding.
2. Hypertension should be treated only if mean arterial pressure is >130 mm Hg. IV nicardipine is titrated according to the response.
3. Oral nimodipine. For the first 10 days following subarachnoid haemorrhage, patients are at risk of intense vasospasm. Nimodipine reduces this risk and accompanying ischaemic complications. Dosage needs to be balanced against the patient's BP (which ideally should be between a mean arterial pressure of 70–130 mm Hg) and a systolic pressure of 120–185 mm Hg. It limits vessel spasm that can occur in response to the haemorrhage.
4. Analgesics and anti-emetics are prescribed. Bed rest is essential to avoid sudden increases in BP. Restlessness and headache are treated symptomatically as necessary. Stool softeners are given to prevent constipation, which can lead to straining.

5. Anticoagulants and antiplatelet drugs are contraindicated.
6. If clinical signs of acute hydrocephalus occur, drainage of CSF should be considered. Excess fluid and blood can be removed using either a lumbar drain inserted into the subarachnoid space of the spinal canal, or a ventricular drain catheter, which is inserted directly into the ventricles.
7. If a cerebral aneurysm is identified on angiography, this can be occluded by either surgical clipping or endovascular techniques to reduce the risks of rebleeding. In many centres today, endovascular coils can be inserted through minimally invasive angiography to occlude the aneurysm. Alternatively, if the aneurysm is accessible surgically, a clip may be placed around it's neck. This however it requires extensive surgery, which is not without risk. The decision as to which treatment is undertaken is usually made by a multidisciplinary team consisting of a neurosurgeon, neuroradiologist, and other health professionals. An important consideration in deciding between clipping and coiling is the location of the aneurysm, its size and the status of the patient. Aneurysms of the middle cerebral artery and its related vessels can be technically difficult to reach endovascularly and are amenable to clipping. Those of the basilar artery and posterior cerebral artery are hard to reach surgically but are more accessible for endovascular techniques. If surgery is indicated, many neurosurgeons prefer to operate within the first 24 h to minimise risk of rebleeding and other complications. After 24 h surgery may be deferred until 10 days have passed. This allows for any cerebral oedema to settle, although there is a risk of further bleeding during this period.
8. In some cases AVMs may be excised, embolised, or treated with high dose, localised radiation (stereotactic radiosurgery). Radiosurgery results in gradual obliteration over several years.
9. If no structural cause is found following angiography, the patient can be reassured that they are not at risk of further bleeds.

7.8 Complications of SAH

SAH is a complex disease that can involve multiple types of neurological injury and systemic organ dysfunction. Well-established risk factors for mortality include poor clinical grade at presentation, older age, aneurysm rebleeding, large aneurysm size and cerebral infarction from vasospasm. Vasospasm, the direct effects of the primary haemorrhage and rebleeding are the most frequent causes of mortality. Cerebral oedema, intraventricular haemorrhage and medical complications also contribute to poor outcomes. Despite advances in medical and surgical management, SAH remains a major cause of premature mortality. Recovery and prognosis are highly variable and largely dependent on the severity of the initial SAH. In general, one-third of patients will survive with good recovery; one-third will survive with a disability or stroke; and one-third will die. Complications include

1. Intracerebral haemorrhage (ICH). This can occur following direct rupture of aneurysm into the brain parenchyma. This commonly occurs with internal cerebral artery (ICA), pericallosal and anterior cerebral artery (ACA) aneurysms.

Secondary rupture of a subarachnoid haematoma into the brain can also occur later. Intraventricular haemorrhage has been reported in up to one third of patients. This is a significant predictor of poor neurological outcome. Subdural haematoma (SDH) is rare following aneurysmal SAH, possibly as a result on tearing of the arachnoid at the dome of the aneurysm and bleeding into the subdural space.

2. Vasospasm. Delayed cerebral ischaemia (DCI) is the most important and preventable morbidity cause after subarachnoid haemorrhage. Blood is an irritant and following a subarachnoid haemorrhage the surrounding vessels can go into intense vasospasm. This can lead to impaired cerebral autoregulation and may progress to cerebral ischaemia and infarction. Often, the terminal internal carotid artery or the proximal portions of the anterior and middle cerebral arteries are involved. Severe cerebral ischaemia can be fatal in 15% of patients. At day 7, up to 70% of patients will have angiographic vasospasm, although this is only clinically manifest in 20–30%. The pathophysiology is not completely understood but the risk is increased following a heavy bleed. In patients who develop vasospasm, hypertensive therapy is often instituted when the aneurysm is secured. This involves an inotrope infusion. If delayed ischaemia does not improve with medical treatment, angiography may be attempted to identify the sites of vasospasm and intra-arterial nimodipine is administered directly into the artery. Continuous EEG (cEEG) has been reported as a possible way to monitor patients for delayed cerebral ischaemia (DCI) and seizures
3. Hydrocephalus. This occurs in about one quarter of patients. Blood in the CSF can result in hydrocephalus by 2 mechanisms: (i) immediate obstruction to the CSF outflow through the sylvian aqueduct, fourth ventricular outlet, basal cisterns, and subarachnoid space (acute, obstructive, noncommunicating type) and (ii) scarring of the arachnoid granulations (delayed, nonobstructive, communicating type). Intraventricular blood is a high risk factor in the development of acute hydrocephalus. A ventriculo-peritoneal shunt may be required.
4. Rebleeding. This can occur in about 20% of patients, usually in the first 2 weeks. Rebleeds in the first few days are thought to be related to an unstable thrombus, later bleeds occur from lysis of the clot. Hypertension, agitation and seizures make rebreeding more likely.
5. Seizures have been reported in 5–10% SAH patients.
6. Electrolyte disturbances. Low sodium can occur as a result of 'cerebral salt wasting'—that is, the development of extracellular volume depletion due to a renal sodium transport abnormality (in patients with intracranial disease and normal adrenal and thyroid function). This rare phenomenon can also occur in head injuries. It is treated by adding sodium orally or intravenously using 1.8% saline. Fluid restriction is dangerous as this may precipitate vasospasm.
7. Myocardial infarction. ECG rhythm changes can occur in >50% of SAH patients. Troponin elevations may also occur. Left ventricular systolic dysfunction is associated an abnormal sympathetic innervation, possibly following excessive release of norepinephrine from the cardiac sympathetic nerves.

8. Pulmonary oedema can occur as a result of the sympathetic discharge following SAH and a raised ICP.
9. In those patients that survive, varying degrees of neurological deficit may persist. These include (i) Speech and language deficits and limb weakness, (ii) visual problems (iii) seizures, (iv) fatigue (v) headaches and problems with higher cerebral functions (short-term memory loss, loss of concentration, changes in perception and personality)

7.8.1 Spontaneous Intracerebral haemorrhage (ICH): Cerebrovascular Accident, or Stroke

The term "cerebrovascular disease" includes all disorders that result in damage to the blood vessels supplying the brain, thereby producing neurologic damage. "Stroke" and "cerebrovascular accident" (CVA) are used to describe an acute neurologic injury resulting from a severe interruption in the flow of blood to the brain. Complete cessation of the flow may render an irreversible cerebral infarct within a period of 3 or 4 min. General symptoms following stroke include variable motor paralysis, sensory loss, visual difficulties, and speech impairment.

Approximately 80% of strokes are associated with atherosclerosis, which leads to embolism, cerebral ischaemia and infarction. Deposition of atheromas in arterial walls predisposes the patient to the development of thrombosis and embolus formation, which can result in infarction of the area of the brain supplied by the occluded vessel. The remaining 20% of cases are caused by cerebral haemorrhage following rupture of a vessel. Clinically these are indistinguishable and it is only following imaging (CT) that the underlying cause can be determined. Nevertheless the distinction between 'haemorrhagic' stroke and 'ischaemic' or 'embolic' stroke is important as treatment differs. Computed tomography (CT) is commonly used in the urgent diagnosis of acute cerebral infarction. With the use of thrombolysis, early signs of ischaemia must be reliably identified, to correctly select patients eligible for thrombolytic therapy or clot removal.

7.8.2 Ischaemic Stroke

Carotid atheroma predisposes patients to thrombosis and cerebral embolus, with infarction of the tissues supplied by the occluded vessel. Atheroma commonly develops in the branching portions of the arterial system, notably at the origin of the internal carotid artery. If this is identified, early referral to a vascular surgeon maybe indicated. Other important sites of thrombus formation include the vertebral, basilar, and middle cerebral arteries. Lacunar infarcts are small lesions that occur in the basal ganglia, pons, cerebellum, internal capsule, and deep cerebral white matter. These are associated with hypertension and diabetes and may be occasionally picked up on CT. Symptoms of lacunar infarcts include unilateral motor or sensory

deficit which may progress over 24–36 h. If these are identified and treated early the prognosis is generally good, often with partial or complete resolution of symptoms over the following 4–6 weeks.

Cerebral infarction usually occurs following ischaemic necrosis in one of the cerebral hemispheres as a result of embolism. Thrombosis within an intracranial vessel may also result in stroke. The resulting neurological deficit depends on the particular vessel involved and the extent of any collateral circulation. Carotid artery atherosclerosis, for example, commonly result in infarction in that part of the brain supplied by the middle cerebral artery. This results in contralateral signs such as facial weakness, flaccid hemiparesis and hemisensory loss. Cerebral infarction can also occur as a complication of other diseases. Emboli can arise from thrombi that have formed in the left side of the heart (following myocardial infarction, atrial fibrillation, or rheumatic heart disease). Hypertension is an important risk factor in the development of thrombosis, particularly at the carotid bifurcation. It has been estimated that the risk of stroke increases approximately sevenfold in patients who have uncontrolled hypertension. Septic emboli are relatively uncommon but may be seen following bacterial endocarditis, particularly when the mitral valve has been involved. Rarer causes of ischaemic stroke include severe hypotension, thrombocytosis, anaemia and cavernous sinus thrombosis.

Stroke caused by embolism develops suddenly. It is usually not preceded by transient ischaemic attacks, but rather the stroke evolves rapidly when a clot suddenly obstructs a cerebral vessel. The resultant infarct may subsequently enlarge over several days as a result of cerebral oedema. These strokes are sometimes referred to as either ‘stroke in evolution’ or ‘completed’. Stroke in evolution indicates that the symptoms are still progressing and as such there is to some extent a potentially reversible element. This should therefore be regarded as a medical emergency. Treatment should commenced immediately. This involves

1. controlling severe hypertension (>185/110). Decreasing mild hypertension may increase infarction in a patient with acute thrombosis, as this may reduce cerebral perfusion.
2. Urgent CT to distinguish ischaemic from haemorrhagic stroke.
3. Thrombolytic agents may decrease the severity of a stroke in carefully selected patients. However any coexisting intracranial haemorrhage is a contraindication to thrombolysis.
4. Endovascular clot retrieval has recently been shown to improve survival and outcomes in selected patients.
5. Anticoagulants (such as heparin) or antiplatelet therapy with aspirin may also be used. Low doses of aspirin taken daily is recommended to decrease the incidence of thromboembolic strokes.

A completed stroke evolves slowly and the full extent of any neurological deficit may take hours or days to emerge. This commonly includes hemiplegia, aphasia, and hemisensory loss as well as speech and swallowing difficulties. Any recovery is dependent on a good collateral circulation. Significant clinical improvement may occur after

3 weeks, when the cerebral oedema has subsided. After a completed stroke, treatment focuses on the prevention of further neurologic damage, through the reduction of underlying risk factors and rehabilitation, including speech and physical therapy.

7.8.3 Cerebral Haemorrhage

Intraparenchymal haemorrhage (IPH) is one form of intracerebral bleeding in which there is bleeding within the brain parenchyma. Bleeding into the ventricles—intraventricular haemorrhage (IVH), can also occur. The commonest cause is hypertension. Bleeding disorders, arteriovenous malformations (AVMs), aneurysms, tumours, and venous hypertension secondary to central venous thrombosis, can also result in intracerebral haemorrhage. Clinically these may all present with signs and symptoms indistinguishable from ischaemic stroke. Urgent imaging is therefore essential (Figs. 7.10 and 7.11).

Clinical features include the following, but not all may be present:

- Headache
- Loss of consciousness
- Focal neurological deficit—if present, the nature of this can often be used to determine the site of the haemorrhage.

Causes of intracerebral bleeding include

1. Hypertension
2. Arteriovenous malformation (Fig. 7.12)
3. Aneurysm rupture
4. Trauma
5. Intracranial neoplasm
6. Coagulopathy
7. Sympathomimetic drug abuse eg cocaine, amphetamines
8. Sickle cell disease
9. Eclampsia or postpartum vasculopathy
10. Infection
11. Vasculitis
12. Neonatal intraventricular haemorrhage
13. Cerebral amyloid angiopathy

In younger patients, vascular malformations (AVMs) are more common. In the elderly, hypertension and amyloid are more common. Cerebellar strokes are uncommon. Patients present with ataxia, ipsilateral facial weakness, gaze paresis, miosis, and decreased level of consciousness. A potential complication of this type of stroke is obstructive hydrocephalus due to compression of the fourth ventricle.

Initial management of a stroke patient commences with resuscitation with IV fluids. Intracranial haemorrhage should be treated as a medical emergency and

may require airway protection with transfer to an intensive care unit. The blood pressure should be maintained at around 140/90. Clotting studies are urgently requested. An urgent CT scan is then required to distinguish between ischaemia and haemorrhage. One of the early CT signs is the loss of gray-white matter interface. CT should be performed as soon as possible after the onset of symptoms, especially if the patient is unconscious or SAH is a possibility. Lumbar puncture in confirmed stroke victims is unnecessary and potentially dangerous. Angiography might also be performed, especially if a clot is close to the Circle of Willis or

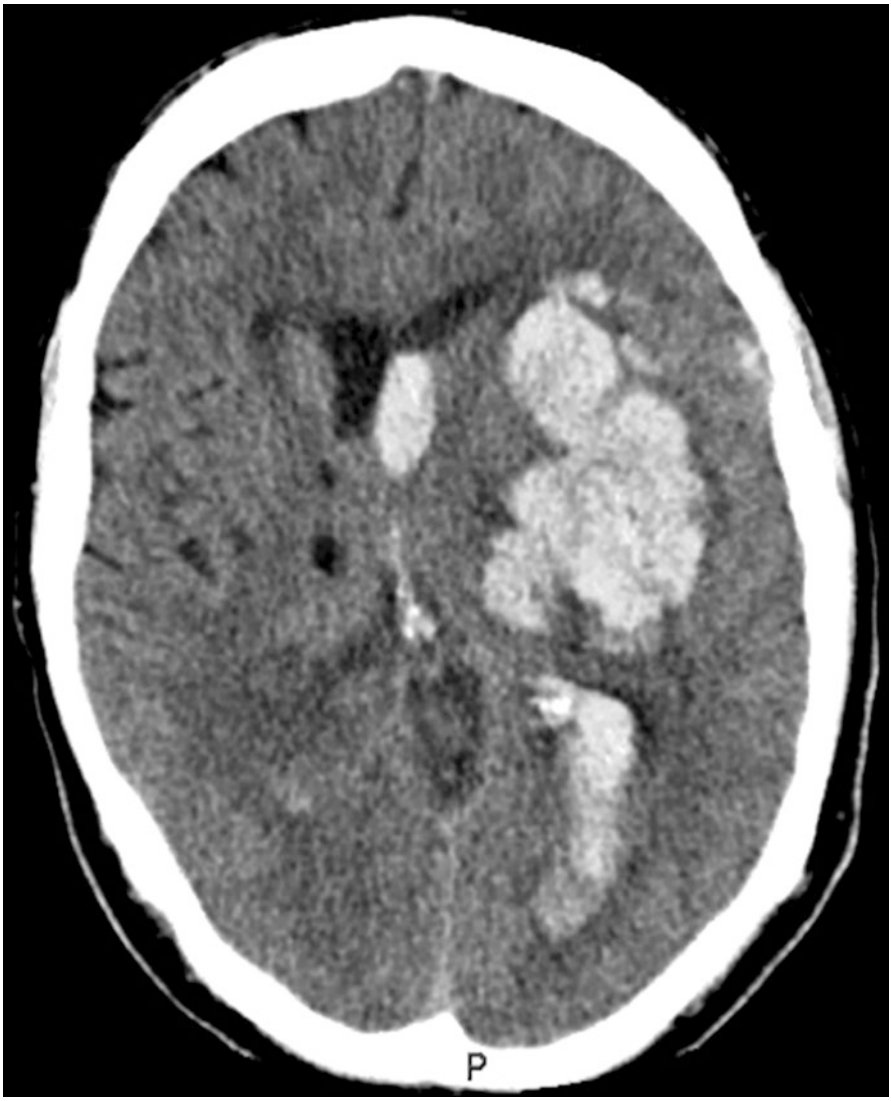

Fig. 7.10 Haemorrhage due to hypertension

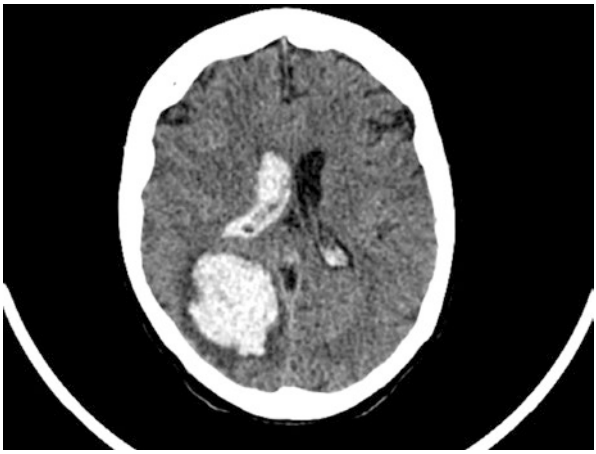

Fig. 7.11 Intracerebral haemorrhage due to AVM

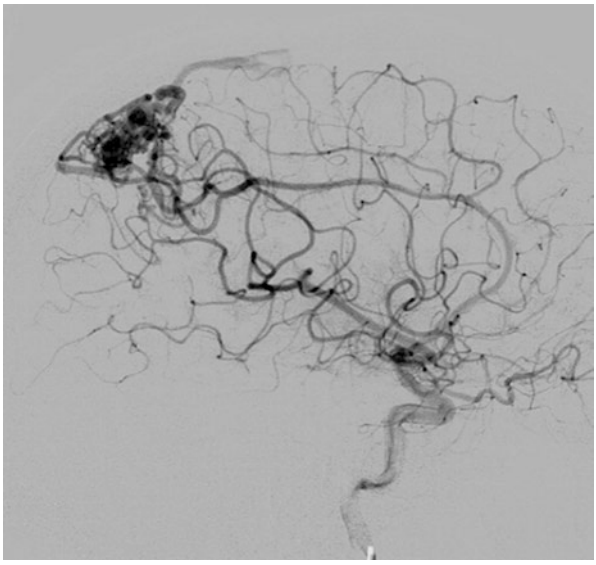

Fig. 7.12 Catheter angiography of occipital AVM

Sylvian Fissure, (indicating a possible aneurysmal cause), or in a younger non-hypertensive patient (suggesting a possible AVM), or if surgical evacuation is being considered. In severe cases neurosurgery may be required (craniotomy and clot evacuation) if the patient is deteriorating due to a raised ICP and the clot is superficial. Deep seated haematomas are not amenable to evacuation eg basal ganglia or thalamus. In those patients that survive, stroke rehabilitation will be necessary. Carotid duplex will also be required later if the patient makes a good recovery. This helps determine whether there is any atherosclerosis of the carotid arteries and further risk.

7.8.4 Intraventricular Haemorrhage

This is bleeding into the brain's ventricular system. It can occur secondary to significant trauma or as part of a stroke. About one third of cases are primary and confined to the ventricular system. These are commonly caused by trauma, aneurysm, vascular malformations and tumours. The remaining two thirds are secondary, arising from an intraparenchymal or subarachnoid haemorrhage. Symptoms are similar to other causes of stroke and include the sudden onset of headache, nausea and vomiting, together with an alteration in the mental state and/or level of consciousness. Focal neurological signs are usually minimal or absent. Diagnosis is confirmed on CT with the presence of blood inside the ventricles. Generally speaking, the prognosis is usually poor when IVH occurs as a result of intracerebral haemorrhage, especially if hypertension coexists and hydrocephalus develops. Intraventricular blood can block the flow of CSF, resulting in obstructive hydrocephalus. This will quickly result in raised intracranial pressure and death unless treated. This type of haemorrhage is common in premature infants or those of very low birth weight. If appropriate, management focuses on the treatment of any underlying causes and monitoring and control of the intracranial pressure via an intraventricular catheter and medication.

7.8.5 Transient Ischaemic Attack (TIA)

A transient ischaemic attack (TIA) is a sudden but transient and reversible neurological deficit that lasts from a few minutes to up to 24 h. It is caused by temporary ischaemia of the brain, spinal cord or retina. However this is not severe enough to result in infarction. TIAs generally have the same underlying cause as strokes which result in a disruption in the cerebral blood flow. As such, they are sometimes referred to as 'mini-strokes'. The severity of TIA varies considerably, from multiple daily attacks over an prolonged period, to a few attacks shortly before a fully blown stroke occurs. Approximately one third of patients with a history of TIA will ultimately go on to develop a stroke within the next 5-years. Diagnosis is therefore important to allow preventive measures to be instituted.

TIAs occur as a result of small (often platelet) emboli. The source of these may be an atherosclerotic plaque in the heart, aorta or internal carotid artery. Haematological causes include polycythemia, sickle cell disease, and other conditions resulting in hyperviscosity of the blood. Risk factors include a family history of stroke or TIA, age >55, male sex, high blood pressure, diabetes and smoking.

Treatment of TIAs should be initiated as soon as the diagnosis is established. However it is not always immediately possible to tell the difference between a small CVA and a TIA. Most patients are therefore usually investigated and admitted as stroke patients, until TIA has been diagnosed. Treatment should initially be directed towards the correction of the immediate problem, with prevention of further episodes. Any

predisposing medical conditions should be treated, notably hypertension, diabetes and any coagulopathy. Anticoagulant therapy is often used, but there is little convincing evidence that anticoagulant drugs are of value in the acute stages. Treatment with aspirin or clopidogrel however, significantly reduces the risks of future TIAs and stroke in high-risk patients. According to local protocols, patients should be referred to a vascular surgeon for consideration of endarterectomy if they are found to have carotid stenosis.

7.8.6 Locked-in Syndrome (LIS)

This is a condition in which there is complete paralysis of nearly all voluntary muscles in the body except for the eyes. Unfortunately, the patient is still completely aware of their surroundings but cannot move or communicate. In some cases the eyes are also paralysed. This condition is also known as cerebromedullospinal disconnection or pseudo-coma. Causes include:

- Poisoning/neurotoxins
- Motor neurone disease/Amyotrophic lateral sclerosis (Lou Gehrig's disease)
- Brainstem stroke
- Multiple sclerosis
- Rapid correction of hyponatremia
- Traumatic brain injury
- Lesions in the brain-stem

In children, the most common cause is a stroke of the pons. Diagnosis can be very difficult. Patients present with quadriplegia and an inability to speak. Only blinking or moving their eyes maybe possible. Locked-in syndrome may therefore mimic loss of consciousness and if respiration is affected it can even resemble death. Imaging is required to exclude other causes. If suspected, EEG can indicate that the patient is not unconscious. Treatment is generally supportive and the prognosis is often very poor. It is extremely rare for any significant motor function to return.

7.8.7 Pituitary Apoplexy

Pituitary apoplexy is bleeding into the pituitary gland. This usually occurs when there is a tumour present. Sheehan's syndrome (Simmond's syndrome or post partum pituitary necrosis) is another form of pituitary gland necrosis which can occur following hypovolaemic shock during childbirth (the gland is hyperpastic during pregnancy with an increased blood supply and is therefore sensitive to ischaemia). In both cases there is major disruption to the blood supply to the pituitary gland resulting in hypopituitarism.

In pituitary apoplexy patients present with sudden onset of headache, which may be associated with a rapidly worsening visual field defect and/or ophthalmoplegia. This is followed in many cases by the symptoms of adrenal insufficiency (Addisonian

crisis), with hypotension, hypoglycaemia and low cortisol levels. Diagnosis is made following CT or MRI and blood tests. These include a complete blood count, urea and electrolytes (notably sodium and potassium), liver function tests, coagulation testing, and a hormonal panel (growth hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone, thyroid hormone).

Prolactin is particularly important as prolactinomas will often respond rapidly to medical therapy and do not require surgery.

Initial urgent treatment requires intravenous fluids and correction of hormone deficiencies (particularly cortisol). Patients are usually very unwell and will require admission and intensive management. Following recovery, the patient will require follow-up by an endocrinologist to monitor long-term consequences. Long-term hormone supplementation is usually required.

7.9 Intracranial and Related Infections

Many intracranial infections present with similar features. Patients are usually unwell with a fever, headache, nausea and altered level of consciousness. Clinically it may not be possible to distinguish the different types of infection from each other. From an emergency perspective this is perhaps less important. Rather it is more important to establish that an intracranial infection is present and requires urgent referral. Initial treatment may be commenced on clinical grounds only, to avoid delays. Nevertheless it is important to obtain appropriate specimens as soon as possible to confirm the diagnosis and determine bacterial sensitivities to antibiotics if these are present. Not all infections present with a pyrexia. Children and the elderly especially can present atypically, sometimes with apparently innocuous symptoms at first. It is therefore very important to maintain a high index of suspicion in any patient presenting with and a unusual headache and signs of cerebral irritation, or an altered level of consciousness. Urgent CT is often the first line of investigation. Lumbar puncture may be required, but this can be contraindicated if there is raised intracranial pressure.

7.9.1 Diffuse Infections in the CSF: Meningitis

Meningitis is an acute inflammatory condition of the meninges usually as a result of infection of the cerebrospinal fluid (CSF). Patients can deteriorate extremely rapidly, making this a medical emergency requiring immediate treatment. Young children often develop nonspecific symptoms, such as irritability, drowsiness, or poor feeding. Therefore it is important to consider meningitis in any irritable child, especially with a rash (non-blanching and petechial). Infection may be caused by viruses, bacteria or other micro-organisms. Bacterial and viral meningitis are contagious and can be transmitted through respiratory droplets during close contact. Viral meningitis can be spread through faecal contamination. Less commonly, certain drugs can result in meningeal inflammation. In most cases the infective pathogen is a virus. Bacterial pathogens need to be quickly isolated, identified and then treated. Bacterial meningitis can result in serious long-term consequences, including deafness, epilepsy, hydrocephalus and cognitive functional deficits if it is not treated quickly.

Some infective causes are preventable with immunisation (meningococcal, mumps, pneumococcal, and Hib vaccines).

The term aseptic meningitis refers to cases of meningitis in which no infection can be found. This is usually caused by viruses but it can also be due to a bacterial infection that has already been partially treated. Rarer infections include spirochetes, borrelia, malaria and amoebae, and these therefore need to be specifically considered if initial investigations fail to identify a cause. Immunosuppressed patients are at risk of fungal infections (cryptococcal sp., Coccidioides sp., Histoplasma sp., Blastomyces sp., and Candida species).

Bacterial meningitis can occur spontaneously. It can also arise following trauma (especially skull fractures), surgery and following insertion of specific devices (e.g. CSF shunts for hydrocephalus). Spontaneous meningitis may be difficult to diagnose, as initial symptoms are indistinguishable from many viral infections (malaise, lethargy, fever, anorexia). Patients with immune deficiencies are particularly susceptible to TB meningitis, fungal, viral, and treponemal infections. Cryptococcal, varicella-zoster virus, cytomegalovirus, and neurosyphilis should therefore all be considered.

The most common symptoms of meningitis are fever, headache and neck stiffness. 'Nuchal rigidity' refers to the inability to flex the neck forwards passively due to severe spasm of the neck muscles. This is a very important clinical sign which should be specifically looked for in any patient with severe headache and a fever. Beware any patient who presents with a high fever, altered mental status and nuchal rigidity. If none of these are present, acute meningitis is unlikely, but if all three are present meningitis is probable. A list of meningitis symptoms and signs could include the following:

1. fever
2. Headache
3. Vomiting
4. Photophobia
5. Irritability
6. Confusion
7. Lethargy
8. Hypersensitivity to loud noises
9. Rash (in over half of cases)
10. Seizures (20% of patients at presentation and an additional 10% of patients within 72 h)
11. Tachycardia/tachypnoea/shock
12. The "jolt accentuation manoeuvre" may help determine meningitis in those reporting fever and headache. This is a variant of nuchal rigidity. The patient is asked to rapidly rotate the head. If this does not make the headache worse, meningitis is unlikely.
13. Kernig's sign. This is very indicative of meningeal irritation. The patient is placed in the supine position, with the hip and knee flexed to 90 degrees. Pain is then induced following passive knee extension, while the hips remain fully flexed. This manoeuvre places traction on the meninges via the sciatic nerve.

14. Brudzinski's sign occurs when flexion of the neck causes involuntary flexion of the knee and hip.

It is important to also look for a rash. If one is present, this may indicate a particular type of meningitis. Neisseria meningitidis ("meningococcal meningitis") typically causes a rapidly spreading, non-blanching, petechial rash, which may precede other symptoms. This can be seen on the trunk, lower extremities and mucous membranes.

Diagnosis in children can be difficult as they do not present with the same features as adults. Small children may only be irritable and appear to be unwell. The presence of a rash in any unwell child should therefore raise urgent suspicion. Age can sometimes be a guide to the underlying cause. In premature babies and newborns, common causes are group B streptococci, *Escherichia coli* and *Listeria monocytogenes* (meningitis in the newborn). Children under five may be infected by *Haemophilus influenza* (if not vaccinated). Older children are more commonly affected by *Neisseria meningitidis* and *Streptococcus pneumoniae*.

In adults, *Neisseria meningitidis* and *Streptococcus pneumoniae* cause about 80% of bacterial meningitis. Staphylococci, Pseudomonas, and other Gram-negative organisms may infect devices, such as cerebral shunts or extraventricular drains.

Tuberculous meningitis is more common in countries in which tuberculosis is endemic, but is also seen in immunosuppressed patients such as AIDS.

The most important test in confirming meningitis is analysis of the cerebrospinal fluid following lumbar puncture (if not contraindicated). Urgent imaging is initially required to assess the status of the ventricles prior to lumbar puncture. This is because obstructive hydrocephalus or an intracranial mass is a relative contraindication to this procedure. If a lumbar puncture is undertaken in such patients, coning can occur. CT may also show evidence of increased attenuation in the basal cisterns and sulci as a result of high concentrations of inflammatory cells. This must not be confused with subarachnoid haemorrhage. Other manifestations of meningeal infection (necrotising panarteritis, septic thrombophlebitis, ischaemic injury and cerebritis) may be detected with diffusion MR imaging, but this is rarely undertaken urgently. Imaging also plays an important role in the detection and management of less aggressive forms of meningitis. TB meningitis, for example, can be difficult to diagnose in patients presenting with headache and cranial neuropathies.

Management of acute meningitis depends on the causative organisms. Bacterial meningitis needs urgent treatment with antibiotics and more recently in some reports, corticosteroids. This helps to ensure recovery and reduce the risk of complications, such as brain swelling and seizures. In one study adjunctive use of dexamethasone decreased pneumococcal meningitis mortality from 30% to 20%. Patients need immediate admission to hospital. Whilst in hospital, other treatments, procedures and investigations will be carried out depending on the patient's condition. Antibiotics are not effective against viruses although, they may be started because the cause of meningitis is not known. Once viral meningitis is confirmed they are usually discontinued. Key elements in management include.

1. If the patient is alert and in a stable condition, oxygen should be administered, intravenous (IV) access established, and immediate admission arranged. It is essential to begin treatment as early as possible. Any delay may contribute significantly to morbidity and mortality.
2. Aggressive resuscitation with IV fluids. This may be necessary the patient is in shock or hypotensive. Crystalloid should be infused until the patient is well hydrated.
3. Monitoring of electrolytes. Hyper or Hypo-natremia can occur in bacterial meningitis as a result of dehydration, inappropriate secretion of antidiuretic hormone (SIADH), or following aggressive intravenous fluid resuscitation.
4. Antibiotics should be given as soon as the diagnosis is suspected and continued until the CSF white cell count is normal. The antibiotic or combination of antibiotics depends on the type of bacteria causing the infection. The penicillins, certain cephalosporins (i.e., third- and fourth-generation agents), carbapenems, fluoroquinolones, and rifampin provide high CSF levels. However it is important to discuss the most appropriate choice of antibiotic with a microbiologist or appropriate specialist. Often these are commenced before bacterial sensitivities are determined. They may therefore need to be adjusted at a later date.
5. Intrathecal antibiotics may be considered in patients with hospital acquired meningitis (for example following neurosurgery or placement of an external ventricular catheter) that does not respond to IV antibiotics.
6. The use of corticosteroids (dexamethasone, 0.15 mg/kg every 6 h for 2–4 days) is controversial but has been reported to improve outcomes by minimising the detrimental effects that can occur secondary to the patient's host defenses (inflammation). However, the anti-inflammatory effects of steroids reduce blood-brain barrier permeability and can therefore impede penetration of antibiotics into the CSF.
7. If the patient's mental status is altered, seizure precautions should be considered, seizures should be treated according to the usual protocol, and airway protection should be considered.
8. A throat swab should be taken for polymerase chain reaction (PCR). This helps to identify the likely organism.
9. Blood is taken for culture and Gram's stain.
10. Computerised tomography (CT) or magnetic resonance (MR) scans of the head may show swelling or inflammation. Computed tomography (CT) of the head should also be performed a before LP is undertaken. If there is no mass effect, LP can be safely performed. X-rays or CT scans of the chest or sinuses may also show infection in other areas that may be associated with meningitis.
11. If there are no contraindications, a lumbar puncture (LP) for cerebrospinal fluid (CSF) examination are indicated to identify the causative organism and in bacterial meningitis determine antibiotic sensitivities.
12. Signs of hydrocephalus and increasing intracranial pressure (ICP) should be closely watched for. Fever and pain should be managed, straining and coughing controlled, seizures prevented and systemic hypotension avoided.

13. Contact Tracing—for single cases it may be necessary to treat close contacts ('kissing contacts'). Usual regimes include rifampicin 600 mg twice daily for 2 days and ciprofloxacin 500 mg as a single dose

Untreated meningitis is often fatal. Systemic complications in those that can still occur and can be severe. These include

1. Gangrene of the limbs (requiring amputation)
2. Systemic inflammatory response syndrome
3. Waterhouse-Friderichsen syndrome—haemorrhaging into the adrenal glands (which is often fatal).
4. Hyponatremia (syndrome of inappropriate antidiuretic hormone secretion)
5. Cerebral oedema and herniation
6. Hydrocephalus
7. Seizures
8. Cardiac arrhythmias and ischemia
9. Cranial nerve palsies (especially eye movements, facial muscles and hearing).
10. Cerebral venous thrombosis, with weakness, loss of sensation, or abnormal movements

7.9.2 Tuberculous Meningitis (TBM)

This is the most commonly seen in children and adolescents. TBM develops when a meningeal, subpial or subependymal tuberculous focus (Rich focus) ruptures into the subarachnoid space or into the ventricular system. Clinical features include

1. Basal exudates
2. Progressive hydrocephalus
3. Vasculitis and Infarction
4. Cranial neuropathies

Formation of a thick, gelatinous exudate occurs, initially confined to basal subarachnoid areas. This rapidly extends to involve the basal cisterns, sylvian fissures, cerebral convexities and the ventricles and choroid plexus. Communicating hydrocephalus is caused by obstruction to CSF flow by thick gelatinous inflammatory exudates within the basal cisterns, over the brain convexities and in the cerebral aqueduct or fourth ventricular foramen. Basal exudates localised to the circle of Willis also result in a vasculitis, with spasm or thrombosis of the vessels and infarction. The vessels at the base of the brain are most severely affected, including the terminal segment of common carotid artery and proximal segment anterior, middle and posterior cerebral arteries. Cranial nerve palsies occurs in about 20–40% of patients. These can be the first clinical feature of TB meningitis. The most commonly affected nerves are II, III, IV, VI, VII. Tubercular encephalopathy is a diffuse cerebral disorder characterised by convulsion, stupor and coma, without signs of meningeal irritation or focal

neurological deficit. It is almost exclusively seen in infants and children receiving antitubercular treatment. It is believed to be an allergic delayed type IV hypersensitivity reaction due to cell mediated immunity to tubercular protein. Isolated calvarial tuberculosis is a rare condition, commonly seen secondary to haematogenous spread from a primary focus elsewhere. The frontal and parietal bones are most commonly involved. This presents as a subgaleal swelling (Pott's puffy tumor) with a discharging sinus. Bony lesions are usually osteolytic, and appear as well defined "punched out" defects.

7.9.3 Non-infectious Meningitis

Non-infectious causes of meningitis may result in diagnostic confusion and inappropriate treatment. Causes include microscopic spread of cancer to the meninges (malignant or neoplastic meningitis), drugs (notably non-steroidal anti-inflammatory drugs, antibiotics and intravenous immunoglobulins), sarcoidosis (neurosarcoidosis), connective tissue disorders (systemic lupus erythematosus), and some vasculitides (such as Behçet's disease). Epidermoid cysts and dermoid cysts have also been reported to result in meningitis following rupture into the subarachnoid space.

7.10 Encephalitis and Meningoencephalitis

This is acute inflammation of the brain. Encephalitis is distinct from meningitis although patients can sometimes present with both. Cerebritis, is an area of unencapsulated inflammation which can develop into a collection of necrotic pus—a brain abscess. Encephalitis can have both infective and non-infective causes. In some patients viral infection can be transmitted via an insect vector (notably ticks and mosquitoes). Rabies virus is transferred following an infected animal bite. Brain inflammation can also occur as a complication of viral infections with measles, mumps, chicken pox. Once it has passed across the blood brain barrier the virus enters neural cells resulting in destruction of function, haemorrhage and a diffuse inflammatory response. Encephalitis can also occur in autoimmune disorders such as multiple sclerosis or Rasmussen's encephalitis. Although Creutzfeldt-Jacob disease (CJD) is due to a prion (which is not an infectious agent in the strictest sense), this is included as part of the differential diagnosis.

Herpes simplex virus, poliovirus, measles virus are common pathogens. Herpes simplex virus deserves special mention. This can initially present with widespread oral ulceration and be erroneously confused with Stevens Johnson's syndrome. If high-dose steroids are given, the patients may develop herpes simplex virus encephalitis. For this reason severe oral ulceration of the mouth should be treated with caution.

Other rare types of encephalitis include Japanese encephalitis, rabies and equine encephalitis. Bacterial encephalitis may occur following meningitis. Parasitic or protozoal infestations, such as toxoplasmosis, malaria, or amoebic infection, can also cause encephalitis. *Cryptococcus neoformans* can occur in immunocompromised patients. Whatever the cause, common symptoms include headache, fever, confusion, drowsiness and fatigue. Seizures, tremors, hallucinations, and memory problems suggest advanced disease. Adults usually present with acute onset of fever, headache, confusion, and sometimes seizures. However children or infants may present with non-specific symptoms such as irritability, drowsiness and fever. In all cases it is important to always check for a stiff neck—this indicates the presence of meningitis or meningoencephalitis.

Several subtypes of this disease exist. Limbic encephalitis is a particular form the disease in which the inflammatory process is confined to the limbic system of the brain. Patients therefore present with disorientation, disinhibition, memory loss, seizures, and behavioural problems. Autoimmune encephalitis presents with catatonia, psychosis, abnormal movements, and autonomic dysfunction. Encephalitis lethargica presents with high fever, headache, delayed physical response and lethargy. Patients can also develop upper body weakness, muscular pains, and tremors.

Meningoencephalitis is the simultaneous infection of meningitis and encephalitis. Causative organisms are the same as those previously described and include viruses, bacteria and protozoans. Specific infections include:

Bacterial

- Listeria monocytogenes
- Neisseria meningitidis
- Rickettsia prowazekii
- Mycoplasma pneumoniae
- Tuberculosis
- Borrelia (Lyme disease)
- Leptospirosis

Viral

- Mumps, a common cause of meningoencephalitis
- Tick-borne meningoencephalitis
- West Nile virus
- Measles
- Epstein-Barr virus
- Varicella-zoster virus
- Enterovirus
- Herpes simplex virus type 1
- Herpes simplex virus type 2
- HIV, a very small number of patient develop meningoencephalitis at the early stage of infection.

Fungal
Cryptococcus neoformans
Protozoal
Primary Ameobic meningoencephalitis can mimic a brain abscess, aseptic or chronic meningitis, or CNS malignancy

- Trypanosoma brucei
- Toxoplasma gondii

Investigations are along the same lines as the previously described intracranial infections. A complete blood count (CBC) with differential should be performed, although findings are often within the normal range. Serum electrolyte levels are usually normal unless dehydration is present (syndrome of inappropriate secretion of antidiuretic hormone occurs in 25% of patients with some types of encephalitis). CT scan should be undertaken if there are focal symptoms or signs, and to exclude brain swelling, raised intracranial pressure, obstructive hydrocephalus, or mass effect. A Head CT also helps exclude brain haemorrhage or infarction as a cause the patients illness. Magnetic resonance imaging is reported to be more sensitive than CT scanning in demonstrating early abnormalities. If there is no evidence of raised intracranial pressure a lumbar puncture can then be undertaken. This should be performed on all patients suspected of having a viral encephalitis. CSF analysis usually shows increased amounts of protein and white blood cells with normal glucose. Specific diagnosis can sometimes be made by the detection of antibodies on polymerase chain reaction. Subsequent MRI imaging can help determine the presence of inflammation and identify other causes. Serological tests may show high antibody titres. EEG may also show characteristic patterns. With the exceptions of HSE and varicella-zoster encephalitis, the viral encephalitides are generally not treatable beyond supportive care. Specific treatments for T gondii and cytomegalovirus (CMV) encephalitis are also available. Patients should initially be resuscitated and referred urgently. Any hydrocephalus or increased intracranial pressure should be treated immediately. Supportive treatment (intravenous fluids/sedation/mechanical ventilation) should be commenced and anti-viral agents administered if the diagnosis is suspected. Systemic complications include hypotension and shock, hypoxemia, hyponatremia,and exacerbation of pre existing chronic diseases. Corticosteroids may also be used to reduce brain swelling, but as previously discussed their use is controversial in the presence of an acute infection.

7.11 Focal Infections with the Potential for 'Mass Effect'

7.11.1 Brain Abscess

Brain abscess is caused by intracranial inflammation with subsequent abscess formation. Infection can enter the intracranial compartment directly or indirectly via 3 routes (i) Contiguous suppurative focus (Direct extension—45–50% of cases), (ii)

following trauma (10% of cases) and (iii) Haematogenous spread from a distant focus (25% of cases). Subdural empyema, sinusitis and middle ear infections are a common cause of brain abscesses, with direct spread intracranially. Haematogenous spread of infection from elsewhere can also occur. Well recognised sites include infective endocarditis and dental abscess. However, In around 15% of cases, no source can be identified. The brain abscess initially begins as a discreet region of inflammation that quickly progresses to form a pus-filled cavity. Common sites are (i) frontal-temporal, (ii) frontal-parietal, (iii) parietal, (iv) cerebellar and (v) occipital lobes (Figs. 7.13, 7.14, 7.15, 7.16 and 7.17).

Clinical features are similar to the other causes of intracranial infection. Headache, nauseas, vomiting, and deterioration in the conscious level are all common. With cerebral irritation the patient may develop focal neurology or seizures. However pyrexia may be absent. Nuchal rigidity and papilloedema are seen in about one quarter of cases, so should be routinely looked for. Untreated, additional localised neurologic signs will eventually be found in most patients. These are due to local pressure/inflammatory affects (for example Cerebellar abscess—Nystagmus and ataxia, Brainstem abscess—Facial weakness, dysphagia and hemiparesis and Occipital abscess- Neck rigidity). Any suddenly worsening headache, followed by emerging signs of meningismus, is often associated with rupture of the abscess.

Investigations are similar to the other causes of intracranial infection, but it is important to note that the white cell count and CRP can be normal, especially if

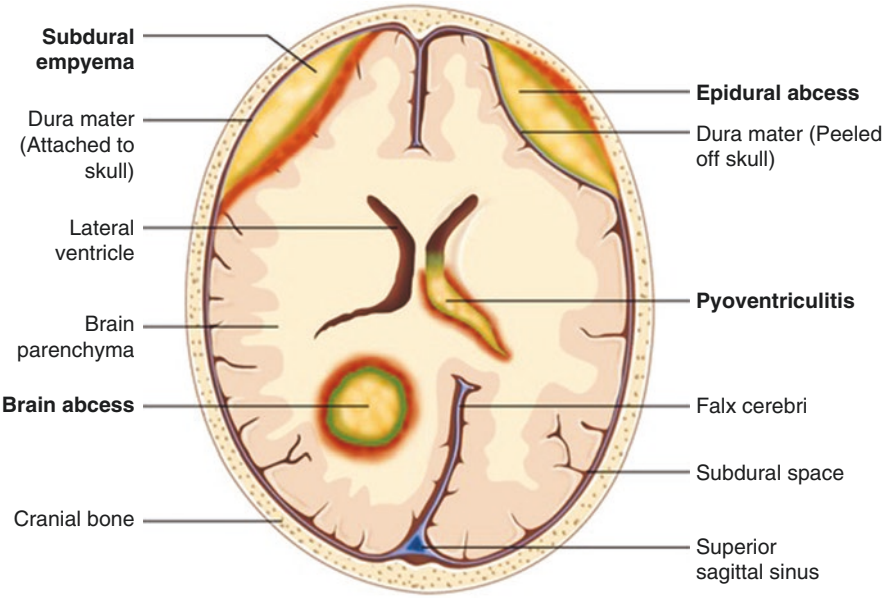

Fig. 7.13 Different types of intracranial suppurative collections

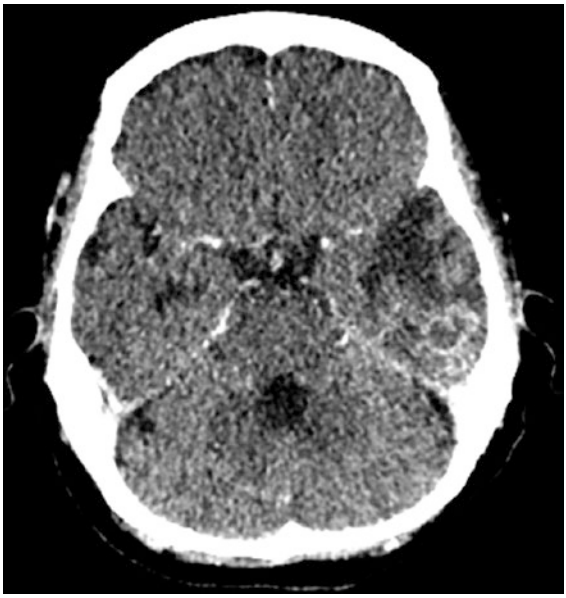

Fig. 7.14 Left temporal abscess due to mastoiditis

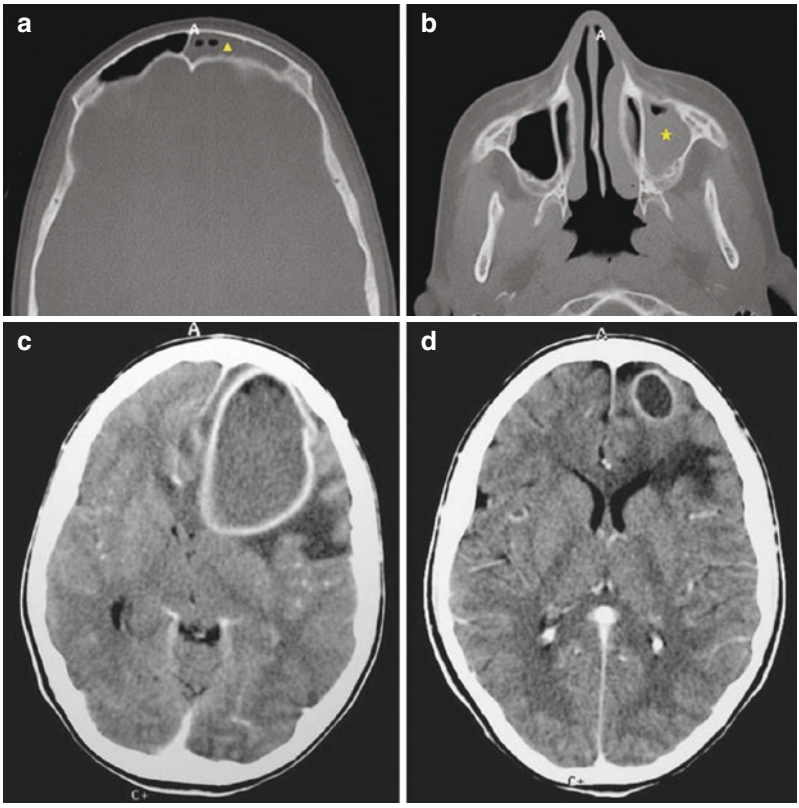

Fig. 7.15 Large frontal brain abscess

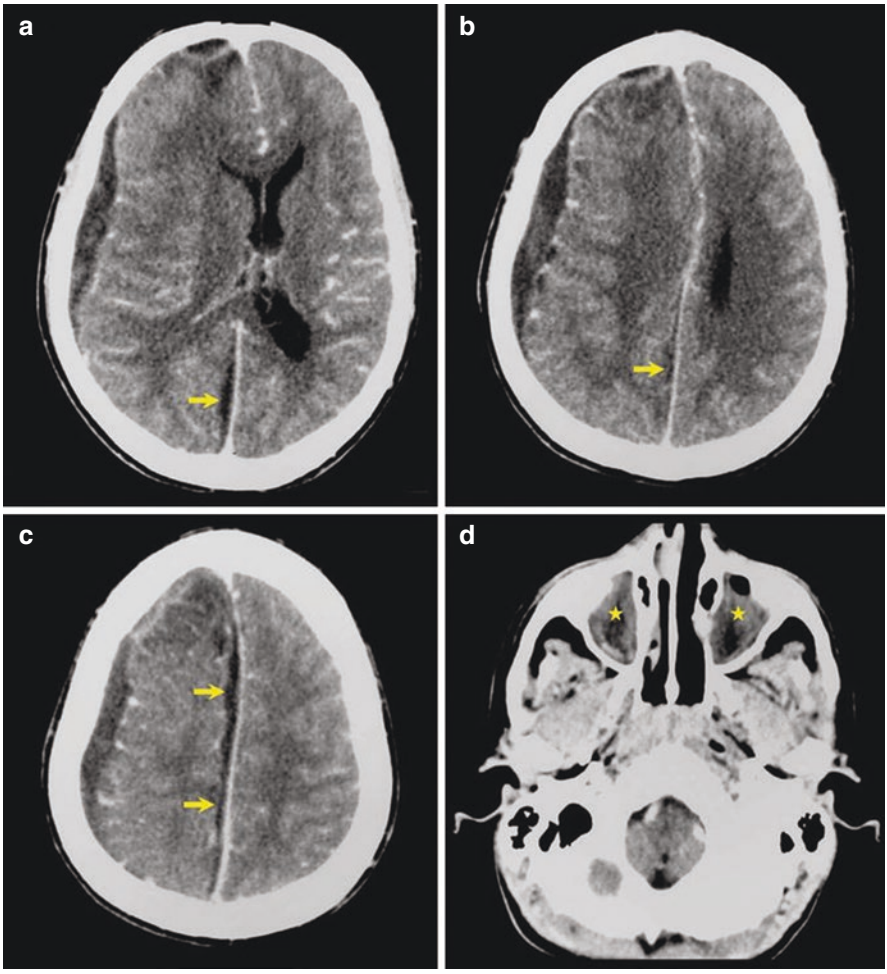

Fig. 7.16 Case 6.5. (**a**–**d**) Axial cranial post-contrast CT scan showing extensive frontoparietal and interhemispheric subdural empyemas on the right side (*arrows*). Note bilateral maxillary sinusitis (*stars*)

there is no primary source. Serological tests should be taken for some pathogens (CSF polymerase chain reaction for Toxoplasma). An urgent CT scans should be undertaken. This usually shows a ring enhancing lesion with surrounding oedema. In contrast to tumours, abscesses are usually perfectly circular with a wall of uniform thickness. They can also be multiple. As with subdural empyema a lumbar puncture should not be performed due to the risk of cerebral herniation (coning). Diagnosis is therefore usually suspected on the basis of an enhancing circular lesion on a CT scan of a patient with an infection elsewhere. Many specialists now consider MRI to be the best diagnostic test in the diagnosis of brain abscess. This is reported to have better sensitivity and specificity.

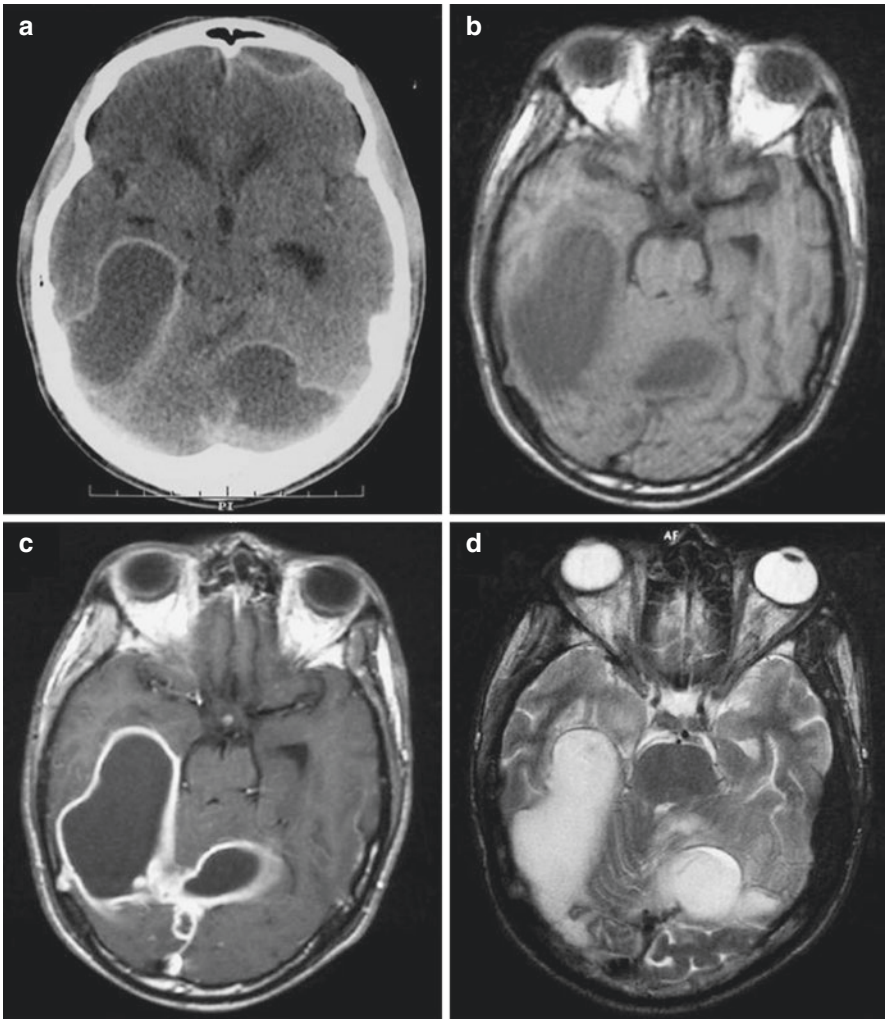

Fig. 7.17 Case 6.4. Axial post-contrast CT scan (**a**). T1-weighted images without (**b**) and with (**c**) gadolinium injection, and a T2-weighted image (**d**) show multiple supratentorial (*right side*) and infratentorial (*left side*) subdural empyemas mimicking intraparenchymal brain abscesses

Early diagnosis is essential. Patients who have only had symptoms for a week or less tend to respond well to medical treatment, although they will require a long course of antimicrobial treatment. However, many patients require urgent surgical drainage. Generally speaking, large abscesses will need to be evacuated or aspirated, whilst smaller ones may be aspirated for diagnostic purposes only. Before the abscess becomes encapsulated, antimicrobial therapy may be beneficial. Once the abscess

has fully formed, surgical drainage combined with prolonged antibiotics (4–8 weeks) is required. Some neurosurgeons prefer to completely evacuate the abscess, while others advocate repeated aspirations. If the patients consciousness is deteriorating, they should be fully resuscitated and steroids and mannitol should be considered prior to transfer. The use of steroids is controversial, however they may be indicated if there is significant mass effect seen on CT, or evidence of significant cerebral oedema. Complications of brain abscesses are partly related to their location. These include hemiparesis, cranial nerve palsies, hydrocephalus, ataxia and optic atrophy. Recurrent seizures may develop in about a third of cases. With early treatment, mortality has been significantly reduced, but since this condition is commonly seen in immunocompromised patients the mortality rate remains around 10–15%.

7.11.2 Subdural Empyema

This is is a collection of pus between the dura mater and the underlying arachnoid. About 95% of subdural empyemas are located within the head, often around the frontal lobe. 5% involve the spine. Most cases are secondary to sinusitis or a middle ear infection. Patients initially present with an illness similar to meningitis, but usually develop a hemiparesis due to cortical venous thrombosis. Seizures are common. The infection has a tendency to spread quickly through the subdural space until it reaches a boundary (falx cerebri, tentorium cerebelli etc.). They are therefore usually unilateral. With progression, the empyema can expand resulting in an increase in intracranial pressure and invasion of the cerebral parenchyma. Cerebral oedema and hydrocephalus can also occur as a result of disruption of the cerebral circulation and normal flow of cerebrospinal fluid. Thrombosis of the cortical veins can result in cerebral infarction. Cavernous sinus thrombosis can also occur.

Infection usually enters through the frontal or ethmoid sinuses. Less frequently it enters through the middle ear, mastoid cells, or sphenoid sinus. Rarely, it occurs by haematogenous spread from distant foci, most commonly the heart or lungs. Common causative organisms are anaerobes, aerobic streptococci, staphylococci, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and other gram-negative bacilli.

Initial investigations and management are similar to meningitis, with the exception of a lumbar puncture. This should be avoided due to the risk of coning. MRI is now the imaging study of choice, being superior to CT scan in defining the extent of the subdural empyema and demonstrating a collection. However CT scan is usually the modality of choice if the diagnosis is uncertain, or if the patient is comatose or critically ill and MRI is not possible. This will also show a thin subdural collection, with pus along the falx. Patients usually require immediate neurosurgical drainage via a craniotomy, which enables good exposure for adequate washout and drainage. Alternatively stereotatic burr hole placement with drainage and irrigation may be undertaken in selected cases. The source of infection should also be identified and treated accordingly (lungs, sinuses).

7.11.3 Other Focal Infections

7.11.3.1 Neurosyphilis

This is an infection which can involve both the brain and spinal cord. It is caused by the spirochete Treponema pallidum. Infection usually occurs in people with long-standing and previously undiagnosed (and untreated) syphilis. In such cases the initial infection may have been acquired decades ago. There are four distinct types of neurosyphilis (i) asymptomatic, (ii) meningovascular, (iii) tabes dorsalis and (iv) general paresis. In rare cases neurosyphilis can been mistaken for Alzheimer's disease. The main symptoms of neurosyphilis include visual impairment, confusion, changing personality, disorientation and an abnormal gait. Patients can sometimes present with seizure. An Argyll Robertson pupil may be present, in which bilaterally small pupils constrict focusing on near objects but not to light. This has been attributed to a dorsal midbrain lesion that interrupts the pupillary light reflex pathway but spares the more ventral pupillary near reflex pathway.

Neurosyphilis can be difficult to diagnose, partly because it is not often considered in the differential diagnosis. Blood tests involve the Venereal Disease Research Laboratory test (VDRL), Fluorescent treponemal antibody absorption (FTA-ABS) and other serology tests (including HIV testing). CT/MRI and samples of cerebrospinal fluid may also be required. Management involves high-dose penicillin.

7.12 Raised Intracranial Pressure (Intracranial Hypertension)

Raised intracranial pressure is not a specific diagnosis, but has many causes. It usually occurs as a result of intracranial pathology. However, in some patients a cause is not found. Causes include:

1. Generalised brain swelling. This has many causes both intrinsic and extrinsic to the brain. Generalised swelling can occur following trauma, prolonged hypoxia (prolonged seizures), severe electrolyte disturbances and infections such as encephalitis. Systemic disease can also result in wide spread cerebral oedema, for example acute liver failure, hypertensive encephalopathy and any condition resulting in hypercarbia
2. Space occupying lesions, such as tumours, haematoma or abscesses. When these grow slowly the intracranial pressure can be compensated for as previously discussed (monroe Kellie doctrine). However when this compensation process becomes exhausted intracranial pressure will rise
3. Obstruction to CSF flow (Aqueduect stenosis, Chiari malformation, meningeal disease)
4. Increased CSF production. Although uncommon a tumour of the choroid plexus can result in overproduction of CSF, which is produced in excess of that which can be resorbed

5. Increase in cerebral venous pressure (venous sinus thrombosis or stenosis, heart failure or mediastinal obstruction)
6. Craniosynostosis—premature fusion of the sutures prevents skull expansion as the brain grows. Depending on the number of sutures involved the extent of elevation of the intracranial pressure varies. Some of these conditions are discussed in the chapter on embryology
7. Idiopathic—this is discussed further below

Worldwide, the most common causes of raised intracranial pressure are (i) subarachnoid haemorrhage, (ii) trauma, (iii) cerebral tumours (iv) stroke (v) meningoencephalitis, and (vi) Hydrocephalus. In many cases, the underlying cause is self-evident and raised intracranial pressure is anticipated as part of the clinical course. Investigations are directed them accordingly to establishing the underlying diagnosis and monitoring the intracranial pressure. Symptoms of raised intracranial pressure are varied and include headaches, vomiting, nausea, loss of concentration, drowsiness, irritability, changes in personality and blurred vision. Vomiting and headaches that occur first thing in the morning, or wake the patient is an important clue to the diagnosis. Because the patient has been laying down the intracranial pressure has risen even further. Symptoms often relieve on getting up. It is perhaps worth noting that caffeine withdrawal can also result in early morning headaches. Management of raised intracranial pressure is directed at the cause. In some cases CSF diversion may be required.

7.12.1 Hydrocephalus

Hydrocephalus is a disturbance of CSF physiology. Secretion of CSF by the choroid plexus is a metabolically active process involving ion pumps and enzyme systems similar to those found in the distal tubule of the kidney. In hydrocephalus there is an abnormal accumulation of cerebrospinal fluid (CSF) within the brain. CSF secretion continues at a constant rate (about 20 mL/h in adults), regardless of intracranial pressure (ICP), so long as the choroid plexus and the brain itself are perfused. This often results in raised intracranial pressure. CSF reabsorption is a purely passive process driven by the pressure differential between the subarachnoid space and the venous circulation. With the rare exception of choroid plexus papilloma (a tumour of the choroid plexus that causes excessive CSF secretion), the diseases that cause hydrocephalus do so by interfering with CSF reabsorption. Symptoms often include headaches, double vision, ataxia, vomiting, sleepiness and mental impairment. In babies there may be a rapid increase in head size, a tense bulging fontanelle and ‘sunsetting’ of eyes. Hydrocephalus can occur as a result of a birth defect (e.g. neural tube defects and those that result in aqueduct stenosis), or it can be acquired, secondary to trauma, intracranial haemorrhage, meningitis and brain tumours. Depending on the underlying drainage mechanisms, hydrocephalus can be classified into communicating and non- communicating (obstructive). Both can be congenital or acquired.

7.12.2 Communicating

Communicating (non-obstructive) hydrocephalus occurs as a result of impaired cerebrospinal fluid reabsorption, but there is still free flow of CSF between the ventricles and subarachnoid space. This type of hydrocephalus is believed to be due to functional impairment of the arachnoid granulations in the superior sagittal sinus (where CSF is normally resorbed into the venous system). Causes of obstruction include subarachnoid and intraventricular haemorrhage, meningitis and congenital absence of arachnoid villi. Scarring and fibrosis secondary to bleeding or infection can also prevent delayed resorption of CSF.

7.12.3 Non-communicating

Non-communicating (obstructive) hydrocephalus, is caused by obstruction to the flow of CSF within the brain. As a result CSF cannot reach the subarachnoid space and builds up within the ventricular system. In this group of patients it is not safe to do a lumbar puncture. These patients are at high risk of coning if this is done. Obstruction to CSF flow can occur at the following sites

1. Foramen of Monro—obstruction may lead to dilation of one or both lateral ventricles.
2. The aqueduct of Sylvius. This can be obstructed by a number of conditions including congenital atresia, haemorrhage, or a tumour. This results in dilation of both lateral and the third ventricles.
3. Fourth ventricle—obstruction here (from a posterior fossa mass) results in dilation of the aqueduct as well as the lateral and third ventricles.
4. The foramina of Luschka and Magendie. These may be congenitally obstructed (e.g. Dandy-Walker malformation).

7.12.4 Common Causes of Hydrocephalus (Figs. 7.18, 7.19 and 7.20)

Prematurity (post haemorrhagic hydrocephalus)
Myelomeningocele
Other congenital or developmental conditions affecting the brain

- Dandy-Walker malformation
- Arachnoid cysts
- Interhemispheric cysts
- Aqueductal stenosis
- Encephalocele

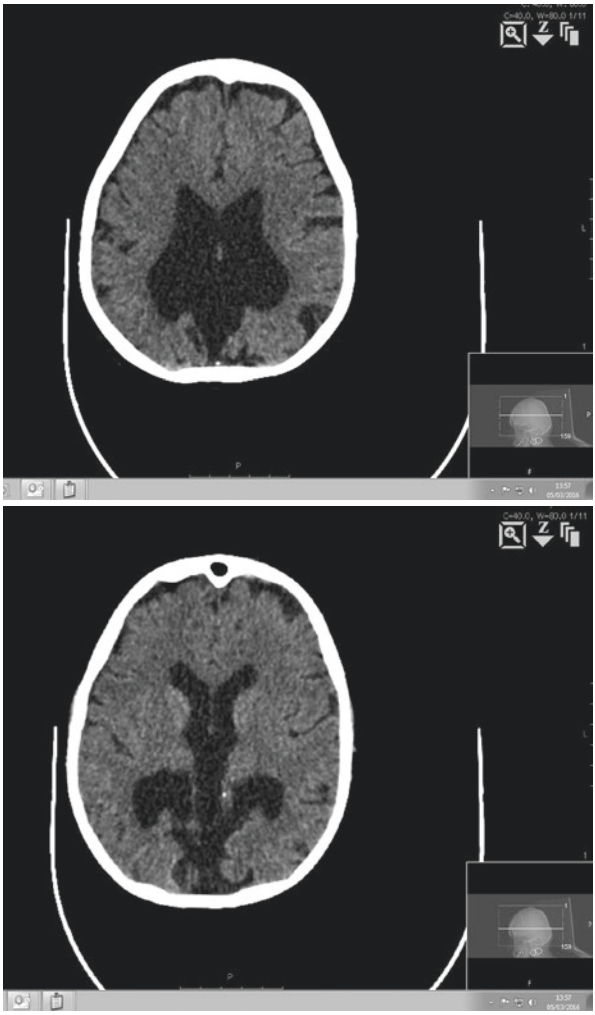

Fig. 7.18 CT scan showing congenital hydrocephalus

Brain tumour

Traumatic brain injury. Post-traumatic hydrocephalus (PTH) can complicate decompressive craniectomy after traumatic brain injury (TBI).

Aneurysmal subarachnoid haemorrhage

Congenital or developmental conditions affecting the skull

- Crouton
- Pfeiffer syndromes
- Achondroplasia

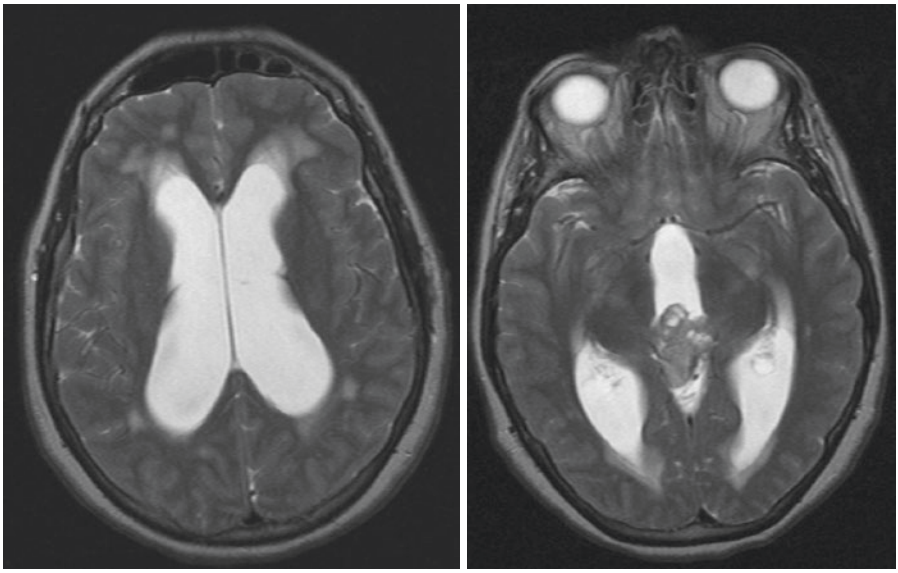

Fig. 7.19 Obstructive hydrocephlaus on T2 MRI due to pineal region tumour

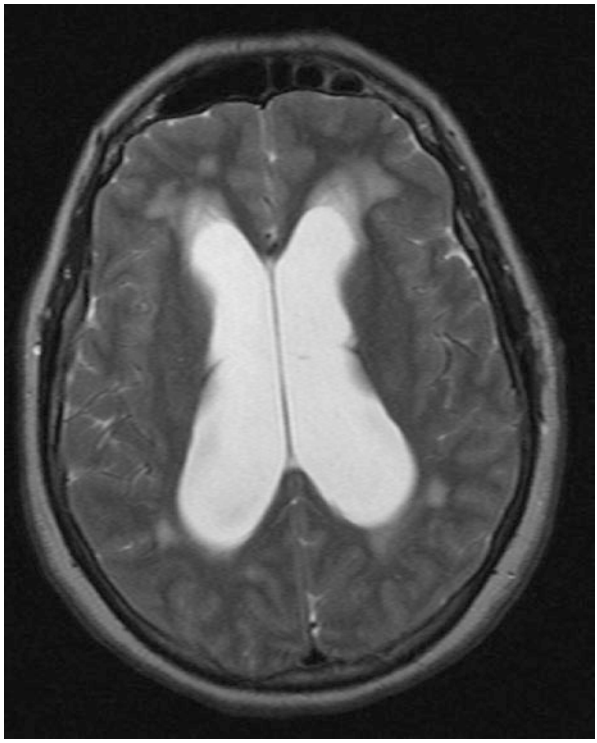

Fig. 7.20 CT scan showing hydrocephalus in an adult

Meningitis.

In many countries today, screening for hydrocephalus is undertaken during pregnancy and shortly after delivery. Routine prenatal ultrasound may detect hydrocephalus during pregnancy in the developing foetus. After birth, the head of the baby is measured regularly. Any abnormalities in head size, especially if accompanied with tense fontanelles require further investigation. Symptoms of hydrocephalus vary with age, disease progression, and individual differences in tolerance by the patient to the condition. For example, an infant's ability to compensate for increased CSF pressure and enlargement of the ventricles differs from an adult's. This is because the bones on the infant skull have not fully ossified and the sutures have not yet closed. The cranial cavity can therefore expand to accommodate the buildup of CSF. In infancy, the most obvious indication of hydrocephalus is often a rapid increase in head circumference or an unusually large head size. Other symptoms may include vomiting, sleepiness, irritability, downward deviation of the eyes (also called "sunsetting"), and seizures. In advanced cases spasticity may occur in the lower limbs.

Older patients present with symptoms of raised intracranial pressure. These may include headache followed by early morning vomiting, nausea, blurred or double vision, urinary incontinence, lethargy, drowsiness, irritability, or other changes in personality or cognition. Neck pain should be regarded with suspicion. This may indicate tonsillar herniation. Blurred vision maybe secondary to papilloedema or optic atrophy. Diplopia may arise secondary to CNVI nerve palsy. Symptoms of normal pressure hydrocephalus include, problems with walking, impaired bladder control leading to urinary frequency and/or incontinence, and progressive mental impairment and dementia. Many of these symptoms may be confused with dementia or Alzheimer's disease. Parkinsonism may also occur.

Investigations usually involve CT scan. This will typically show ventricular dilatation. Ultrasonography, magnetic resonance imaging (MRI), and pressure-monitoring techniques may also be undertaken in borderline or uncertain cases. The fourth ventricle is usually dilated in communicating hydrocephalus, but may be small in non-communicating hydrocephalus. MRI may also be necessary if a third ventriculostomy is being considered, to visualise the basal cisterns and local anatomy. It can also look for Chiari malformation or cerebellar or periaqueductal tumours. In infants, ultrasound through the anterior fontanelle may be undertaken.

7.12.4.1 Hydrocephalus Is Most Often Treated by Surgically Inserting a Shunt

These consist of three parts (i) a ventricular catheter, (ii) a valve, and (iii) a distal catheter. The ventricular catheter passes from the ventricle of the brain through the skull, where it joins the valve. The valves prevents excessive drainage of CSF. Most include a reservoir that can be punctured with a needle for diagnostic purposes and to remove CSF. The valve is also connected to a distal catheter that carries the CSF to another part of the body, where it can be reabsorbed back into the venous circulation. Common sites include the peritoneal cavity, pleural cavity, right atrium, and the

internal jugular vein. Shunt systems thus divert the flow of CSF from the CNS to another area of the body where it can be absorbed as part of the normal CSF circulatory process. This will hopefully control the intracranial pressure. Whenever possible the underlying cause is also corrected. Complications of shunts include mechanical failure, infections, obstructions and the need to lengthen or replace the catheter. If these occur, the shunt system usually requires replacement. Shunt systems require monitoring and regular follow up. In patients with normal pressure hydrocephalus a lumbar puncture maybe undertaken to determine the suitability of a shunt. Following removal of CSF from the puncture, if symptoms improve (gait, or cerebral functions), then placement of a shunt will probably help. Repeated lumbar puncture may also be indicated in patients with hydrocephalus secondary to intraventricular haemorrhage. This particular type of hydrocephalus can resolve spontaneously.

Treatment of hydrocephalus has changed in recent years with better imaging and introduction of endoscopic procedures as well as enhanced shunts. Third ventriculostomy creates an internal bypass by creating a stoma between the floor of the third ventricle and the basal cisterns. Endoscopic third ventriculostomy (ETV), with or without with choroid plexus cauterisation (CPC), is an emerging technique that provides restoration of cerebrospinal fluid flow and a shunt-free option for hydrocephalus children. In severe cases external ventricular drainage may be required. This can be done at the bedside. CSF drains via a manometer into an external collecting system. This may also be performed if there is infection or bloodstained CSF preventing shunt insertion.

7.12.5 Shunt Assessment

It is important to know how to assess a shunt. If a shunt becomes blocked the intracranial pressure can rise very quickly and patients can become very unwell. Consider shunt blockage in any patient known to have a shunt who begins to act erratically, becomes confused or becomes drowsy. If the patient is severely unwell and unresponsive a diagnostic aspirate may be taken from the reservoir. If this improves the patient's clinical condition a blockage in the distal catheter is likely to be the problem. If fluid cannot be aspirated a blockage in the ventricular catheter may be the cause (commonly from the choroid plexus). In other patients if time allows, diagnosis of shunt blockage can be made following CT scan. However CT imaging requires careful interpretation, depending on the underlying pathology. Neuroendoscopy techniques can also be used to reveal the cause of shunt obstruction. Plain films of the whole of the shunt (Shunt series) may be helpful if there are concerns regarding the distal catheter, which can break, disconnect, or migrate.

7.12.6 Shunt Infection

Infection is a common complication of ventriculoperitoneal shunt (VP) placement, reportedly occurring in nearly 10% of patients. Patients with hydrocephalus secondary to IVH or meningitis are especially at risk as well as those receiving a shunt

under 1 year of age. This may be due to the poorly developed immune system in infants under 1 year of age, the immaturity of the skin barrier in early infants, and the characteristics of the bacterial flora in this age group.

Infection generally develops within the first 2 months after surgery, with *Staphylococcus epidermidis* being the most common cause. However, P. aeruginosa and Klebsiella and other multi resistant gram-negative bacteria have also been reported, making this a very difficult problem to treat. *Candida* is an incredibly rare but serious cause of ventriculoperitoneal (VP) shunt infections. Contamination most likely occurs at the time of placement or soon after. Breakdown of the wound and dehiscence over the shunt account for most infections. Shunt infections usually occur within a few weeks of surgery and are mostly secondary to contamination from skin bacteria. An infected VP shunt will often become secondarily obstructed by omentum, localising the infection. Patients present with symptoms of a blocked shunt accompanied by a fever. Meningism is uncommon. Infected Ventricular-Atrial (VA) shunts usually will not block and so the infection may continue undetected for a long period. Symptoms of an infected VA shunt include vague ill health and a low-grade temperature. When a shunt infection is suspected, percutaneous needle aspiration of the shunt reservoir is usually diagnostic. CSF is sent for microscopy and culture. The preferred treatment of CSF shunt infections involves intravenous antimicrobial therapy, surgical removal of the infected shunt, installation of an external ventricular drainage (EVD) device, and insertion of a new shunt once the CSF is sterile. Prophylactic antibiotics have not been shown to prevent shunt infections.

7.12.7 Shunt Overdrainage

Occasionally a shunt will excessively drain CSF, so that the patient develops low-pressure headaches. This may cause persistent low-pressure headaches, subdural collections, collapse of ventricles, bleeding or in cases of lumbo-peritoneal shunt, downward shifts of the brain resulting in herniation. In these cases, headache complaints are minimal when the patient is lying down but become more severe when the patient sits up or stands. In some patients if the ventricles are very large, any sudden change in pressure can cause them to collapse, tearing the delicate cortical veins and resulting in subdural haematoma. Low-pressure headaches are treated with reassurance and advising a high fluid intake. Caffeine has been reported to be helpful. The shunt can be revised if symptoms persist. Low-pressure headaches can also occur in up to a third of people who have had a spinal tap, usually hours to a day or two afterward—cerebrospinal fluid sometimes continues to leak out of the puncture site.

7.13 Idiopathic (Benign) Intracranial Hypertension (IIH)

Idiopathic intracranial hypertension (IIH), sometimes called benign intracranial hypertension (BIH) or pseudotumor cerebri (PTC), is a neurological disorder in which there is increased intracranial pressure, sometimes in the absence of an obvious cause. It can occur in all age groups, but is most common in women aged 20–40.

It is often associated with obesity. Whilst this is called 'benign', this is a misnomer. Untreated it can result in visual loss. The condition occurs in about one per 100,000 people. Symptoms include early morning headaches, nausea, and vomiting. Headaches are often made worse by any activity that increases the intracranial pressure further, such as coughing and sneezing. There may also be pulsatile tinnitus, cranial nerve deficits and visual symptoms.

Physical examination is usually normal apart from the presence of papilloedema. Diagnosis therefore relies on a careful history and a high index of suspicion. Cranial nerve palsies may be noted (the patient may have a squint secondary to a third, fourth, or sixth nerve palsy). If the condition has been longstanding, the visual fields may be constricted. Longstanding papilloedema can result in optic atrophy.

The cause of the raised intracranial pressure in this condition is unknown. Three theories exist (i) an excess of CSF production, (ii) increased volume of blood or brain tissue, (iii) obstruction of the veins that drain blood from the brain. Congestion of venous blood may result from a generalised increased in venous pressure, which has been linked to obesity. Other causes of raised intracranial pressure must be considered and excluded. Venous sinus stenosis can be treated by endovascular stenting if appropriate. Medications including high-dose vitamin A derivatives (e.g. isotretinoin for acne), long-term tetracyclines and hormonal contraceptives have also been reported to increase intracranial pressure. Other rare conditions include obstructive sleep apnea, systemic lupus erythematosus, chronic kidney disease, and Behçet's disease.

IIH is diagnosed following CT or MRI. These usually appear to be normal, although slit-like ventricles and an "empty sella sign" (flattening of the pituitary gland due to increased pressure) may be noted. An MR venogram may be performed to exclude the possibility of venous obstruction or cerebral venous sinus thrombosis. Lumbar puncture is often required to measure the CSF pressure, as well as to obtain a sample of CSF to exclude other possible causes. If the pressure is significantly increased, some CSF may also be removed to reduce symptoms. In some cases it may be necessary to monitor the ICP. Diagnosis is often made using the Modified Dandy criteria

1. Symptoms of raised intracranial pressure (headache, nausea, vomiting, transient visual obscurations, or papilloedema)
2. No localising signs with the exception of abducens (sixth) nerve palsy
3. The patient is awake and alert
4. Normal CT/MRI findings without evidence of thrombosis
5. LP opening pressure of >25 cmH2O and normal biochemical and cytological composition of CSF
6. No other explanation for the raised intracranial pressure

7.13.1 Management Aims to Prevent Visual Loss and Symptom Control. Measures Include

1. Weight loss, including bariatric surgery
2. Lumbar puncture. In some cases, this may be sufficient to control symptoms, and no further treatment is needed. The procedure can be repeated if necessary.

Repeated lumbar punctures are sometimes required to control the ICP urgently if the patient's vision deteriorates rapidly
3. Acetazolamide (Diamox) reduces CSF production. Furosemide (Frusemide) may be used as an alternative if acetazolamide is not tolerated
4. Occasionally surgery may be offered if medical therapy fails or if it is not tolerated. This includes optic nerve sheath fenestration (to reduce the pressure locally) or placement of a shunt
5. If venous sinus stenosis is diagnosed, venous sinus stenting may be performed

7.14 Intracranial Thrombosis

Cerebral venous drainage is comprised of two systems, the superficial and the deep venous systems. Draining blood passes into the major dural sinuses—Superior sagittal sinus (SSS), inferior sagittal sinus (ISS), lateral sinus (LS), cavernous sinus and straight sinus, and then to the internal jugular vein (IJV). Many anastomoses can be found between these two cerebral venous systems. Clinically the dural sinuses are divided into posterior superior (P-S) and anterior inferior groups (A-I). P-S comprises the SSS, ISS, LS, straight sinus, and occipital sinus. The A-I group comprises the superior and inferior petrosal sinuses and the cavernous sinus. Inside of dural sinuses are found the Pacchioni's or arachnoid granulations, which play an essential role in the cerebrospinal fluid (CSF) physiology. SSS is located anatomically in the attached margin of falxcerebri, and drains almost all cerebral cortex. The LS drains the cerebellum, brain stem and the posterior portions of brain hemispheres. In the skull base are also the cavernous sinuses, through which the oculomotor, trochlear, abducens, the ophthalmic and maxillary branches of the trigeminal nerves pass. Thrombosis within any of these sinuses can have devastating consequences. Several types can occur. They can arise following a number of predisposing conditions. Trauma, hyperviscosity syndromes and tumours need to be urgently identified.

7.14.1 Dural Venous Sinus Thrombosis

Venous sinus thrombosis can affect any age and either sex, but most commonly affects young and middle-aged females. It is a sporadic cause of headache, with an unpredictable prognosis. Diverse aetiologies have been reported to play a major role in the development of this condition. Thrombosis can arise following trauma over the sinus, or tumours nearby and in relation to nearby infections from paranasal sinusitis, otitis, mastoiditis, meningitis and intracranial abscess. It may also occur following neurosurgical procedures. Maxillary sinusitis has been reported as a rare cause. When thrombosis occurs, the venous pressure rises, impeding CSF absorption. This can result in raised intracranial pressure. Patients present with symptoms of raised pressure, notably headaches, especially in the morning, visual disturbances and papilloedema. In severe cases, venous infarction of the cerebral cortex can occur resulting in severe focal neurological deficits. Thus, this condition should be considered in all young women who percent with an unusual and

progressive headache accompanied with focal neurological signs. Diagnosis is usually made following CT or MRI scans which usually show some degree of brain swelling and in some cases haemorrhagic infarctions (Fig. 7.21). The 'delta' sign is a triangular filling defect in the sinus on a CT scan with contrast. Other useful signs include the 'string sign' and the 'dense triangle sign'. MRI and CT venography are also useful imaging modalities. Management aims to control or resolve the underlying cause, control any intracranial hypertension, treat or prevent seizures or focal neurological deficits resulting from cerebral oedema or infarction. Seizures can occur in around one third of cases. Anticoagulation either with heparin or other oral anticoagulants is usually required in most cases, whilst in others, endovascular administration of thrombolytic agents maybe indicated. In selected cases endovascular and other surgical techniques have been used to remove the clot. In extreme cases decompressive craniectomy maybe necessary. Prognosis is highly variable, but recurrence of thrombosis is particularly high inpatients with known risk factors.

7.14.2 Cavernous Sinus Thrombosis

This is a rare infective disease. It continues to have a high mortality, despite widespread availability of antibiotics. Significant morbidity includes residual cranial nerve palsies and blindness. Early diagnosis is essential and the possibility of CST should be considered in any patient who presents with sudden proptosis, accompanied by erythema, chemosis, diplopia and a headache.

The cavernous sinus is trabeculated and as such acts as a sieve, filtering bacteria and thrombi from diverse sources (such as the maxillary sinus, midface and orbits) CST is

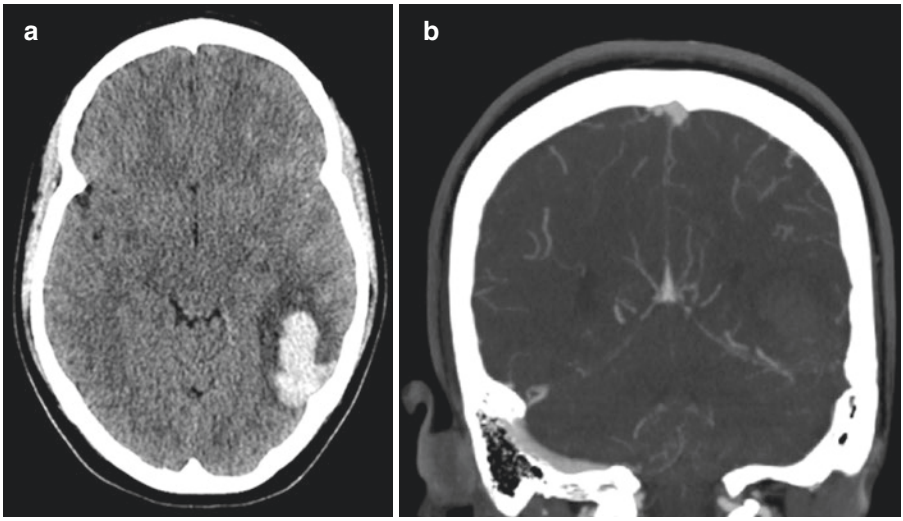

Fig. 7.21 CT brain of Left temporo-parietal ICH and CT venogram demonstrating occlusion of left sigmoid sinus by thrombus

most commonly a septic (infected) thrombosis that develops within the cavernous sinus. This may result from any infection of the tissues drained by the cavernous sinus, such as the face, tonsils, soft palate, teeth and ears. The commonest reported organism is methicillin-resistant *Staphylococcus aureus* (MRSA), followed by MSSA. However various streptococci, other staphylococci, oral anaerobic flora, and gram-negative organisms have also been reported. Fungal infections (Aspergillus fumigatus) are rare but are seen in immunocompromised patients, such as diabetes, haematological malignancies, those taking immunosuppressants, or patients who have had a bone marrow transplant. Not surprisingly prognosis is poor in this immunocompromised group.

Most commonly infection arises from an initial focus of infection in the face (usually the orbital, notably orbital cellulitis), but can also arise from paranasal sinus infection (ethmoiditis). At these sites (i.e. the central midface) the venous drainage communicates directly with the cavernous sinus. Infected emboli can freely pass into the sinus, since the facial, angular, ophthalmic and pterygoid plexus of veins do not possess valves. Thrombosis can then spread into other venous sinuses resulting in subdural empyema or meningitis. Infective endocarditis and extension of thrombosis to the internal carotid artery (which passes through the sinus) are rarer causes. Clinical features include

1. Systemic upset: fever, tachycardia and sweating
2. Facial or peri-orbital pain
3. Signs of Venous obstruction—eyelid oedema, chemosis, dilated conjunctival vessels
4. 'Pulsating exophthalmos' a transmitted carotid pulse with periorbital oedema (Fig. 7.22)
5. Blindness with papilloedema and retinal haemorrhages
6. Ophthalmoplegia: classically CNVI first followed by CNIII and IV

Imaging studies, such as contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) have had a significant impact on the diagnosis of CST in recent decades. High-resolution contrast-enhanced CT or MRI is useful in the assessment of suspected cavernous sinus thrombosis. This may reveal the primary source of infection, thickening of the superior ophthalmic vein, and irregular filling defects in the cavernous sinus. However, MRI is more sensitive than CT in the detection of septic CST because it can visualise the blood vessels better. Blood tests include inflammatory markers and coagulation studies. These patients are generally very unwell and the prognosis is often quite poor. The current consensus on treatment is that it should include high-dose intravenous antibiotics directed at the most likely pathogens together with surgical drainage of the original source of infection (usually the paranasal sinuses). Antibiotics should be continued for at least 2 weeks beyond the time of clinical resolution. This has been suggested to be necessary because the bacteria sequestered within the thrombus may not be killed until the dural sinuses start to recanalise. The role of corticosteroids and anticoagulants in treatment is unclear. Surgery to the cavernous sinus itself is difficult and not recommended.

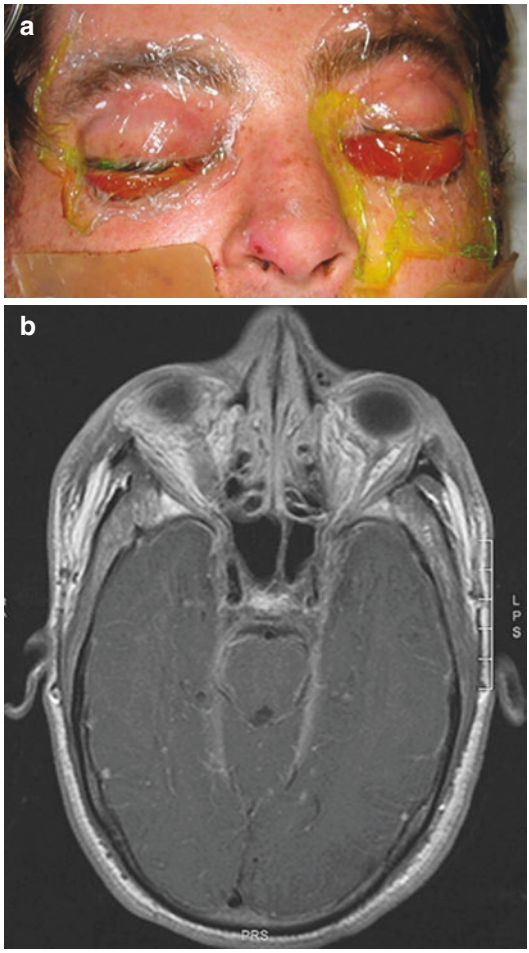

Fig. 7.22 (**a**, **b**) Cavernous sinus thrombosis from methicillin-resistant. *Staphylococcus aureus* (MRSA). The patient was a previously healthy man who suffered a minor injury to the skin next to the right nostril 3 days earlier. (**a**) Examination showed bilateral ophthalmoplegia, proptosis, and a right nasal skin lesion. (**b**) Magnetic resonance imaging (MRI) demonstrated enhancement of the cavernous sinuses and prominence of the right superior ophthalmic vein, suggesting early thrombus formation. Reproduced from Munckhoff et al., with permission from John Wiley and Sons

7.15 Intracranial Tumours

A large number of CNS tumours and cysts exist which are both benign and malignant in nature. Even 'benign' tumours (ie non-metastasising) can be life-threatening by virtue of their mechanical pressure effects within a confined space. Commonly tumours present with one or more of three symptoms:

- Raised intra-cranial pressure
- Progressive neurological deficit
- Epileptic fits

7.15.1 Primary Tumour Types

- Gliomas including astrocytoma, glioblastoma (Fig. 7.23), oligodendroglioma
- Pituitary adenoma

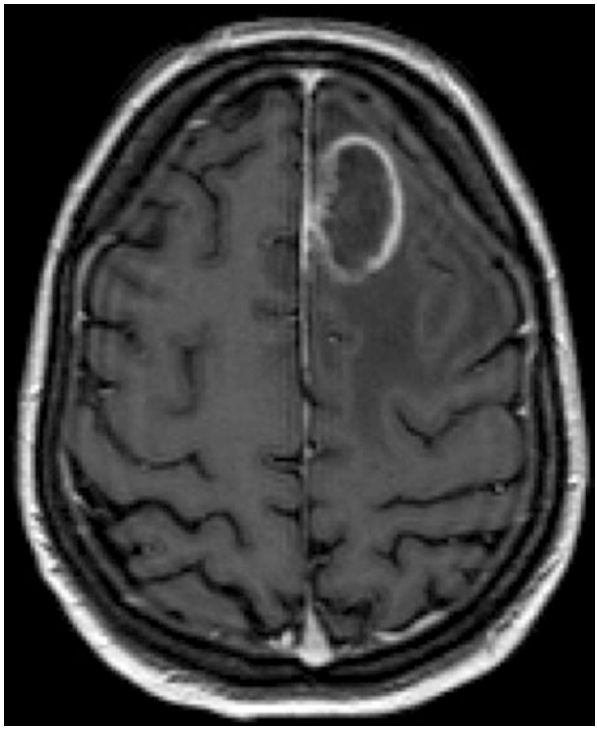

Fig. 7.23 Intracerebral tumour

- Craniopharyngioma (Figs. 7.24 and 7.25)
- Meningioma
- Acoustic neuroma
- Choroid plexus (Fig. 7.26)
- Pineal region (Fig. 7.27)
- Colloid cyst
- Primary CNS lymphoma (Fig. 7.28)
- Haemangioblastoma

In the presence of unexplained neurological symptoms urgent investigations are indicated. MRI scan is now the definitive investigation of choice, but CT scan, with and without contrast, is usually the first line investigation acutely. Malignant tumours are seen as irregular enhancing cystic or solid lesions, which usually show some degree of mass effect and surrounding oedema. The three commonest tumours are:

- Metastases. These are often identified as small round 'cannon ball' lesions. They are usually multiple and at the grey-white matter junction, most commonly in the MCA territory. Suspicious lesions require further investigation (CT chest/abdomen/pelvis). Sometimes it is easier to biopsy the primary source, rather than the metastasis (so long as the clinical evidence in favour of malignancy is strong).

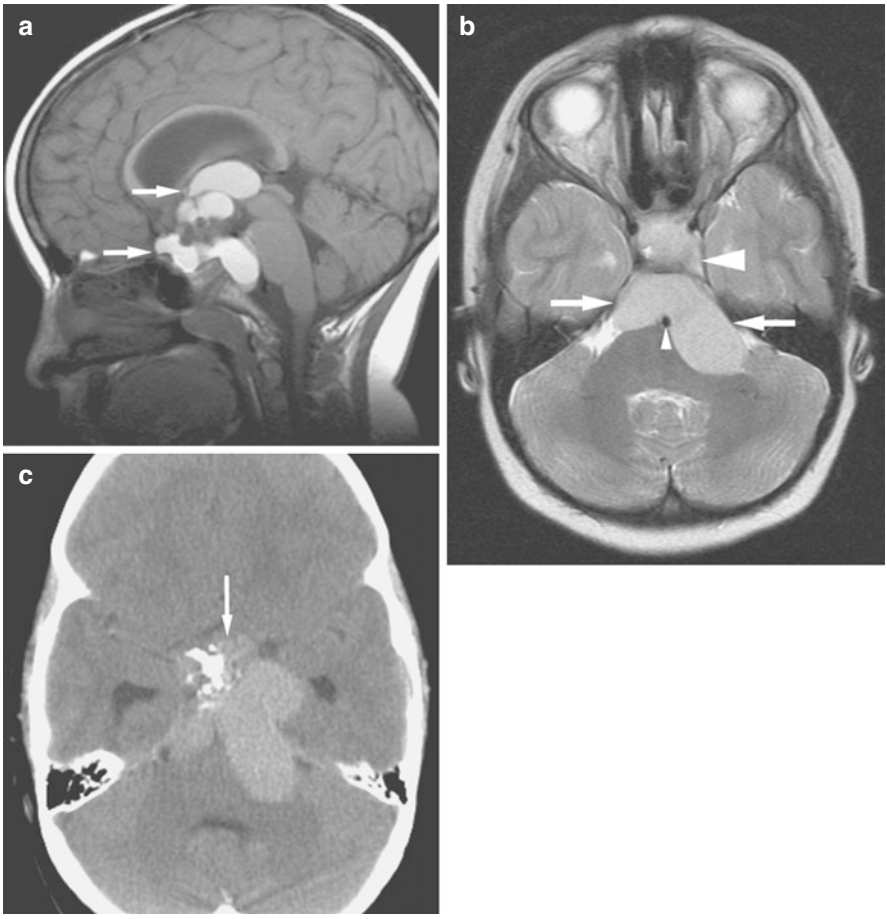

Fig. 7.24 Craniopharyngioma: 7-year-old female with history of longstanding headache. (**a**) Sagittal T1-weighted MRI shows a large lobulated sellar/suprasellar mass extending upwards to third ventricle and posteriorly into prepontine cistern (*arrows*). Most cysts show hyperintensity. (**b**) Axial T2-weighted MRI shows extension into cerebellopontine angles more to left (*arrows*) with left parasellar extension (*arrowhead*) and encasement of basillar artery (*small arrowhead*). (**c**) Axial CT shows eccentrically located calcification within a hyperdense lobulated mass at suprasellar region (*arrow*)

- Gliomas. These are primary neuronal tumours and usually appear as large irregular lesions with indistinct margins. Several grades of malignancy are described. Generally the prognosis is poor in high grade gliomas.
- Meningiomas. These arise from and are attached to the dura. Although usually benign if left untreated they can result in focal pathology and mass effects. They appear homogeneous on contrast enhancement.

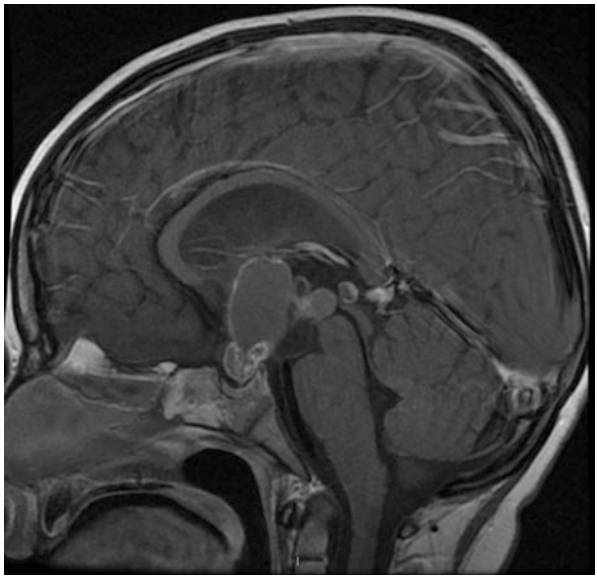

Fig. 7.25 Sagittal T1 MRI with gadolinium of craniopharyngioma

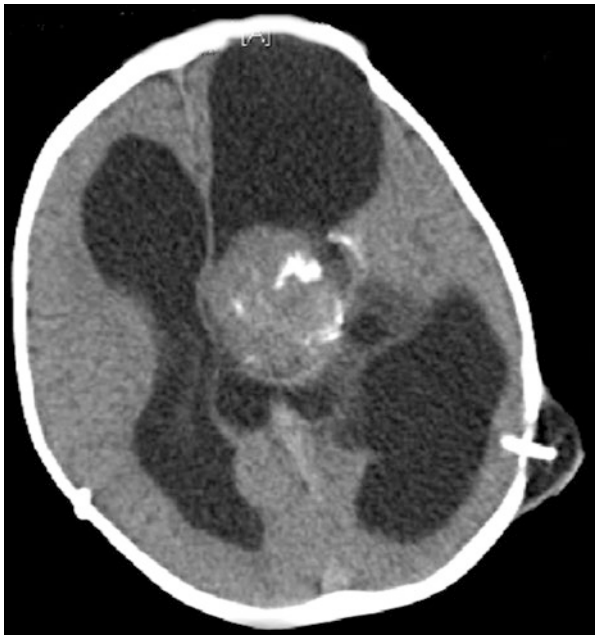

Fig. 7.26 T1 axial MRI showing choroid plexus tumour

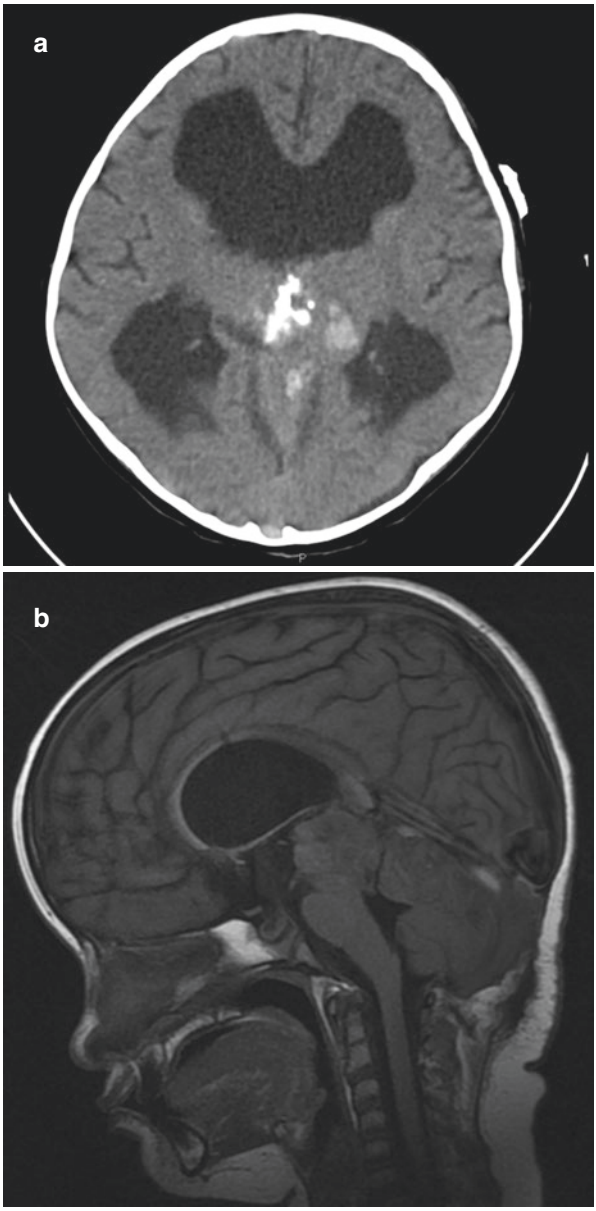

Fig. 7.27 t1 axial and sagittal MRI showing pineal region tumour

Chordomas are uncommon, but malignant tumours that arise from the remnants of the embryonic notochord (see chapter on embryology). Most occur in the sacro-coccygeal region, but around one-third occur in the skull base. These are found in the region of the spheno-occipital synchondrosis. Aberrant notochordal rests can occur in the clivus, vertebral bodies, nasopharynx, pharynx and spine. Thus chordomas can arise in any of these sites. There is still some debate about whether some chordomas

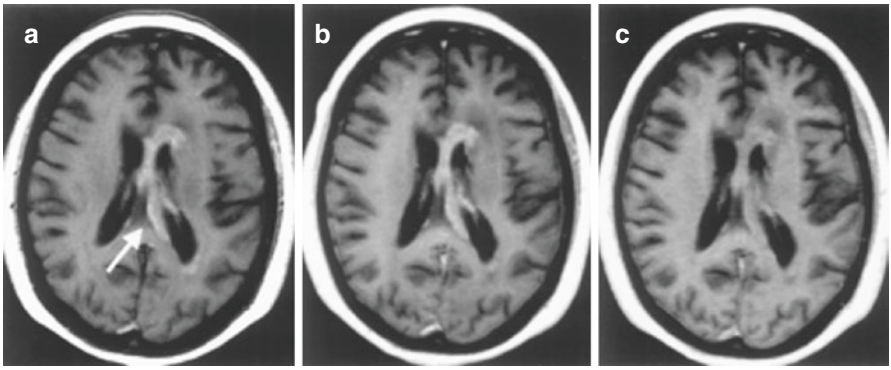

Fig. 7.28 t1 axial MRI showing primary CNS lymphoma

are chondroid variants of chordoma or true chondrosarcoma. Ideally these should be resected, but this is not always possible and multiple recurrences are common. Proton beam stereotactic guided radiosurgery has greatly improved survival. Conventional external beam radiation is not as effective.

Management of other cerebral tumours depends on their site, size and specific pathology. The age and general health of the patient is also a key determining factor. Some tumours are deep seated and effectively incurable. In such cases heroic treatments may leave the patient with significant morbidity and with little benefit. In other cases tumours may be small, superficial and detected early. Surgery and/or chemoradiotherapy may then be indicated. Management principles include

1. Urgent neurosurgical referral. Whenever possible, excision of the tumour is the preferred treatment. However, this may not be possible due its site, extent or nature, or because the patient is too frail. In these cases a biopsy or debulking may be performed, or a palliative course of management may be indicated.
2. Steroids to reduce oedema—typically dexamethasone 4 mg, four times daily is prescribed, with gastric protection (proton pump inhibitor). Rarely, if the patient is rapidly deteriorating, intravenous mannitol and megadose dexamethasone should be given pending neurosurgical transfer and emergency surgery.
3. Anticonvulsants should be prescribed if the patient has a history of fits. Some neurosurgeons advocate prophylactic anticonvulsants even in the absence of seizures.
4. In high grade malignant tumours, patients will usually require adjuvant therapy with radiotherapy with or without chemotherapy. Currently ongoing advances in this field are based on molecular profiling of tumours.
5. More recently, Gamma Knife radiosurgery (GKRS) is being considered as a first line of treatment in a number of malignant and benign intracranial diseases, including some astrocytomas. This has shown promising results and can avoid the need for risky neurosurgical resections with deep-seated tumours and toxic side effects of chemotherapy. Morbidity is often less then 5%. However, the effectiveness of GKRS is not known for all tumours.

7.15.2 Meningiomas

Meningiomas are a diverse group of tumours arising from the arachnoid cells of the meninges (Fig. 7.29). They account for up to a quarter of all intracranial tumours. Many produce no symptoms at all and if discovered by chance require no treatment other than follow-up and serial CT scanning. Although these are usually benign in nature, a small percentage of meningiomas can become malignant. Surgery is still the treatment of choice in symptomatic cases, particularly when the tumour infiltrates the skull base or vascular structures. However complete resection may not be possible without significant morbidity and mortality. Debulking may then be indicated for symptomatic cases (e.g. proptosis following orbital infiltration).

Meningiomas may be discovered purely by chance when the patient undergoes a head CT scan or MRI of the head for some other reason. The most common ones originate along the cerebral convexities. However patients may present with

1. Focal seizures
2. Progressive weakness or sensory disturbance
3. Aphasia
4. Raised intracranial pressure
5. Diplopia or unequal pupils

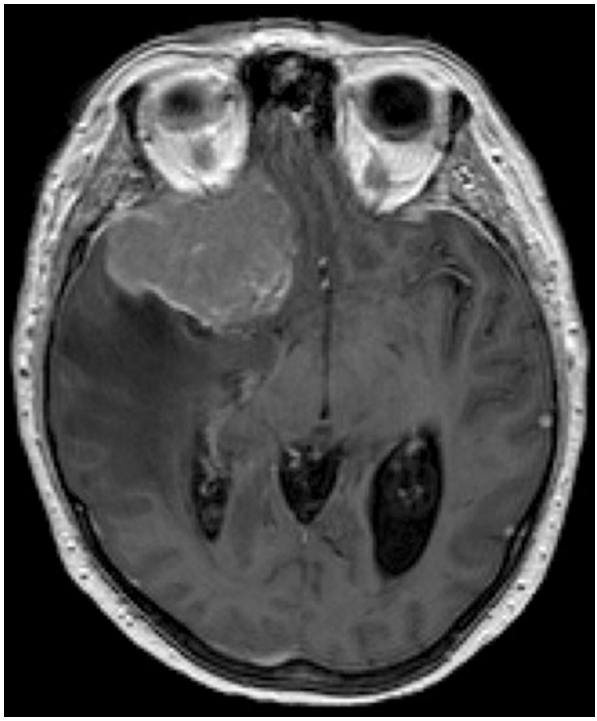

Fig. 7.29 T1 MRI with contrast showing sphenoid wing meningioma

Some tumours can invade into the adjacent bone (intra osseous meningioma). This commonly occurs in the orbital region (greater wing of sphenoid), resulting in diplopia, orbital dystopia and vision-threatening proptosis. Similar symptoms can occur with cavernous sinus meningiomas (Fig. 7.30). Involvement of the orbital apex can also result in pressure on the optic nerve with eventual loss of sight. Meningiomas arising entirely outside of the CNS are rare. However extracranial meningiomas can occur in the calvarium, scalp, orbit, nose, paranasal sinuses, middle ear and infratemporal fossa. Lesions of the cheek, neck, and parotid have even been reported. Most extracranial meningiomas are simply extensions of the intracranial component, such as those arising from the skull base. Others occur as a result of growth along nerve sheaths, such as the optic sheath meningioma. Rarely some are metastases from malignant varieties. Ectopic extracranial meningiomas can arise in the nests of arachnoid cells which were deposited in extracranial sites during the early stages of neural tube closure. Such ectopic clusters may be found along the optic nerve, trigeminal nerve and where cranial nerves III, VII, and IX–XII penetrate the dura. Most involve the orbit, basal skull and upper sinonasal region.

The causes of meningiomas is not known. Most cases are sporadic, although some are familial. Radiation and a history of head trauma appear also to be predisposing factors. Patients with neurofibromatosis type II have a 50% chance of developing one or more meningiomas, suggesting a genetic basis to the disease (possibly chromosome 22q). Although predominantly intracranial, meningiomas may also occur in the spinal canal.

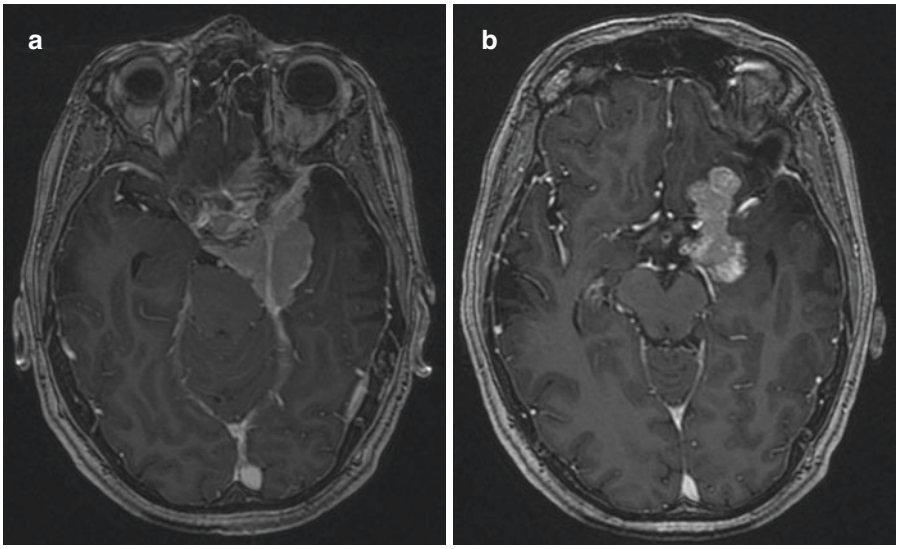

Fig. 7.30 T1 MRI with contrast showing cavernous sinus meningioma

Diagnosis is usually made the following contrast CT or MRI. The WHO classification system grades meningiomas as.

1. Benign (Grade I)
2. Atypical (Grade II)—this includes brain invasion. The mean survival is approximately 12 years
3. Anaplastic/malignant (Grade III). Mean survival is approximately 3 years.

In many cases treatment is not required if there are no symptoms and the patient can be kept under follow-up with regular imaging. However this is generally not recommended if the tumour is causing symptoms, or there are concerns regarding its precise nature. Many tumours can be removed surgically, if their location and size is favourable. Although many are confined to the dural region, intra osseous meningioma can infiltrate the bone widely, making total resection impossible. Radiation therapy may then be indicated with, proton-beam or fractionated external beam radiation. This may also be indicated in small tumours which are surgically inaccessible, or in patients who are unfit for surgery. Radiation may also be considered if there has been incomplete resection of a tumour or recurrence of a high grade tumour.

7.15.3 Astrocytoma (glioma)

Astrocytomas (also referred to as gliomas) originate in the glial cells, or astrocytes. They are the commonest glioma and can occur in most parts of the brain. They rarely arise within the spinal cord. Several subtypes exist, but these are often simply referred to as low or high-grade, the latter carrying the worst prognosis. Astrocytomas can develop at any age and do not metastasise. Low- grade tumours are more often found in children or young adults, while high-grade tumours are more common in adults.

Astrocytoma causes symptoms as a result of compression, invasion and eventual destruction of the brain parenchyma. Secondary symptoms may be caused as a result of mass effects or obstruction to CSF circulation and raised intracranial pressure. Tumours are usually identified following CT scan or MRI, both of which may be required to define the size, location, vascularity of the lesion, and any secondary effects on the ventricles. These are important in planning surgery. Most tumours will require a biopsy to confirm the diagnosis and determine the grade of lesion. The World Health Organization (WHO) grading system is based on four histological grades from I to IV, with I being the least aggressive (Fig. 7.31) and 4 (Fig. 7.32) being the most aggressive. High grade astrocytoma (grade IV) is the most common primary nervous system cancer and the second most frequent brain tumour, after cerebral metastasis.

Management of astrocytomas often requires surgery and radiotherapy. With low grade astrocytomas, excision of the tumour may allow patients to survive for many years. In some reports, the 5-year survival has been around 90%. However this often

comes with a risk of residual neurological deficit, depending on the location of the tumour and the amount of brain tissue resected. Complete resection of high grade astrocytomas is often not possible due to their widely infiltrative nature. These inevitably recur following treatment (both surgery or radiotherapy).

Glioblastoma (WHO grade IV) is the most malignant type of tumour. It is the most common primary brain tumour and typically affects the older age group, with a slight male predominance. These tumours are sometimes divided into primary and secondary, depending on whether they arise de novo (primary), or start out as a less malignant tumour (secondary). These tumours are commonly found in the

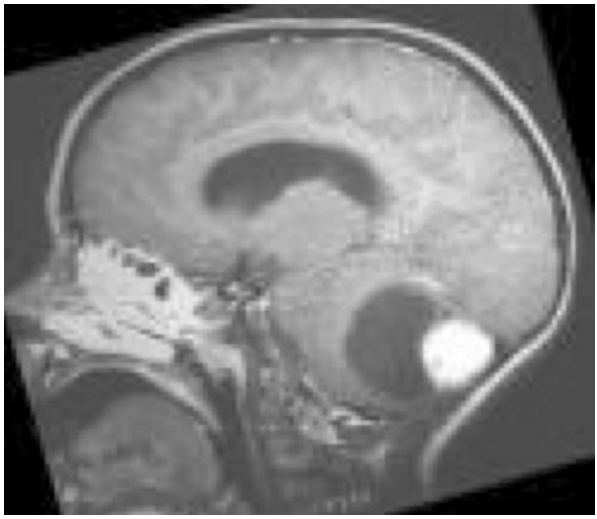

Fig. 7.31 T1 sagittal MRI with gadolinium showing a cerebellar pilocytic astrocytoma

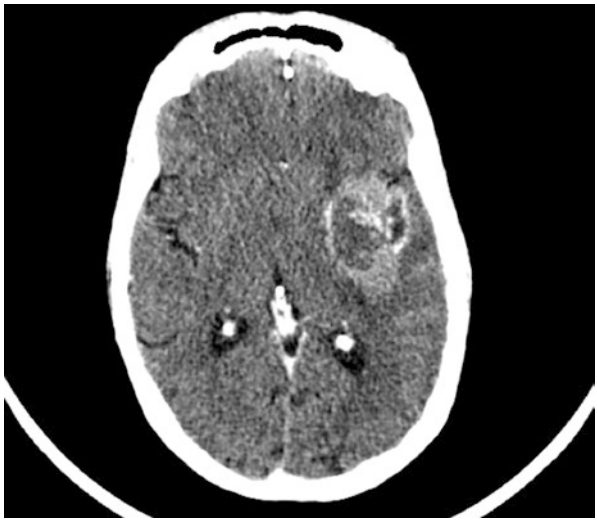

Fig. 7.32 CT with contrast of left peri-sylvian glioblastoma

sub-cortical white mater but they can also spread through the corpus callosum and present as a "butterfly glioma". Current treatment follows the 'Stupp protocol' which was published in 2005. This includes a maximal safe surgical resection followed by conformal external beam radiotherapy with adjuvant temozolamide. However there is no consensus on the treatment of recurrent Glioblastoma with clinical trials currently in progress. Immunotherapy may have a role.

7.15.4 Pituitary Adenoma

The pituitary gland (hypophysis), is an endocrine gland about the size of a pea. It is located at the base of the brain, just behind the optic chiasma. The gland rests in the midline hypophyseal fossa of the sphenoid bone (sphenoid fossa or sella turcica) in the middle cranial fossa. The anterior pituitary (adenohypophysis) regulates several important physiological processes (including stress control, growth, reproduction and lactation). The posterior pituitary gland (neurohypophysis), produces ADH (antidiuretic hormone). All these hormones are important in growth, maintenance of blood pressure, functioning of the sex organs, thyroid glands and metabolism, as well as many aspects of pregnancy and childbirth. They also control water/salt concentration within the kidneys, temperature regulation and pain relief. Not surprisingly then, disturbance of the gland can result in a wide range of complex disorders.

Pituitary tumours are relatively common and are mostly adenomas (Fig. 7.33). These are benign, slow-growing tumours, which originate from one of its specialised cells. If the tumour produces an excess of one or more hormones, it is called a "functional" adenoma. Examples include (i) prolactinoma, (ii) growth hormone secreting tumour (resulting in acromegaly in adults or gigantism in children), and (iii) cortisol secreting tumours resulting in Cushing's disease. Nonfunctioning adenomas can also occur.

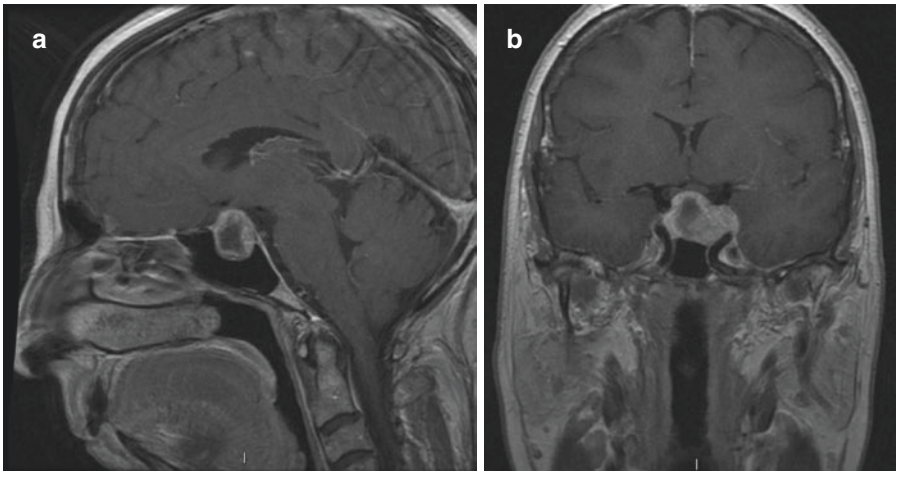

Fig. 7.33 Sagittal and coronal T1 MRI with gadolinium of pituitary macroadenoma

Microscopic pituitary adenomas are reported to occur in about one in five adults. These are often discovered following MRI of the head for some other reason. However, the majority of these will never grow or cause symptoms. Rare tumours include (i) Atypical pituitary adenoma, which grows quickly and is more likely to recur (ii) Pituitary carcinoma, a malignant variant which can metastasise (iii) Multiple endocrine neoplasia type 1 (MEN 1), which is characterised by simultaneous tumours of the pituitary, pancreas and parathyroid glands. Pituitary adenomas develop in 25 percent of patients with MEN 1.

Clinical features can be considered as a result of mechanical effects and whether hormones are secreted. They can therefore vary. Large tumours can compress the optic chiasm, resulting in bitemporal hemianopia. Hormone-producing adenomas can produce symptoms related to the hormones released (notably Prolactin, Growth hormone, ACTH, TSH). Very large tumours can compress the remaining gland resulting in pituitary failure. This can present as decreased sexual drive, impotence, loss of body and facial hair, infertility, hypothyroidism, fatigue, low blood pressure, electrolyte abnormalities. If severe, this can be fatal. Diagnostic tests include hormone assays and imaging (MRI).

Treatment depends on several factors, including:

1. Hormone production by the tumour
2. Tumour size
3. The extent that the tumour has invaded surrounding structures
4. Patient's general health

Hormone-producing adenomas can sometimes be treated medically. Prolactinomas may not require surgery. Medication also plays an important role in managing the symptoms of Cushing's disease and acromegaly. Surgical management now involves minimally invasive endoscopic techniques. Tumours are removed endonasally. Very large tumours may require a craniotomy. Radiotherapy is reserved for large, non resectable or high grade tumours.

Ectopic pituitary tissue is rare and related diseases are also rare. Because the anterior lobe of the pituitary develops as an invagination of endoderm from the developing nasopharynx (Rathkes pouch), residual cells can deposit along its path of migration. This can result in functioning glandular tissue or tumours anywhere from the nasopharynx to the suprasellar cistern. Cystic change can also occur and is normally asymptomatic, being discovered by chance. This is usually found in the mucoperiosteum of the roof of the nasopharynx, where the vomer attaches. Pituitary adenomas sited within the nasopharynx are usually downward extensions of lesions arising in the pituitary fossa. Invasive pituitary adenomas can occasionally invade the nasopharynx, ethmoids and nasal cavity. Others can extend to the cavernous sinus. If very invasive, these these can involve much of central skull base. Pituitary carcinomas also show locally invasive features, but will also metastasise. Treatment may be surgical resection and/or chemoradiotherapy, depending on the nature and extent of the lesion.

7.16 Sudden Disturbance in Cerebral Function

Like lethargy, a sudden disturbance in cerebral function can have many causes, many arising outwith the CNS. This can take many forms, such as changes in behaviour and the development of an acute confusional state ('delirium')—characterised by an acute fluctuating impairment of cognitive functions and inattention. Delirium may be the result of a variety of systemic or cerebral diseases or from drug intoxication or withdrawal. Investigations may include a full blood count, biochemistry (serum sodium, potassium levels and blood sugar), liver, renal and thyroid functions, arterial blood gas analysis, chest X-ray, ultrasound abdomen, CT brain and cerebrospinal fluid (CSF) analysis. Further details of the assessment of an acute confusional state fall outside the scope of this book, but it should be noted that some (such as hypoglycaemia and alcohol withdrawal) can be fatal if not treated. Treatment is directed towards the underling cause, some of which have been previously discussed. From a more 'intracranial perspective' sudden disturbances in function can arise form a temporary or permanent disruption in neural physiology. Perhaps the best examples of this are CNS infections, stroke, epilepsy and concussion, although other causes exist. Acute confusional migraine has also been described. This is a migraine variant that manifests with acute confusion, agitation, disorientation, altered mental status, speech difficulties and memory deficits.

7.16.1 Epilepsy

Seizures ('fits') can result from wide variety of disorders, some of which are intracranial in nature, whilst others are extracranial. Epilepsy is a type of seizure but is not a single condition. It is characterised by abnormal, recurrent, and excessive neuronal discharges within the central nervous system, which can be precipitated by a variety of causes. The seizures often occur spontaneously, usually resulting in loss of consciousness, with sensory and motor deficits. Underlying causes include a genetic predisposition, structural or metabolic problems. Common causes of seizures include

- Genetic and various rare syndromes
- Brain tumours
- Stroke
- Head injury
- Toxic ingestion/Chronic alcohol abuse/withdrawal
- Metabolic disorders
- Infections of the central nervous system such as meningitis/encephalitis
- Cerebral arteriovenous malformations
- Tuberous sclerosis
- Autoimmune encephalitis
- Hypothalamic hamartomas.

In many cases the cause is not found. Although the disease can occur at any age, the age at the time of onset of seizures is often associated with specific causes.

1. Infants—complications during birth, anoxia, intracranial injury, metabolic disorders, and congenital malformations.
2. Children and adolescents—trauma and febrile infections.
3. Young adults—alcohol or drug abuse.
4. Older adults—cerebrovascular disease and tumours.

Various classifications exist, but a descriptive classification is the most useful. Seizures are divided into generalised and those that affect only part of the brain (partial seizures). Simple partial seizures originate from a discrete area of the brain. Typically they do not result in loss of consciousness. However, complex partial seizures (referred to as temporal lobe or psychomotor) are associated with impairment in consciousness. The majority of generalised seizures are either 'absences' (petit mal) or tonic-clonic seizures—('grand mal'). The remaining seizures (myoclonic or infantile, and clonic, tonic, and atonic) usually occur in childhood. These have a poorer prognosis with regards to childhood development. "Status epilepticus" refers to recurrent seizures without recovery between them. This is a medical emergency. All seizures are at risk of progression to status epilepticus.

Clinically, nonspecific symptoms such as headache, a change in mood or lethargy may herald the onset of an impending seizure. These are distinct from the aura that occurs just before a generalised seizure. The most common type of seizure is the tonic-clonic, or grand mal seizure. About 90% of epileptics experience this at some point during their illness. This begins with an 'aura'—an emotional feeling or hallucination (hearing, vision or smell) which is quickly followed by sudden unconsciousness and spasms. This is the 'tonic' phase, which lasts about 30 s. Because of the muscle spasm, the patient usually falls to the ground and becomes cyanosed. The tonic phase is then followed by a clonic phase, in which the patient undergoes jerking movements (convulsions), incontinence and tongue biting. This can last a few minutes. Following this, a postictal state develops, during which the patient slowly recovers. The patient may be confused, lethargic and occasionally develop a focal but temporary neurological deficit.

Petit mal or 'absences' are the second most common type of seizure. These occur mostly in children and often resolve during their teen years. A typical seizure lasts just a few seconds. There is no aura, or tonic-clonic phase. Instead the patient loses awareness, becomes 'vacant' and appears to stare into space. Many continue normal activities immediately after the seizure has finished, unaware it has occurred. Petit mal attacks may occur several times a day. Severe cases may interfere with school and social activities. Around 50% of patients develop tonic-clonic seizures at puberty.

Diagnosis of epilepsy is usually made based on the description of the seizure. More than one is necessary to make a diagnosis. Following a first seizure of any kind, all patients should be referred to a specialist for investigation. Patients should be screened for acute problems such as low blood glucose, metabolic conditions,

sepsis, toxins, withdrawal states, and stroke. Blood glucose, electrolytes, calcium, thyroid hormone, electroencephalography and CT or MRI may all be required to rule out metabolic or structural causes. Brain lesions commonly associated with epilepsy include cortical malformations, gliosis, vascular disorders, and small tumours. In addition, magnetic resonance spectroscopy (MRS), functional MRI (fMRI) and Diffusion MRI may be used to measure metabolic activity and involved visualise key areas. Positron emission tomography (PET) and single photon emission computed tomography (SPECT) can also help map physiochemical brain processes and brain perfusion patterns.

Once fitting has been controlled management involves investigations for underlying treatable causes and prevention of further seizures. During a seizure, rolling the patient onto their side and into the recovery position helps prevent aspiration and injury. If a seizure lasts longer than 5 min this should be considered as status epilepticus. The airway should be protected and midazolam or a suitable alternative given. Once the patient is stabilised treatment then involves use of anticonvulsant medication, preferably under the supervision of a specialist. A number of medications are available (such as phenytoin, carbamazepine and valproate). The choice of drug depends on the type of seizure to be treated. Drug treatment is continued until there have been no further seizures for at least 3 years. In some patients surgery may be indicated to control persistent focal seizures. Mesial temporal lobe epilepsy (MTLE) is a common cause of medically intractable epilepsy. This may be treated with temporal lobectomy. Gamma Knife stereotactic radiosurgery is an alternative to surgery. This appears to be quite promising.

First seizures should be reported to the Driver and Vehicle Licensing Agency (DVLA) in the UK or the equivalent body internationally. Currently in the UK, if the first seizure is unprovoked, investigations are normal, and no neurological deficit is present, driving can usually be permitted after 6 months. Otherwise, driving is usually permitted after 12 months of being seizure free. Commercial licences are subject to more stringent regulation.

7.16.2 Vertigo

Vertigo is the subjective feeling that one is moving when they are not, often described as spinning or swaying. This may be associated with nausea, vomiting and unsteadiness. It is typically worsened when the head is moved. The condition is classified into peripheral or central, depending on the location of the underlying dysfunction. Common causes are benign paroxysmal positional vertigo, Ménière's disease, and labyrinthitis. These are described in the chapter on the Ear. Less common central causes include stroke, brain tumours, trauma, multiple sclerosis, and migraine. Rare causes may include carbon monoxide poisoning, alcohol and aspirin.

7.16.3 Central Vertigo

Vertigo that occurs as a result of a disorder within the brainstem or cerebellum is called central vertigo. Vestibular migraine is the association of vertigo and migraines. The cause of this is not known, but it has been suggested to arise as a result of stimulation of the trigeminal nerve in migraine sufferers. Other possible causes include imbalanced vestibular nuclei activity in the brainstem, or vasospasm of the central vestibular pathway vessels. CNS infarctions/haemorrhage, cerebellopontine angle tumours, epilepsy, cervical spondylosis, degenerative disorders, migraine, multiple sclerosis and parkinsonism can all result in central vertigo. Patients may also have accompanying neurologic deficits (such as slurred speech and double vision), and nystagmus. Central vertigo can last along time. In some patients it may not resolve. If a central cause is suspected CT or MRI is indicated, to identify strokes and tumours. Treatments include anticholinergics, anticonvulsants, antihistamines, beta blockers and corticosteroids.

7.16.4 Multiple Sclerosis (MS)

This a chronic inflammatory autoimmune demyelinating condition which affects the myelin sheaths of the nerves in both the brain and spinal cord. Onset is usually during young adulthood. Due to its random distribution of CNS involvement, this gives rise to a wide range of neurological signs and symptoms. The disease is classified into several clinical types.

1. Primary progressive—in this form symptoms steadily get worse.
2. Progressive relapsing—This is characterised by a steady functional decline with later superimposed acute attacks.
3. Relapsing remitting—This is the most common form (85% of cases). Patient's are affected in distinct episodes which completely resolve. In between attacks, patients have no worsening of symptoms.
4. Secondary progressive—here the symptoms only partially resolve. There are no acute attacks.

The primary cause of MS is inflammation of central nervous system. Both T cells, and B cells and their products appear to be involved in the pathogenesis resulting in loss of oligodendrocytes. Where myelin is lost, a neurone can no longer effectively conduct electrical signals. Autopsy studies have shown multiple, discrete pink or grey rubbery plaques within the white matter. These are composed of areas of myelin and oligodendrocyte loss, with infiltrates of inflammatory cells and scar tissue. Relative preservation of the axons and neurones themselves within these lesions helps to differentiate MS from other disorders. What precipitates this is unknown,

although genetic, environmental and infectious agents have been suggested. A 40-fold increased susceptibility among first degree relatives of MS patients has been reported, possibly related to chromosomes 6p21, 10p15, 5p13, and 1p36. Sunlight exposure, deficiency in vitamin D, human herpes virus type 6, Epstein Barr virus, and mycoplasma pneumoniae have also all been implicated, although the mechanisms by which they act are still unknown. Proposed mechanisms include the hygiene hypothesis and the prevalence hypothesis.

1. The hygiene hypothesis—exposure to certain infectious agents early in life is protective, the disease being a response to a late encounter with such agents.
2. The prevalence hypothesis—the disease is due to an infectious agent more common in regions where MS is common and where in most individuals it causes an ongoing infection without symptoms.

Diagnosis should be suspected whenever two distinct episodes of neurological symptoms are separated by both anatomy and time. Common symptoms include changes in vision (unilateral visual loss, diplopia), weakness, dyscoordination, sensory loss or distortions, or changes in bowel and bladder function. Less common symptoms include cognitive change, fatigue, and mood disturbance**.** Progression of MS can eventually result in severe disability. Plaques of demyelination can be seen on MRI scans. No single diagnostic test exists for MS. Evidence for a viral cause include the presence of oligoclonal bands in the brain and cerebrospinal fluid of affected individuals. Currently to make a diagnosis of MS there must be

1. evidence of damage in at least two separate areas of the CNS (brain, spinal cord, and optic nerves).
2. Symptoms must last for more than 24 h.
3. evidence that the damaged areas developed at least 1 month apart.
4. exclusion of all other possible diagnoses.
5. MRI evidence (the most sensitive imaging test for MS).
6. a positive spinal tap for oligoclonal bands.

Treatment aims to prevent relapses and progression. Medication in relapsing forms targets different parts of the immune system to avoid further inflammation. However they do not cure the disease or reverse existing damage. These include interferon β analogs, monoclonal antibodies, cytotoxic drugs and steroids. Other drugs are undergoing phase II and III trials.