Syphilis

23

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Syphilis is a chronic and systemic sexually transmitted disease (STD) caused by *Treponema pallidum* (TP). It mainly spreads via sexual contact, blood, and vertical transmission. The disease has extremely complex clinical manifestations, involving nearly all organs in the human body. During its early stage, syphilis invades the genitals and the skin, while during the late stage, the cardiovascular system, nerve, skeleton, eyes, and other organs. Syphilis can be transmitted to fetus via placenta of infected mother, which is hazardous to human health.

23.1 Etiology

In 1905, Schaudinn and Hoffmann discovered *Treponema pallidum* (TP) in the primary lesion of a patient with syphilis. TP is also known as treponema pallor, which is categorized into the genus of *Treponemas*, the family of treponemas, the order of spirochete. The thallus of TP is slim with its length ranging from 5 to 20 μm (a mean length of 6–10 μm) and its transverse diameter being about 0.15 μm. The thallus has an even arrangement of 6–12 spirals and is invisible to the naked eyes. And only its refractivity can be observed by dark-field microscopy. TP is active, with moving patterns of spinning, crawling, and flexing. At the anterior part of TP, there are 4–6 flagella like fine fiber bundles, with curling endings. Without any impact from external factors, the spirals are regular in shape, with slow and regular motion. The commonly applied dyes fail to stain them, but the bacteria can be observed by dark-field microscopy or phase contrast microscopy. TP, an anaerobic microorganism, can survive and reproduce for a long period of time in the human body. And they can hardly survive in vitro, which can be rapidly killed by boiling, dryness, sunshine, soap water, and common disinfectants. However, it is cold tolerant, being capable of surviving 48 hours at 0 °C refrigerator, 3 days at 4 °C, and even being infectious at −78 °C for several years.

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23.2 Epidemiology

23.2.1 Source of Infection

Patient with syphilis is the only source of infection, and TP can be found in their skin lesions, blood, seminal fluid, and breast milk. Caries callosa in the cases of primary syphilis and syphiloderm in the cases of secondary syphilis contain large quantities of TP.

23.2.2 Route of Transmission

23.2.2.1 Sexual Contact

Sexual contact is the major route of transmission, accounting for about 95 % of all syphilis cases. It spreads via tiny injuries of skin and mucosa. The untreated patients are the most infectious during the initial 1–2 years after the infection, and their infectivity is decreasing along with the development of the disease. The patients with an illness course of above 4 years hardly transmit the disease by sexual contact.

23.2.2.2 Vertical Transmission

Infected pregnant woman can transmit the disease to her fetus via placenta to cause intrauterine fetus infection. It mostly occurs after 4 months of gestation, leading to fetus syphilis, abortion, premature birth, and stillbirth. It is

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generally believed that pregnant women with a shorter course of syphilis are at a higher risk of transmitting the disease to the fetus. Their infectivity is decreasing along with the development of syphilis. However, woman with syphilis for 2 years can still transmit the disease to her fetus via placenta.

23.2.2.3 Other Routes

TP can also spread via indirect contact. Occasionally, patients are infected via kissing, shaking hands, breast feeding, or contacts to secretions of the patients, contaminated clothes, or contaminated utensils by the patients with syphilis.

23.2.3 Susceptible Population

The high-risk populations of infecting syphilis include prostitutes, male homosexuals, and drug abusers. And male homosexuals have especially high risk of infection. Currently, an increasingly large population is infected with syphilis, with common occurrence in sexual workers, peasant workers, and senior citizens. Syphilis is the most commonly found in the age group of 20–50 years, who have active sexual behaviors. In addition to no congenital immunity against syphilis in human being, this age group is generally susceptible to syphilis regardless of gender.

23.2.4 Epidemiological Features

Syphilis is an endemic sexually transmitted disease throughout the world. According to WHO, about 12 million new cases of syphilis are reported all over the world each year, with common occurrence in South Asia, Southeast Asia, and Africa. In Southeast Asia, the most new cases are reported each year, with its peak incidence age at 15–30 years and with no significant difference between males and females. In the early stage after the People's Republic of China was founded, syphilis was the major sexually transmitted disease, with more occurrence in residence areas of minorities than that in urban areas. With implementation of a series of control measures, sexually transmitted diseases were basically eradicated in China during the 1960s. However, after the 1980s, the incidence rate of syphilis has been increasing along with increasingly more international communications. By May 31, 2013, the yearly reported cases of syphilis was 189,559 in China, which increased by 0.7 % compared to the reported cases of the previous year (totally 188,321 cases). The geographic region with incidence of syphilis is increasingly large and the hazards caused by the disease are increasingly serious.

23.3 Pathogenesis and Pathological Changes

23.3.1 Pathogenesis

After TP gains its access into the human body via mucosa or skin defect, it invades the adjacent lymph nodes within several hours. After 2–3 days, it enters into the blood stream to spread throughout the body. After 2–3 weeks incubation period after its invasion into the human body, characteristic primary skin lesions form at the defected mucosa or skin, typically caries callosa. After that, antibodies are produced in the body. An experimental study on rabbits with syphilis has demonstrated that syphilis at the early stage is histologically characterized by mononuclear cell infiltration, with lymphocyte infiltration at day 6 after the infection. Meanwhile, TP can be found in the epithelial cell space of caries callosa and in the depressions or phagosomes of epithelial cells. Otherwise, TP can be found between the fibroblast plasma cells and the endothelial cells of tiny capillaries, in the lymphatic vessels, or in regional lymph nodes. Due to rapid elimination of TP from the lesions by immunity, most TPs are killed 24 days after the infection and the conditions develop into asymptomatic incubation period, namely, the primary incubation of syphilis.

23.3.2 Pathological Changes

23.3.2.1 Endarteritis Obliterans and Minor Perivascular Inflammation

Endarteritis obliterans refers to proliferation of endothelial cells and fibrocytes in arterioles, which leads to thickened vascular wall as well as stenosis and occlusion of vascular lumen. Minor perivascular inflammation refers to perivascular infiltrations of mononuclear cells, lymphocytes, and plasmocytes. And constant emergence of plasmocytes is one of the characteristic pathological changes in the cases of minor perivascular inflammation.

23.3.2.2 Syphilitic Gumma

Syphilitic gumma, also known as syphiloma, has grayish white lesions with different sizes. Under a microscope, the

structure of lesion can be observed like tuberculous nodule, with central coagulative necrosis. Morphologically, the lesion resembles to caseous necrosis. But necrosis of the lesion is incomplete, with preservation of elastic fibers. By staining of the elastic fibers, the outline of original vascular walls in the lesion can be observed. In the granulation tissue around necrosis, there are abundant lymphocytes and plasmocytes but rare epithelioid cells and Langerhans cells. Endarteritis obliterans and periarteritis definitely occur. At the late stage of syphilitic gumma, the lesion can be absorbed, with following occurrence of fibrosis, and finally develops into deformed organs but rare occurrence of calcification. Syphilitic gumma may involve any organ in the human body, commonly skin, mucosa, liver, bone, and testis. Lesions of vasculitis can be found at any stage of syphilis, while syphilitic gumma commonly occurs in the cases of tertiary syphilis.

23.4 Clinical Symptoms and Signs

23.4.1 Acquired Syphilis

23.4.1.1 Primary Syphilis

The common manifestations include caries callosa and sclerotic lymphadenitis, usually with no systemic symptoms.

Caries Callosa

Caries callosa commonly occurs about 3 weeks after the infection, with 90 % of the cases at external genital organs. During the early stage, the lesion is a red bean-sized hard nodule, which develops necrosis at its surface to form painless ulcers with accompanying edema. By palpation, hardness of the lesion touches like cartilage, with serous secretion at the surface, which is known as caries callosa. It contains a large quantity of TP, with strong infectivity.

Sclerotic Lymphadenitis

Sclerotic lymphadenitis occurs 1–2 weeks after emergence of caries callosa, commonly with unilateral groin or adjacent lymph nodes involved. The lesion is a hard protrusion, with no redness, swelling, and ulceration at the surface and being painless. It usually disappears after several months. By puncture of the lymph node, a large quantity of TP can be detected.

23.4.1.2 Secondary Syphilis

In the cases with untreated or incompletely cured primary syphilis, TP disseminates throughout the body along with the blood flow and local lymph nodes to cause skin and mucosa lesions as well as systemic lesions, which is known as secondary syphilis. It commonly occurs 7–10 weeks after the infection, or 6–8 weeks after emergence of caries callosa.

Skin and Mucosa Lesion

In patients with secondary syphilis, 80–85 % of the cases develop skin and mucous lesion. The common manifestations include syphiloderm, condyloma, syphilitic alopecia, and mucosa lesion.

Bone and Joint Lesion

Invasion of TP into the skeletal system can cause periostitis, arthritis, osteitis, osteomyelitis, bursitis, or tenosynovitis. And the periostitis is the most common, with common involvement of long bone. For instance, syphilitic periostitis is commonly found at the tibia, with manifestations of slightly thickened periosteum, subjective persistent dull pain, obvious tenderness, slight conditions during daytime, and physical activities and aggravated conditions at nights. Arthritis commonly involves shoulder, elbow, knee, hip, ankle, and other joints, which is usually symmetric with manifestations of articular effusion, articular swelling, and tenderness. The symptoms are slight during daytime and serious at nights.

Ocular Lesion

Ocular lesion is the most common in the cases of secondary syphilis and its incidence rate is low. The lesion is commonly caused by iritis, iridocyclitis, choroiditis, and retinitis, with adverse effect on vision in different degrees.

Neurological Lesion

The neurological lesion is mainly caused by asymptomatic neurosyphilis, syphilitic meningitis, and cerebrovascular syphilis. Asymptomatic neurosyphilis is only manifested by abnormalities of cerebrospinal fluid, and syphilitic meningitis can cause symptoms of intracranial hypertension, cerebral nerve palsy, and others. Cerebrovascular syphilis is commonly concurrent with syphilitic meningitis, mainly invading the cerebral artery to cause thickened vascular wall and vascular stenosis, which further lead to insufficient blood supply to the brain.

Multiple Sclerotic Lymphadenitis

The incidence of multiple sclerotic lymphadenitis is 50–80 %, with manifestation of systemically enlarged painless lymph nodes.

Organ Syphilis

Organ syphilis rarely occurs, which may involve the liver, kidney, bile duct, and gastrointestinal tract to cause syphilitic hepatitis, syphilitic nephritis, pericholangitis, and gastrointestinal lesions.

23.4.1.3 Tertiary Syphilis

Tertiary syphilis is also known as advanced syphilis, with a history of above 2 years. About 40 % of untreated patients or patients incompletely cured with early syphilis may experience the development of the conditions into tertiary syphilis after 3–4 years.

Skin and Mucosa Lesion

The manifestations include nodular syphiloderm and syphilitic gumma.

Bone Syphilis

Bone syphilis has the most common manifestation of periostitis, which is characterized by affected limb pain, periosteal proliferation, thickened diaphysis, and saber-shaped tibia in the cases with involved tibia. In the cases with osteomyelitis, osteitis, and arthritis, pathological fracture, osteoperforation, and joint deformity can be found.

Ocular Syphilis

The manifestations resemble to those of secondary syphilis, including iritis, iridocyclitis, retinitis, optic neuritis, interstitial keratitis, and other ocular lesions.

Cardiovascular Syphilis

Its incidence rate is 10 %, which commonly occurs 10–30 years after the infection. The manifestations include simplex aortitis, incomplete closure of aortic valve, stenosis of coronary orifice, aortic aneurysm, and myocardial gumma.

Neurosyphilis

Its incidence rate is 10 %, which commonly occurs 3–20 years after the infection. Neurosyphilis can be classified into several types, and the commonly found types include asymptomatic neurosyphilis, meningeal syphilis, meningovascular syphilis, brain parenchymal syphilis, and gumma neurosyphilis.

23.4.2 Congenital Syphilis

Congenital syphilis is also known as placenta transmitted syphilis, which is caused by spreading of TP from mother to the blood flow of the fetus via placenta and the umbilical vein. It can be categorized into early congenital syphilis, advanced congenital syphilis, and latent congenital syphilis. Congenital syphilis is characterized by no occurrence of caries callosa. The early lesions of congenital syphilis are more serious than those of acquired syphilis. Compared to acquired syphilis, congenital syphilis has rarer involvement of the cardiovascular system but more common involvement of the skeleton and sensory organs. Congenital syphilis may affect the growth and development of the infant. Otherwise, physical signs of congenital syphilis permanently remain.

23.4.2.1 Early Congenital Syphilis

Early congenital syphilis commonly occurs in infants at the age of less than 2 years. Patients usually experience premature delivery, with retarded growth, malnutrition, elderly like appearance, weak and hoarse crying voice, and restlessness. The skin and mucosa lesions resemble to those in the cases of secondary acquired syphilis. Perioral and perianal rhagades commonly occur, with formation of radiating shaped scars after healed, which are characteristically early congenital syphilis. Bone syphilis is relatively common, with possible manifestations of chondritis, osteomyelitis, periostitis, and syphilitic dactylitis, which further cause syphilitic pseudoparalysis, such as limbs pain and limited limbs activities. In addition, the common manifestations also include syphilitic rhinitis, systemic lymphadenectasis, hepatosplenomegaly, and meningitis.

23.4.2.2 Advanced Congenital Syphilis

It commonly occurs at the age of above 2 years, generally at the age of 5–8 years. Various symptoms consecutively occur at the age of 13–14 years, mainly invading eyes, teeth, and nervous system but rarely invading the cardiovascular system. In the cases of skin and mucosa syphilis, syphilitic gumma is common, while in the cases of bone syphilis, periostitis is common, with possible occurrence of saber-shaped tibia and Clutton joint. Neurosyphilis is mainly characterized by cranial nerve lesions, especially auditory nerves and optic nerves. In some rare cases, juvenile paralytic dementia and juvenile tabes can be found. In addition, parenchymatous keratitis, Hutchinson teeth, and nerve deafness are integratively known as Hutchinson triad.

23.4.2.3 Latent Congenital Syphilis

Latent congenital syphilis may be asymptomatic. Otherwise, the early symptoms are untreated but disappear. However, both cases are serologically detected positive for syphilis.

23.4.3 Latent Syphilis

The cases with a history of syphilis, no symptoms or disappearance of symptoms, serologically positive for syphilis but no other positive findings, and normal findings in cerebrospinal fluid examination are defined as latent syphilis. Its occurrence is related to strong immunity of the human body or temporary suppression of TP due to therapies.

23.5 Syphilis-Related Complications

Syphilis-related complications are commonly found in the cases of tertiary syphilis, which involve multiple organs with variant clinical manifestations. The common complications include bone syphilis, cardiovascular syphilis, and neurosyphilis.

23.5.1 Bone Syphilis

Bone syphilis is caused by infection of TP by bones and joints. Based on the route of infection and time of onset, bone syphilis is categorized into congenital and acquired. Congenital bone syphilis occurs due to spread of TP from the blood flow of mother into fetus via the placenta, which is divided into early onset and late onset. The cases with syphilis occurring in infants aged under 2 years is referred to as early congenital bone syphilis, while the cases with syphilis occurring in children aged above 2 years are referred to as late congenital bone syphilis. Acquired bone syphilis occurs due to sexual contact, blood contact, or other ways of contact.

23.5.1.1 Early Congenital Bone Syphilis

It is mainly manifested as metaphysitis, periostitis, and osteomyelitis, among which metaphysitis is more common. And its clinical manifestations are various, including skin rashes, large bullous or large flakes of desquamation, systemic lymphadenectasis, bone changes, and hepatosplenomegaly, among which skin rash and bone changes are more common.

23.5.1.2 Late Congenital Bone Syphilis

Late congenital bone syphilis is caused by reactivation of potential lesion after invasion of TP into fetal bone. Generally, its onset occurs in children aged 4–15 years, which is clinically characterized by keratitis, deafness, saddle nose sign, and saber tibia sign. In addition, it also leads to swelling of joint, difficulty walking, even developmental disorder, and hypophrenia.

23.5.1.3 Acquired Bone Syphilis

Its onset is caused by invasion of TP, along with blood flow, to bones, which commonly occurs in patients suffering from secondary and tertiary syphilis. The main symptoms include obvious local stabbing pain and tenderness, which may aggravate during rests. The serological test for syphilis is positive. The manifestation is commonly periostitis. And osteitis and osteomyelitis are also possible manifestations.

23.5.1.4 Syphilitic Arthritis

Both congenital and acquired syphilis can lead to syphilitic arthritis. In the early stage, the disease firstly involves synovium of joint, with manifestations of joint swelling and effusion as well as widened joint space. When the disease further develops to involve articular cartilage and destruct the bone under articular cartilage, the articular space is narrowed, with blurry, discontinuous, and absence of bony articular surface. In the cases with the epiphysis involved, the lesions develop toward the diaphysis, with extensive osteoproliferation and bone destruction.

23.5.2 Neurosyphilis

Neurosyphilis is a systemic chronic infectious disease caused by invasion of TP into the central nervous system, accounting about 10 % of the syphilitic cases. It is more common in young and middle-aged male adults. Neurosyphilis can be found at any stage of syphilis infection. Inappropriate and insufficient treatment of early syphilis is an important factor contributing to the occurrence and development of neurosyphilis. The disease can mainly be categorized into the following types.

23.5.2.1 Asymptomatic Neurosyphilis

It refers to the cases with positive findings by laboratory cerebrospinal fluid examination, such as positive VDRL in the cerebrospinal fluid, but no symptoms and signs related to the nervous system.

23.5.2.2 Meningeal Syphilis

Meningeal syphilis usually onsets 2 months to 2 years after the infection, with main manifestations of syphilitic

meningitis, which is clinically characterized by fever, headache, nausea, vomiting, psychiatric disorder, positive meningeal irritation sign, and manifestations of involved cranial nerve. And the commonly involved cranial nerves include the facial nerve and the vestibulocochlear nerve.

23.5.2.3 Meningovascular Syphilis

Its onset is usually 4–7 years after the infection, with typical manifestation of diffuse encephalitis complicated by focal lesions of the nervous system. Its early symptoms include changes of personalities, emotional change, changes of consciousness, and insomnia.

23.5.2.4 Brain Parenchymal Syphilis

Its onset is usually 4–7 years after the infection, which is more common in males, including paralytic dementia and myelophthisis. Paralytic dementia is manifested as diffuse parenchymal lesion of the cerebral cortex, with psychiatric and neurological changes. Myelophthisis is manifested as degeneration and atrophy of posterior root of spinal nerves and posterior column of spinal cords, with lightening pain of lower limbs, abnormal sensation, absent reflexes, and ataxia. The characteristic manifestations of brain parenchymal syphilis include absent lower tendon reflexes and deep sensory disturbance, which develop slowly but may have acute onset.

23.5.2.5 Gumma Neurosyphilis

Gumma neurosyphilis can be categorized into cerebral gumma and spinal gumma. Cerebral gumma neurosyphilis is manifested like brain tumor, brain abscess, or brain tuberculosis, while spinal gumma neurosyphilis is manifested as dural granuloma.

23.5.3 Cardiovascular Syphilis

Cardiovascular syphilis, one of the conditions that may cause death in the cases of advanced syphilis, is a cardiovascular disease caused by invasion of TP into the human body. Cardiovascular syphilis mostly derives from acquired syphilis, lasting for 10–25 years from the infection of TP to the onset of cardiovascular syphilis. In rare cases, symptoms of cardiovascular syphilis occur 1–2 years after the infection. Most patients with cardiovascular syphilis simultaneously experience neurosyphilis. Cardiovascular syphilis can be divided into the following five types, simplex syphilitic aortitis, syphilitic incomplete closure of aortic valve, syphilitic aortic aneurysm, syphilitic stenosis of coronary orifice, and syphilitic myocardial gumma.

23.5.4 Other Syphilis-Related Complications

In the advanced stage, TP can also invade multiple organs to cause various complications, including respiratory syphilis, gastrointestinal syphilis, hepatosplenic syphilis, urogenital syphilis, and endocrine glands syphilis. In addition, TP may also involve the eyes, ears, and lymph nodes to cause complications.

23.6 Diagnostic Examinations

23.6.1 Laboratory Tests

The laboratory tests for diagnosis of syphilis include pathogenic test, serological test, histopathological test, genetic diagnosis, and cerebrospinal fluid examination. Serological test and cerebrospinal fluid examination are commonly applied tests for diagnosis and assessment of syphilis.

23.6.1.1 Pathogenic Test

By dark-field microscopy, the finding of TP with typical morphology and characteristic motion is defined as positive, which is applied to define the diagnosis.

23.6.1.2 Serological Test

The serological test for diagnosis of syphilis can be divided into the following two types.

Serological Test for Non-TP Antigen

1. Venereal disease research laboratory test (VDRL): It can be quantitatively and qualitatively applied by using cardiolipin, lecithin, and cholesterin as the antigen.
2. Rapid plasma reagin test (RPR): It is an improved version of VDRL, with availability of results by naked eyes. It is one of the commonly used examinations across mainland China.
3. Unheated serum reagin test (USR): It is also an improved version of VDRL, with its sensitivity and specificity being close to those by VDRL.

Serological Test for TP Antigen

1. Fluorescent treponemal antibody absorption test (FTA-ABS): The test is the most sensitive examination for TP, but its technical operations are relatively challenging.
2. *Treponema pallidum* hemagglutination assay (TPHA): It is more applicable than FTA-ABS with favorable stability. However, it is less sensitive to primary syphilis than FTA-ABS.
3. *Treponema pallidum* particle assay (TPPA): Its sensitivity to syphilis is close to that by TPHA and is mainly applied to screen and define the suspected positive cases. TPPA is one of the commonly used laboratory tests to define TP infection. Meanwhile, it is also one of the examinations for definitive diagnosis of TP infection adopted by CDC of the United States.

Molecular Biological Detection

PCR is an important laboratory test for the diagnosis of syphilis and can be applied for various clinically collected specimens, with both high sensitivity and specificity. It can also be applied to define the genotype of TP. Currently, it is the most complicated examination for the diagnosis of TP infection.

Cerebrospinal Fluid Examination

Cerebrospinal fluid examination is applied for the diagnosis of neurosyphilis, whose indices include WBC count, protein, VDRL test, PCR detection, and colloidal gold test. VDRL test provides reliable evidence for the diagnosis of syphilis. In the cases with active neurosyphilis, the WBC count usually increases ($>5\times10^6$/L). Therefore, it is also a sensitive indicator for assessing therapeutic efficacy of the therapies against syphilis.

23.6.2 Diagnostic Imaging

23.6.2.1 X-Ray

X-ray examination of bones has relatively high sensitivity and specificity to congenital bone syphilis. Chest X-ray can also facilitate the diagnosis of cardiovascular syphilis.

23.6.3 Ultrasound

Ultrasound is a commonly used examination for cardiovascular syphilis.

23.6.3.1 CT scanning

CT is a commonly applied examination for the diagnosis of cardiovascular syphilis and neurosyphilis.

23.6.3.2 MR Imaging

MR imaging is commonly applied for understanding of the location, range, and severity of neurosyphilis.

23.7 Imaging Demonstrations

23.7.1 Bone Syphilis

23.7.1.1 Early-Onset Congenital Bone Syphilis

About 10 % of infant patients aged within 1 year show negative by serological test for syphilis. Therefore, radiological examination is important for the diagnosis of congenital bone syphilis. Early-onset congenital bone syphilis is the most commonly manifested as metaphysitis, followed by periostitis and osteomyelitis. It is characterized by multiple symmetric lesions, which is mainly metaphysitis with accompanying diffuse irregular osteoproliferation and bone destruction.

Syphilitic Metaphysitis

The lesions are multiple and symmetric, with common occurrence at the long bone of four limbs, such as femur and tibia. And the lesions are especially obvious at distal ulna and radius, proximal medial tibia, and proximal humerus. The early manifestations include widened area of prior calcification with marginal high density and serrated appearance as well as unevenly increased density. With the development of the lesions, the prior calcification area is coarse, with inferior transparent strips and dense lines to form sandwich sign. Along with granulation, unilateral bone destruction of metaphysis occurs to show bone defects, with clearly defined margin, which is known as cat-bite sign (Figs. 23.1, 23.2, and 23.3). The metaphysis at the bilateral superior medial tibia and the bilateral inferior medial femur shows symmetric bone destruction, which is surrounded by osteoproliferation with irregularly increased density. Such lesions are known as Wimberger sign, which has diagnostic value for early-onset congenital bone syphilis. After the lesions develop into the advanced stage, the prior calcification can be destructed, with partially or completely destructed metaphysis and different degrees of osteoproliferation. The lesions usually show no involvement in epiphysis, which is also characteristically early-onset congenital bone syphilis.

Syphilitic Periostitis

Periostitis, the most common condition in the cases of congenital bone syphilis, usually coexists with metaphysitis. The lesions are commonly found at radius, ulna, and femur. X-ray examination demonstrates linear, stratified, or shell-like thickening of periosteum at diaphysis, which parallels to diaphysis of long bone (Fig. 23.4). The lesions develop in a wide range and commonly involve the whole diaphysis and metaphysis. In some cases, periosteum is subject to obvious thickening to form sarcophagus sign. Some parts of thickened periosteum fuse into the diaphysis to show appearance of thickened diaphysis.

Syphilitic Osteomyelitis

It may occur at long bone, mostly resulted from expansion of metaphysitis toward diaphysis. The range with lesions is relatively large, and the lesions may involve more than half of the length of the diaphysis. The manifestations include local worm-eaten-like destruction of bone cortex, relatively wide osteoproliferation and sclerosis, thickened periosteum, and absence of bone marrow cavity, but no formation of sequestrum. Syphilitic osteomyelitis usually coexists with metaphysitis and periostitis. X-ray examination demonstrates transparent areas in the diaphysis with different sizes, which are actually bone destruction caused by syphilis.

23.7.1.2 Late-Onset Congenital Bone Syphilis

Its X-ray demonstrations resemble to those of early-onset congenital bone syphilis. However, late-onset congenital bone syphilis has obviously decreased range with lesions and obviously less serious conditions, with only diffuse changes of chronic periostitis. Periostitis is the most commonly found at the bilateral tibia, with stratified or lacelike proliferation of periosteum. The typical X-ray demonstrations include proliferation of convex periosteum at bilateral tibia and thickened diaphysis, which appears like a curved knife and is known as saber shin.

23.7.1.3 Acquired Bone Syphilis

The most common change of acquired bone syphilis is syphilitic osteomyelitis, which mainly involves diaphysis of long bone. The manifestations include periosteal proliferation in different degrees, which are common at tibia, skull, rib, and sternum. Periosteal proliferation at the anterior margin of bilateral tibia results in thickened bone cortex, appearing like a saber. Osteitis is manifested as diffuse osteoproliferation and osteosclerosis, thickened bone cortex, as well as thickened and deformed diaphysis with internal low-density areas, which are caused by bone destruction. Focal lesion of osteitis is syphilitic gumma, which is commonly found at bone cortex. The manifestations include defective bone cortex at certain part of bone, which is surrounded by osteoproliferation and osteosclerosis as well as periosteal proliferation.

Case Study 1

Syphilitic metaphysitis and syphilitic periostitis

For case detail and figures, please refer to Peng F et al. *Journal of Medical Radiology*, 2011, 21(6): 912 (In Chinese).

Case Study 2

A baby girl patient aged 20 days, with tenderness of the right lower limb for 2 days.

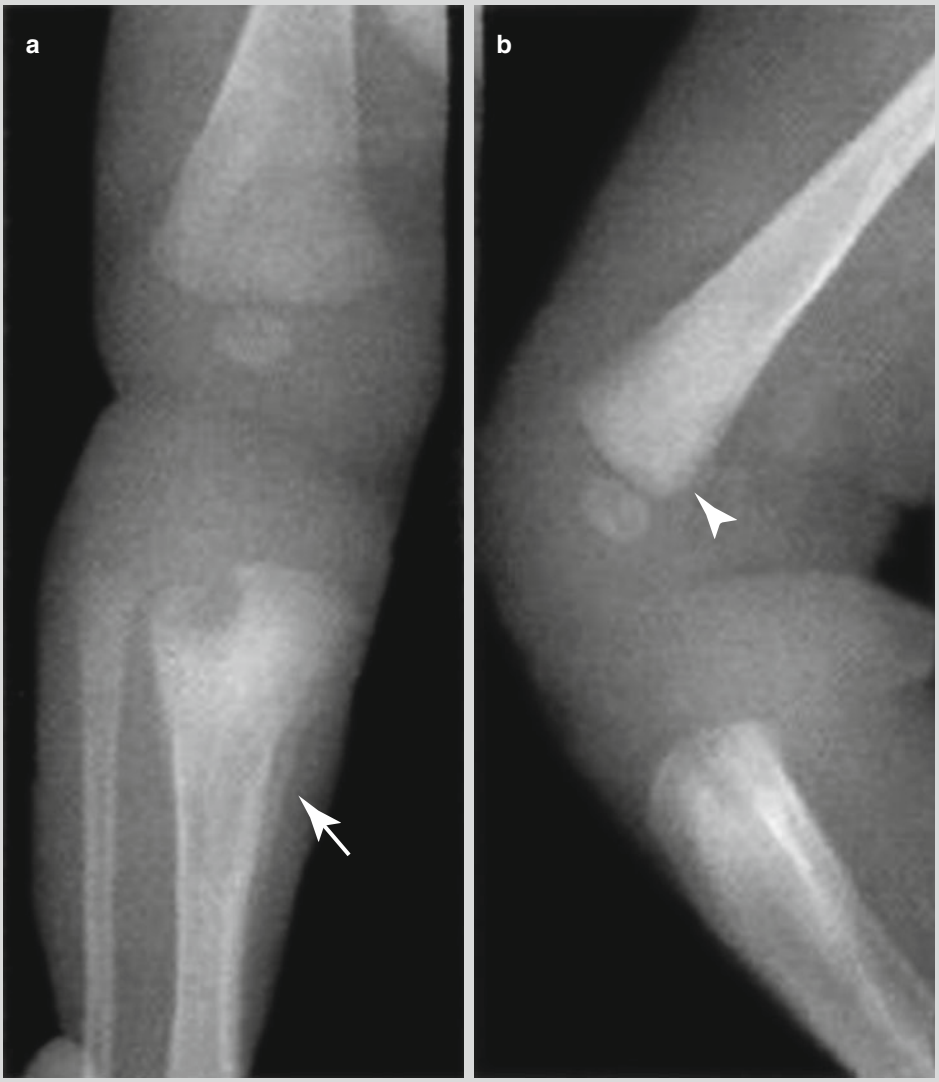


Fig. 23.1 Syphilitic osteomyelitis complicated by metaphysitis and periostitis. (**a**) Posterior-anterior and lateral X-rays demonstrate worm-eaten-like bone destruction at the left superior tibia, with surrounding high-density area and neighboring periosteal thickening (indicated by *arrow*). (**b**) Linear transparent area of bone destruction is demonstrated at the metaphysis of left distal femur (indicated by *arrowhead*)

Case Study 3

A baby boy patient aged 2 days, with RPR of 1:128.

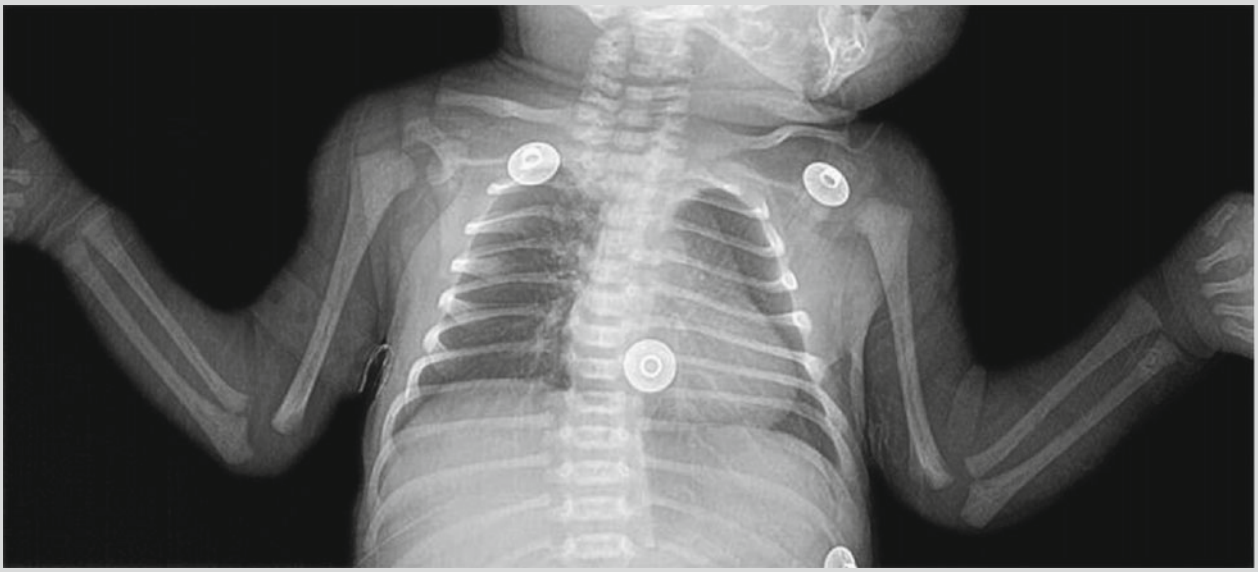


Fig. 23.2 Syphilitic metaphysitis. X-ray demonstrates round-like low-density bone lesion at the right inferior humerus

Case Study 4

A baby boy patient aged 2 months, with skin rashes for 1 month and fever and abdominal distension for 5 days.

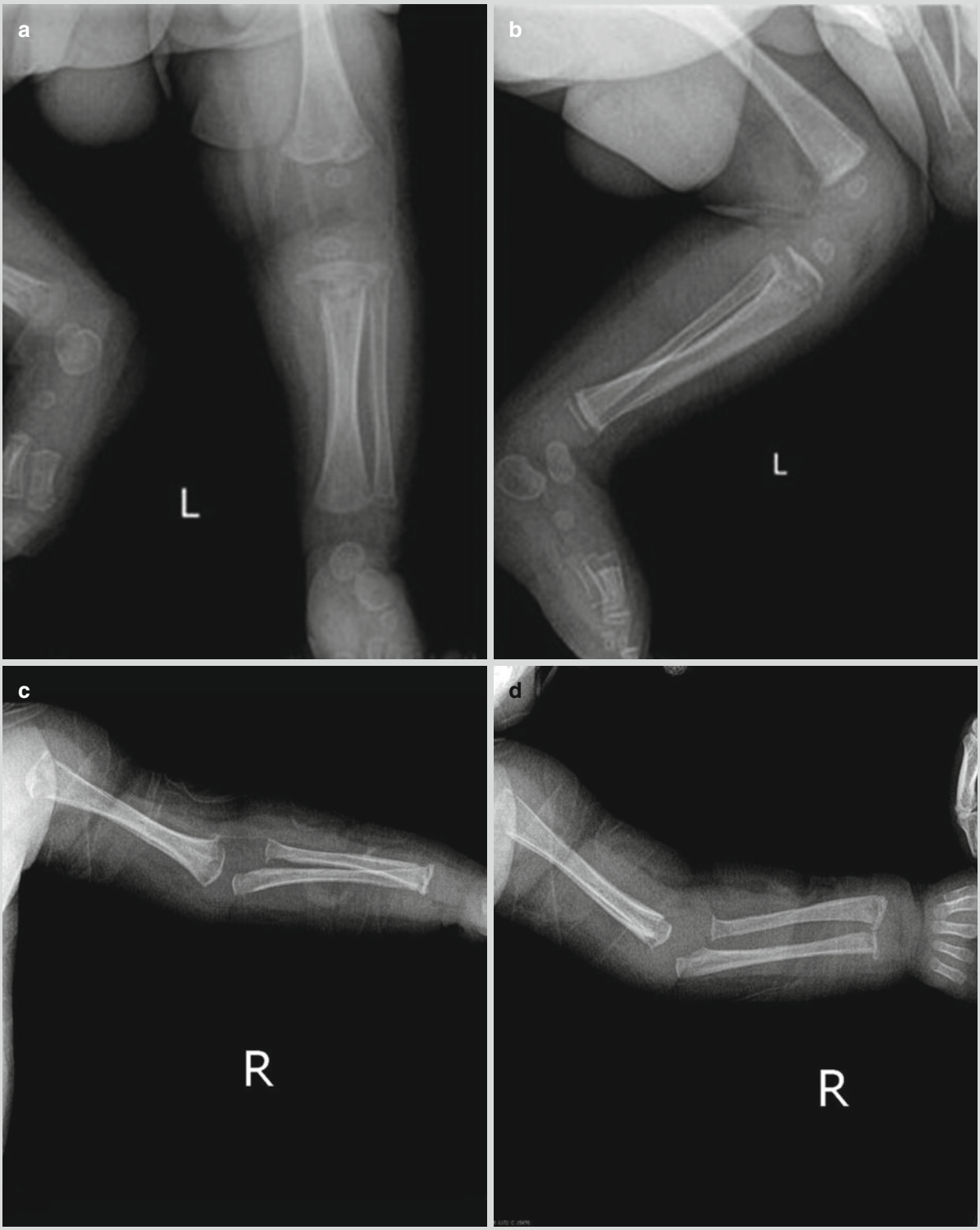


Fig. 23.3 Syphilitic metaphysitis. (**a**, **b**) Posterior-anterior and lateral X-rays demonstrate bone destruction at the proximal metaphysis of left tibia, widened space between metaphysic and swollen adjacent soft tissue; (**c**, **d**) Posterior-anterior and lateral X-rays demonstrate coarse bone cortex at the metaphysis of right radius and ulna

(The case study 2 and the case study 3 as well as the figures are provided by Zhang N et al. from the Department of Radiology, Chengdu Infectious Diseases Hospital, Sichuan, China)

Case Study 5
A baby boy patient aged 5 months, with abnormalities by serological test for above 3 months.

For case detail and figures, please refer to from Zhang GY et al. *Journal of Medical Research*, 2012, 41(2): 166 (In Chinese).

Case Study 6
A baby boy patient aged 10 weeks, with pain at bilateral upper limbs. He was suspected with greenstick fracture of the left humerus.

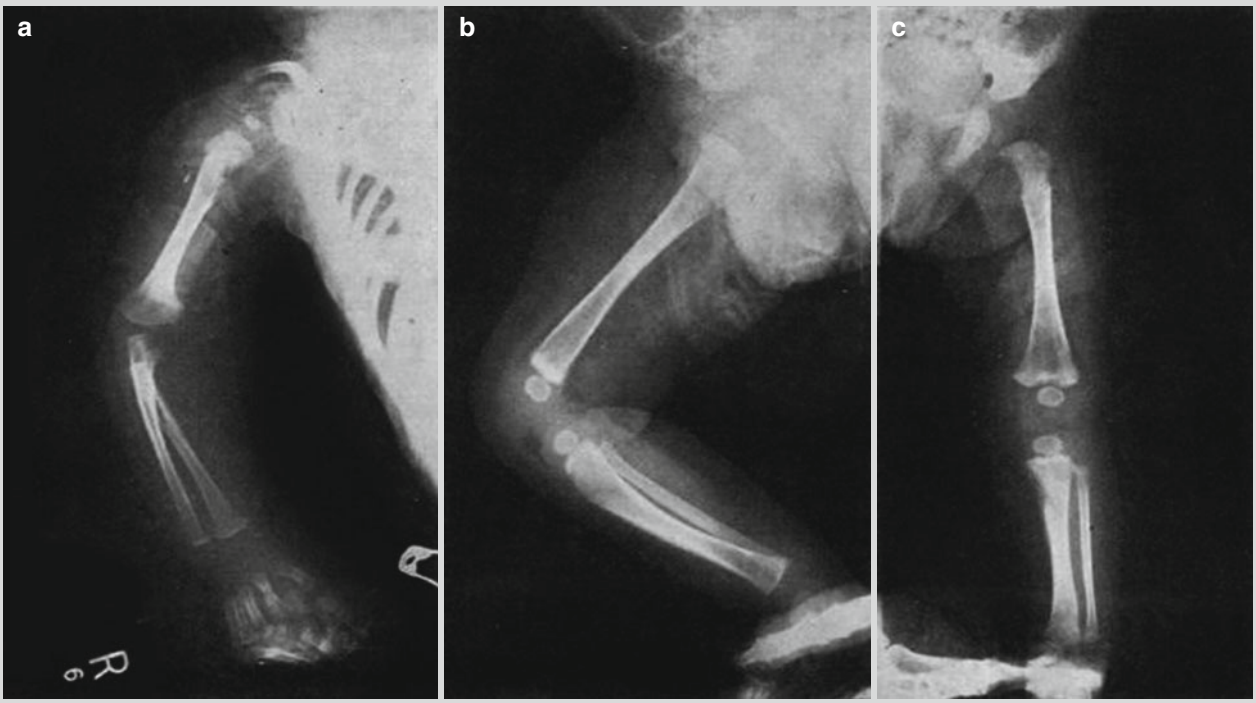


Fig. 23.4 Syphilitic metaphysitis and periostitis. (**a**) X-ray demonstrates parallel thickening of periosteum at the right radius and ulna and transparency shadow below the metaphysis. (**b**) Thickened prior calcification is demonstrated at the left femur. (**c**) Irregular decalcification is demonstrated at the left proximal tibia (Reprint with permission from Marks KL. *Br Med J*, 1954, 1 (4869): 1018)

23.7.2 Neurosyphilis

The radiological examinations for the diagnosis of neurosyphilis mainly include CT scanning and MR imaging. X-ray and ultrasound provide information with limited diagnostic value.

23.7.2.1 Asymptomatic Neurosyphilis

The radiological examinations usually demonstrate no abnormalities of the brain parenchyma.

23.7.2.2 Meningeal Syphilis

In its early stage, CT scanning demonstrates no abnormalities. But by contrast scanning, linear enhancement of meninges sometimes can be demonstrated. By MR imaging, the meninges and brain surface are demonstrated with diffuse linear long or equal T_1 signal and long T_2 signal. The meningeal lesions are generally more serious at the base of brain, which can be demonstrated with obvious enhancement by contrast imaging (Fig. 23.5). There are also demonstrations of swollen adjacent brain tissues, enlarged and widened cisterns and sulci, and increased signal strength of cerebrospinal fluid. Due to accumulated and increased inflammatory exudates at the base of brain, communicating hydrocephalus commonly occurs. The meningeal lesions can disseminate along the cranial nerves at the base of brain to invade the cranial nerves, with common involvement of VII and VIII cranial nerves. Syphilitic myelitis is demonstrated as long T_1 long T_2 signals of the

involved spinal cords. By contrast imaging, uneven enhancement can be demonstrated (Figs. 23.6 and 23.7). Due to common involvement of the meninges, the condition is also known as syphilitic meningomyelitis, manifested as inflammatory thickening of dura matter and its adhesion with pia matter of arachnoid membrane. The condition may further develop to cause lesions at the supplying vascular vessels and the nerve roots of the spinal cords, leading to spinal cord degeneration.

23.7.2.3 Meningovascular Syphilis

Meningovascular syphilis is pathologically characterized by proliferation of arteriolar endothelial cells and fibrocytes, thickening of vascular walls, stenosis, and blockage of the vascular lumen. After formation of cerebral infarction, MR imaging demonstrates typical T_1WI low signal and T_2WI high signal. By contrast imaging, the lesions are demonstrated with patches and cortical gyrus-like enhancement. After occurrence of encephalomalacia, the signal is the same as that of the cerebrospinal fluid.

23.7.2.4 Brain Parenchymal Syphilis

Brain parenchymal syphilis includes paralytic dementia and myelophthisis. In the early stage of brain parenchymal syphilis, CT scanning demonstrates extensive low-density change, with accompanying edema. In the advanced stage of brain parenchyma syphilis, the cortex is subject to diffuse atrophy and expanded lateral ventricles, but no ischemia and inflammatory changes. T_1WI and T_2WI of MR imaging demonstrate atrophy of different degrees at bilateral frontal and temporal lobes that is more obvious at the anterior parts, bilaterally symmetric dilation of brain ventricles, and glial proliferation of subcortex and hippocampus (Fig. 23.8).

23.7.2.5 Gumma Neurosyphilis

Gumma neurosyphilis can be found at any part of brain tissues, mostly at the cerebral cortex and subcortex. The round-like lesions may be singular or multiple, with a diameter of 2–2.5 cm. By T1WI, the central caseous necrosis of the lesion is demonstrated as low signal or equal low mixed signal, with surrounding low signal due to a large area of edema that shows space-occupying effect. By contrast imaging, the lesions are demonstrated with irregular ring-shaped enhancement and adjacent meningeal enhancement that indicates meningeal involvement Fig. 23.9. Intramedullary gumma neurosyphilis is manifested as swollen and thickened spinal cord, round-like or nodular lump that resembles to intracranial gumma, as well as enhancement and thickening of adjacent meninges.

Case Study 7

A male patient aged 53 years complained of dizziness with illusion for 1 month. He also experienced loss of memory, depression, and behavioral abnormalities. By laboratory tests, RPR was 1:8 and TPPA positive.

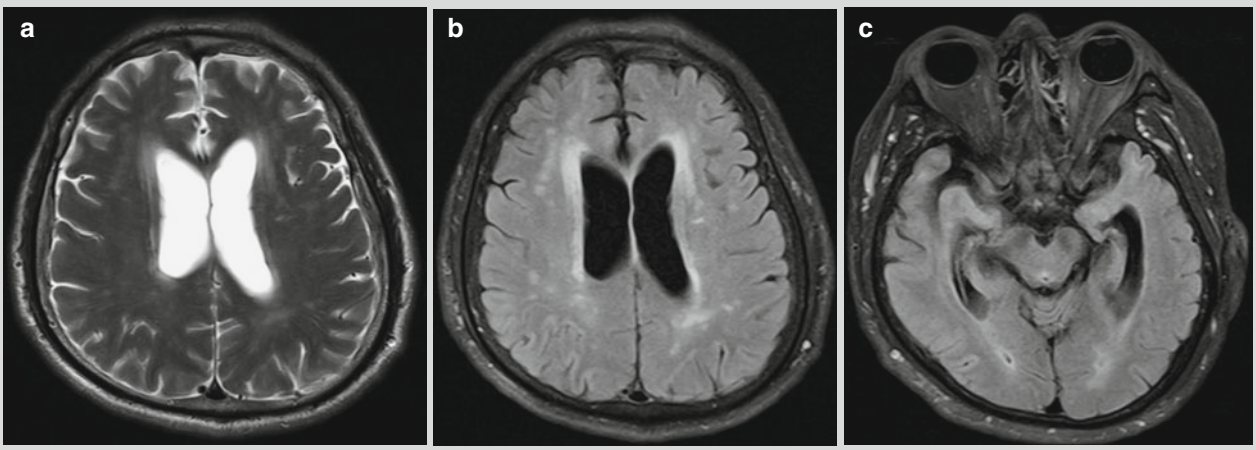
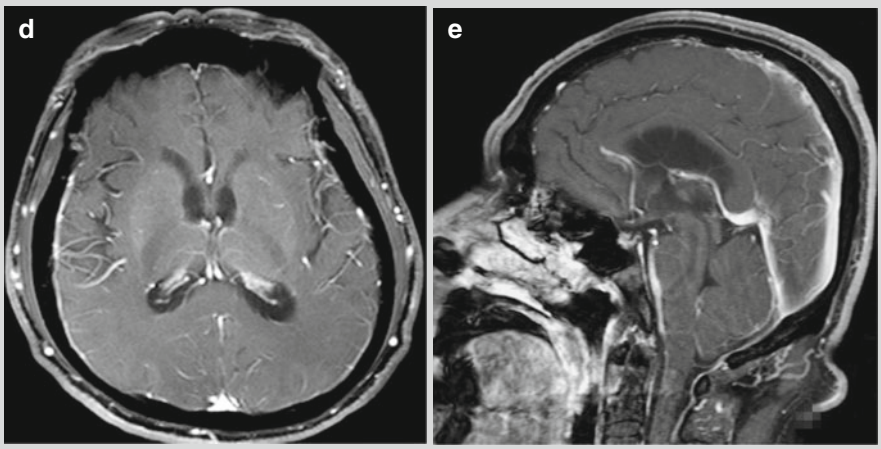


Fig. 23.5 Meningeal syphilis. (**a**, **b**) Transverse T2WI demonstrates multiple patches of long T1 long T2 signals at the bilateral semioval centrum and beside the bilateral lateral ventricles. By water and fat suppression T2WI, high signal can be observed. (**c**) The cortex at the inferior pole of bilateral temporal lobes and hippocampus is demonstrated to be thinner. (**d**, **e**) Contrast imaging demonstrates thickening and enhancement of the right temporal lobe and the meninges of brainstem; slight dilation of bilateral lateral ventricles

Fig. 23.5 (continued)



Case Study 8

A male patient aged 46 years experienced progressive instability of gait and dysuria. By physical examinations, deep reflex of both lower extremities was sensitive, bilateral Babinski sign was positive, and sensory disturbance was below L1. By laboratory tests, cell counts and protein level in the cerebrospinal fluid increased, while immunological assay of both cerebrospinal fluid and serum for syphilis was positive. The clinical diagnosis was syphilitic myelitis.

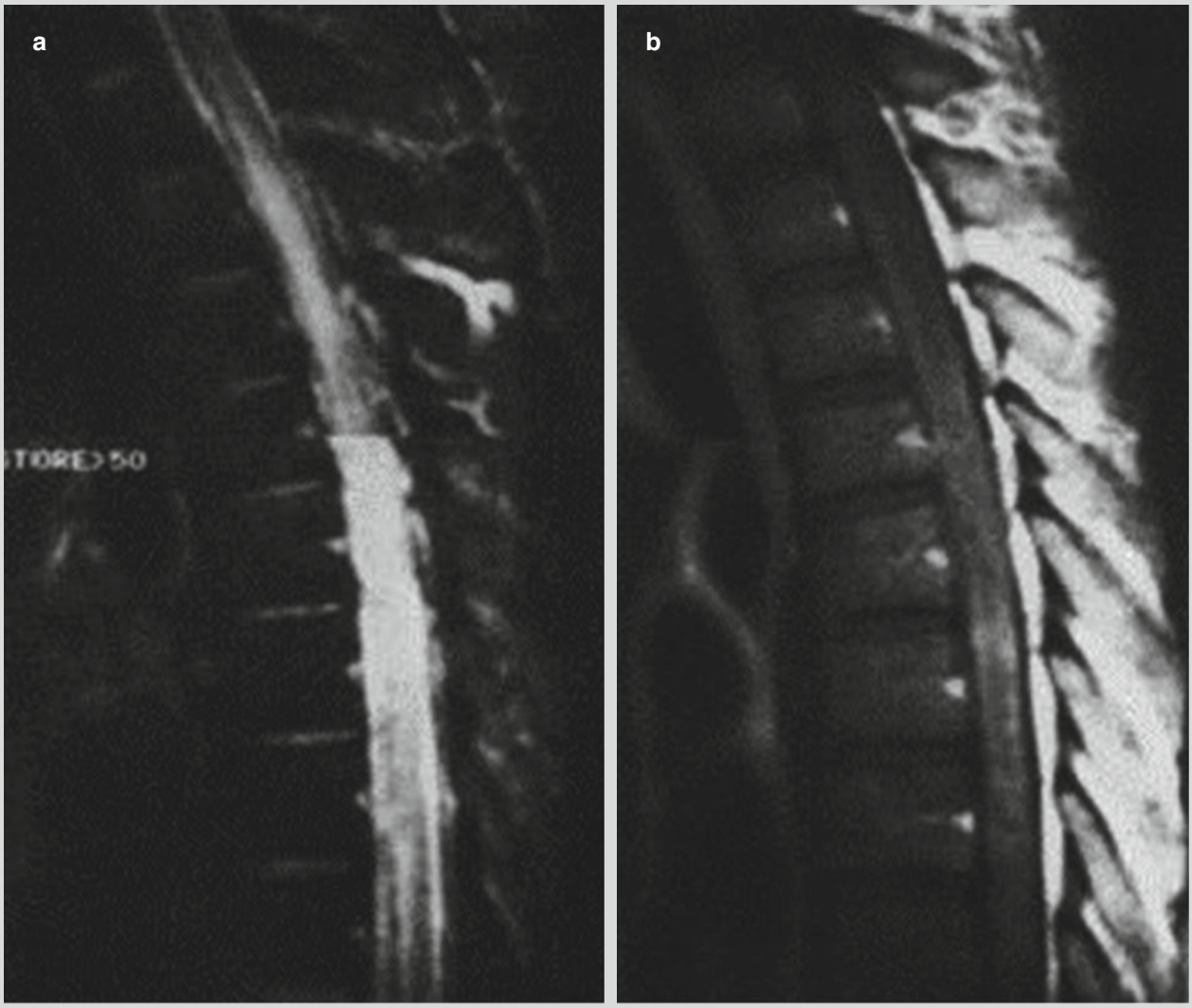


Fig. 23.6 Syphilitic myelitis. (**a**) Sagittal T2WI of MRI demonstrates high signal at the thoracic spinal cord. (**b**) Gd-DTPA contrast sagittal T1WI demonstrates uneven enhancement of the thoracic spinal cord, diffusive swelling of the spinal cord with internal low signal (Reprint with permission from H. Nabatame, et al. *Neuroradiology*, 1992, 34 (2): 105)

Case Study 9

A female patient aged 45 years complained of low back pain and upset with no known causes for 2 months that exacerbated for 2 weeks. The pain was especially obvious in the posture of supine at nights that affected her sleeping. In addition, she also experienced right lower-limb pain. By laboratory tests, RPR was positive, TPPA was positive, titer was 1:1,024, and HBV was positive. The pathological diagnosis was chronic inflammation with accompanying necrosis at T_{12}-L_1 spinal cord that is consistency with manifestations of syphilitic myelitis.

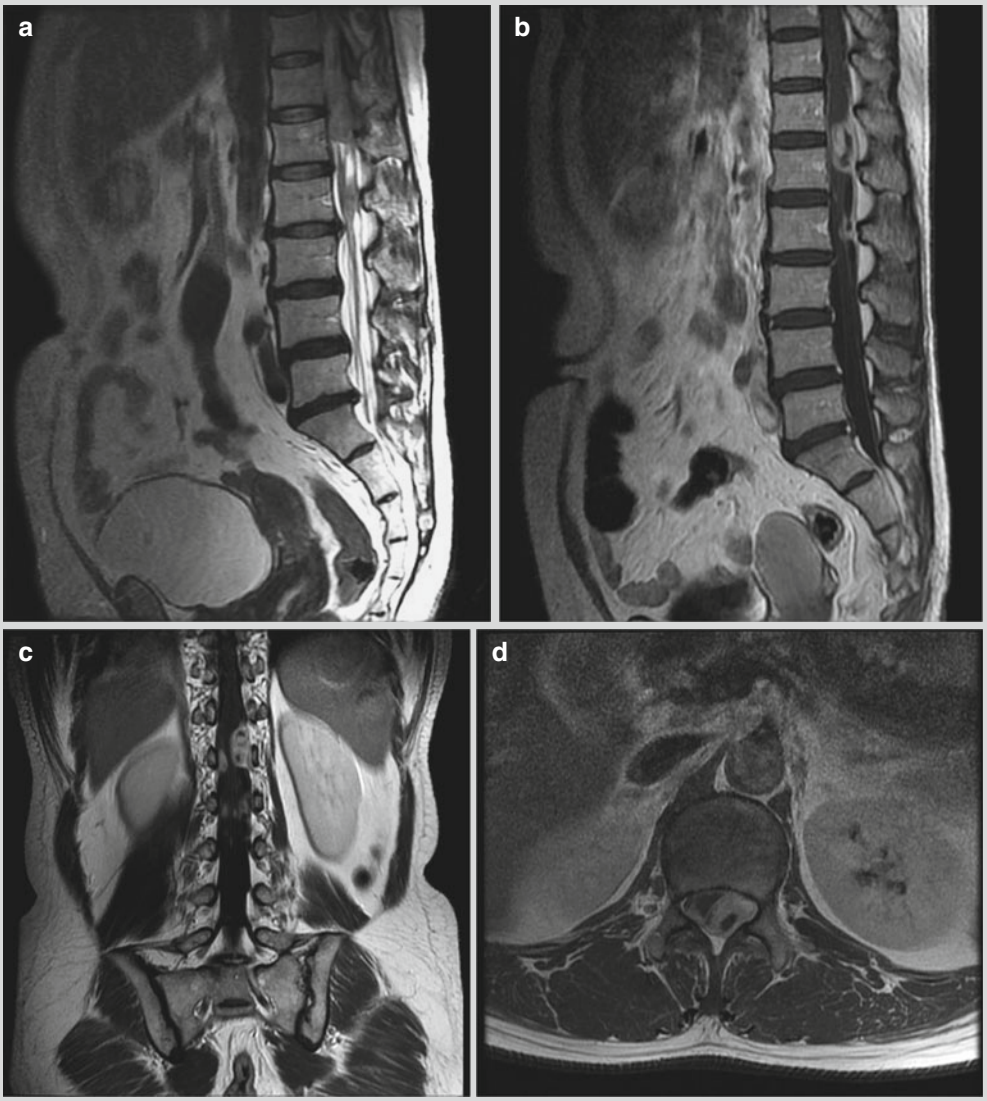


Fig. 23.7 Syphilitic myelitis. (**a**) T_2WI demonstrates heterogeneous signal shadows at the T_{12}-L_1 spinal cords. (**b–d**) Contrast imaging demonstrates the posterior wall of T_{12}-L_1 horizontal spinal canal with multiple lumps of ring-shaped enhancement, which adhere to dura mater at the posterior wall of spinal canal. The adjacent dura mater is also demonstrated with enhancement

(The case and figures were provided by Tang YH at Ruijin Hospital, Shanghai, China)

Case Study 10

A male patient aged 49 years experienced unclear language expressions, loss of memory, emotional instability, tremor of upper limbs, poor orientation, uncoordinated gait, hypermyotonia of the four limbs, and tendon hyperreflexia. By laboratory tests, serological test for TP antigen was positive; VDRL of the cerebrospinal fluid was qualitatively positive and quantitatively 1:8. The clinical diagnosis was paralytic dementia.

For case detail and figures, please refer to Peng FH et al. *Chinese Journal of Radiology*, 2005, 39 (9): 957 (In Chinese).

Case Study 11

A male patient aged 44 years was detected syphilis positive more than 1 month ago. He had histories of unhealthy sexual life and drug abuse. And he experienced psychiatric disorder, loss of memory, and intelligence decline. By laboratory tests, TPPA was positive and RPR was 1:32.

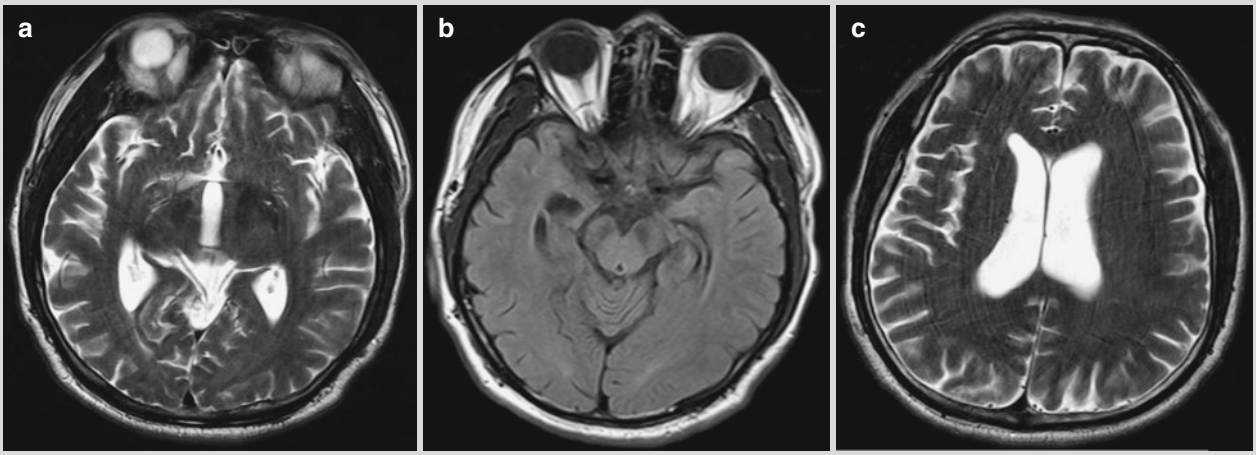


Fig. 23.8 Brain parenchymal syphilis. Transverse T2WI demonstrates multiple spots and strips of long T1 long T2 signals at the bilateral basal ganglia. (**b**) Atrophy of bilateral hippocampus and parahippocampal gyri is demonstrated. (**a**, **c**) Dilation of the bilateral lateral ventricle and the third ventricle is demonstrated

Case Study 12

A female patient aged 40 years complained of blurry vision for 1 month, with defects of bilateral lower right vision.

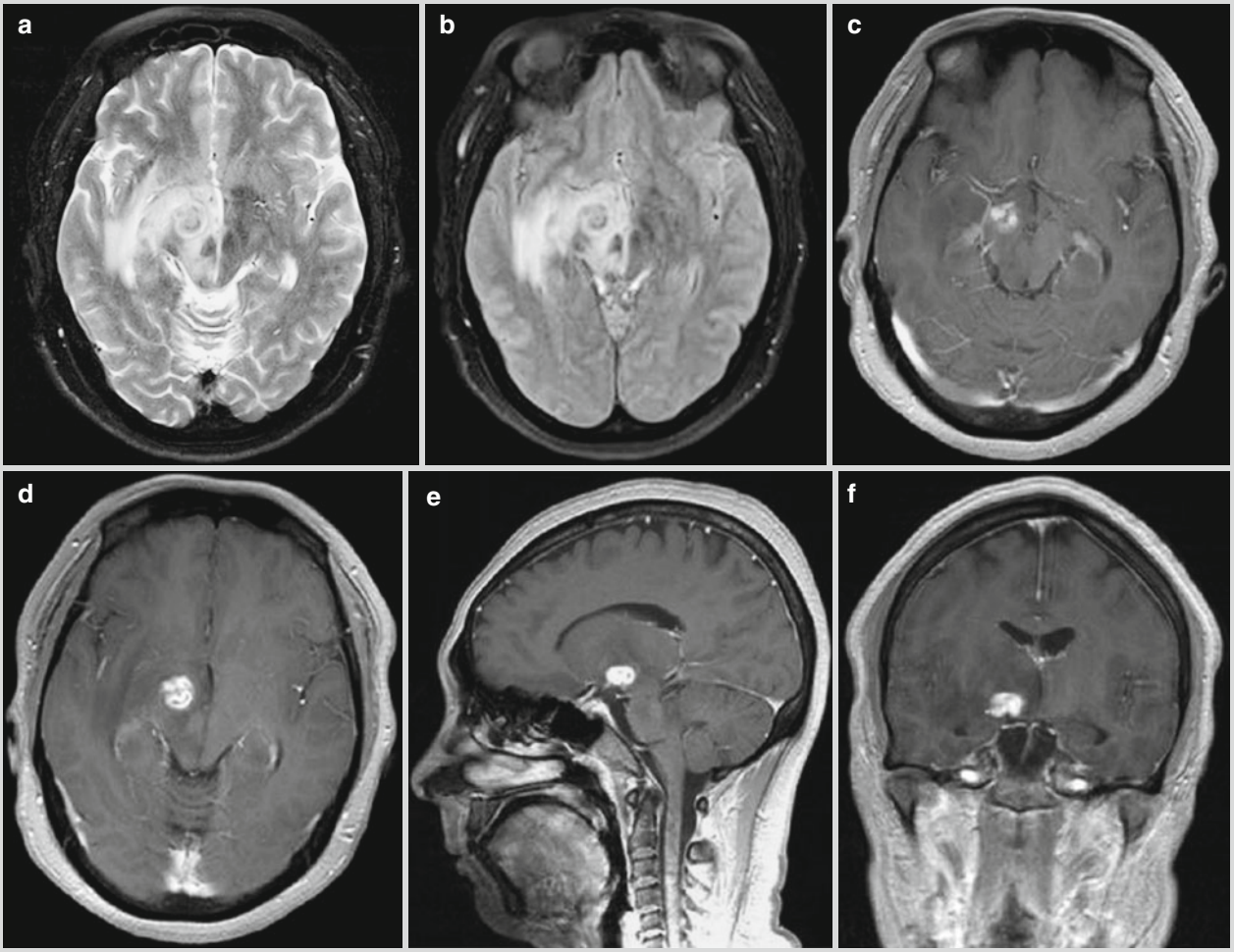


Fig. 23.9 Gumma neurosyphilis. (**a**, **b**) Transverse MR imaging demonstrates round-like long T2 signal at the right mesencephalon and cerebral peduncle, with internal uneven and mixed signals. The center of the lesion is demonstrated with slightly low signal. And the lesion is demonstrated with surrounding large flakes of high-signal edema. And the midline structure is demonstrated to shift slightly leftward. (**c**–**f**) Contrast imaging demonstrates obvious enhancement of the lesion, with well-defined boundary, and slight enhancement of the adjacent meninges

(Note: the case and figures were provided by Xia S at the Department of Radiology, the First Central Hospital, Tianjin, China.)

Case Study 13
A male patient aged 56 years experienced IV degree myodynamia of the left lower limb and hyperalgesia of the left lower limb. He had a history of unhealthy sexual life. By laboratory tests, RPR was negative and TPPA was 1:640 to be positive.

For case detail and figures, please refer to Liu H et al. *Journal of Clinical Radiology*, 2008, 27 (9): 1275 (In Chinese).

23.7.3 Cardiovascular Syphilis

23.7.3.1 Syphilitic Aortitis
Syphilitic aortitis is commonly complicated by incomplete closure of aortic valve, stenosis of coronary orifice, and other conditions. Ultrasonocardiography demonstrates dilated aorta, aortic regurgitation, and enlarged left ventricle.

23.7.3.2 Syphilitic Incomplete Closure of Aortic Valve
Ultrasonocardiography indicates abnormal enlargement of the aortic circle, dilated ascending aorta, different degrees of aortic regurgitation with following enlarged left ventricle, and widened outlet of the left ventricle. Color Doppler demonstrates colored regurgitation bundle during diastole from aortic circle to the outlet of left ventricle.

23.7.3.3 Syphilitic Aortic Aneurysm
X-ray demonstrates mediastinal mass shadow. Both CT scanning and MR imaging demonstrate the location, size, and morphology of aortic aneurysm, which is usually cystiform or spindle-shaped aortic aneurysm shadow (Figs. 23.10 and 23.11).

23.7.3.4 Syphilitic Stenosis of Coronary Orifice
The condition mainly involves the proximal coronary orifice. By coronary angiography, morphology of the coronary artery and the location, severity, and range of its obstructive lesion can be defined. And such an examination is currently the only way to observe the morphology of coronary artery. Coronary angiography can define the location and severity of stenosis of coronary orifice.

Case Study 14
A male patient aged 74 years experienced stable angina pectoris and accompanying aortic regurgitation. Ultrasonocardiography demonstrated dilated aortic root and obvious aortic regurgitation.

For case detail and figures, please refer to Pugh PJ et al. *N Engl J Med*, 2002, 346 (9): 676.

Case Study 15
A male patient aged 76 years experienced progressive dyspnea and accompanying swelling of the lower limbs. He had a history of chronic syphilis, but no history of receiving therapies.

For case detail and figures, please refer to Rajab TK et al. *N Engl J Med*, 2011, 364 (13): 1258.

Case Study 16

A male patient aged 57 years experienced chronic hypertension, lipid metabolism disorder, and a history of smoking and drinking. Ultrasonocardiography demonstrated dilated ascending aorta, normal diameter of aortic root, moderate hypertrophy of the left ventricle, and favorable ventricular systole. No lump in the cavity of aortic regurgitation and no communication between the atria and ventricles were found.

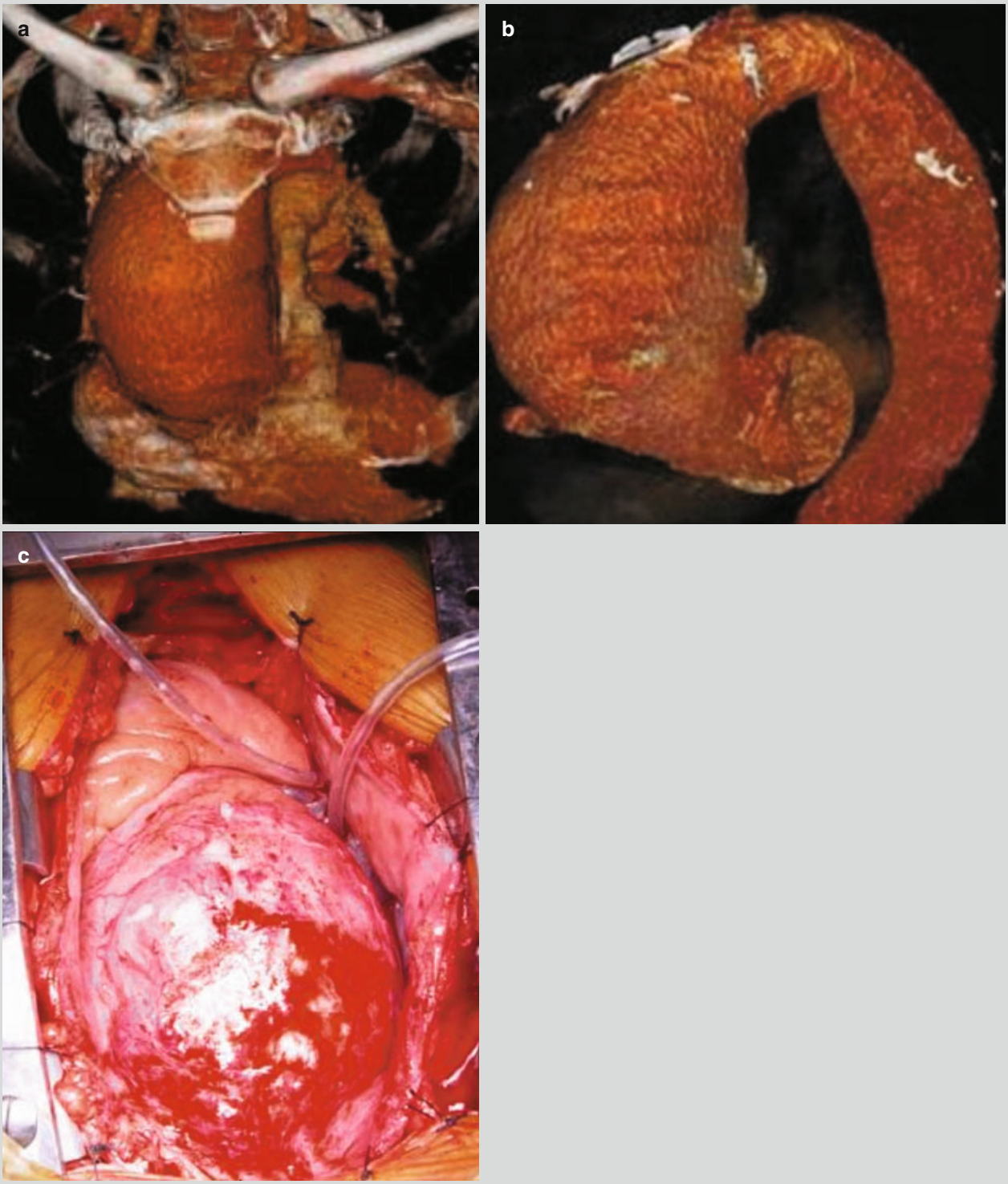


Fig. 23.10 Syphilitic aortic aneurysm. (**a**, **b**) VR of CT scanning demonstrates aneurysm at the ascending aorta. (**c**) Observations during surgery to remove the aneurysm (Reprint with permission from Paulo N, et al. *Interact Cardiovasc Thoracsurg*, 2012, 14 (2): 193)

Case Study 17

A male patient aged 38 years experienced sudden dyspnea, sharp stabbing pain at the chest, and cardiac shock.

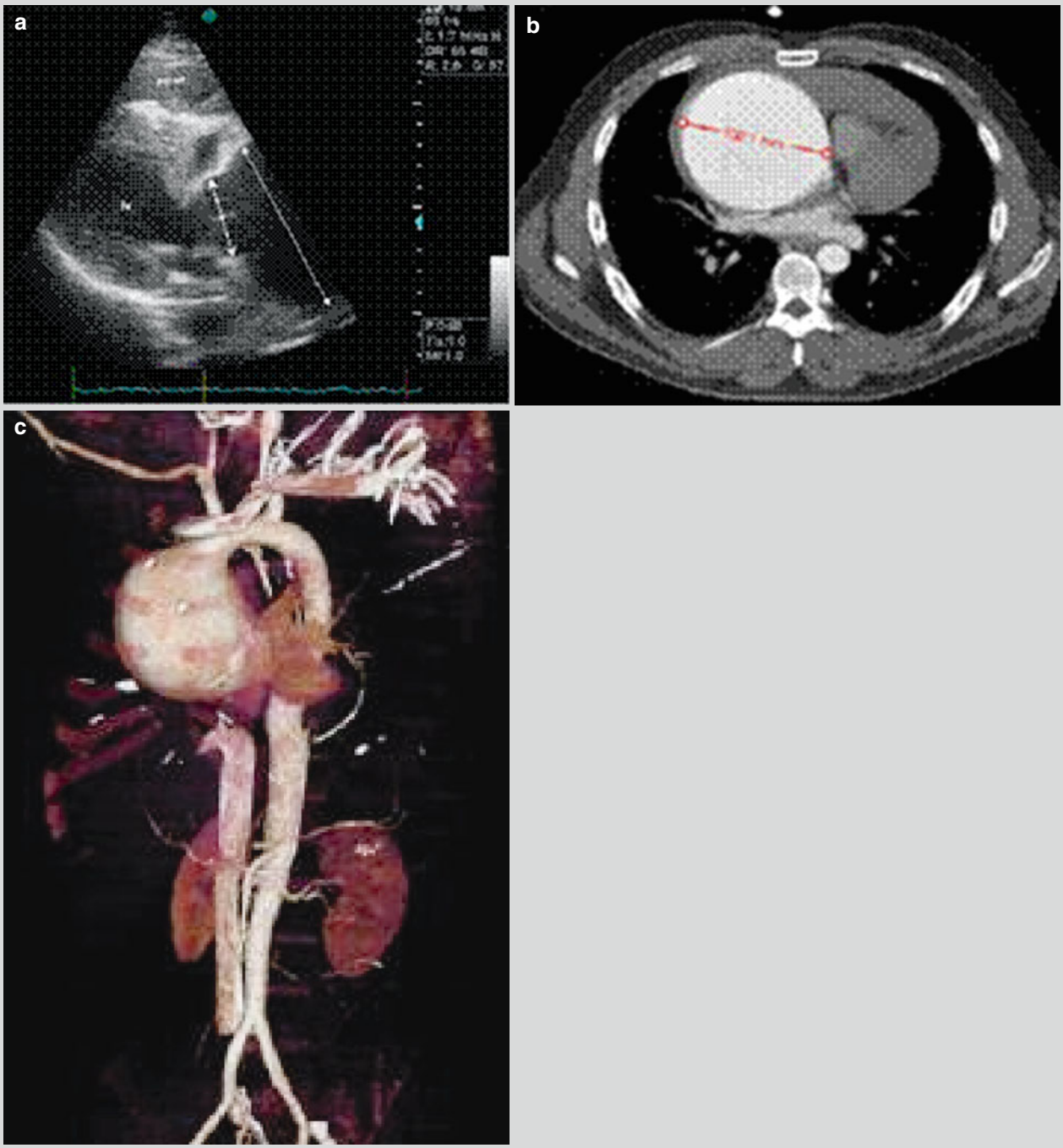


Fig. 23.11 Syphilitic aortic aneurysm. (**a**) Ultrasonocardiography demonstrates serious dilation of the ascending aorta and accompanying moderate incomplete closure of aortic valve. (**b**, **c**) CT scanning demonstrates dilated ascending aorta with a diameter of about 10 cm and compressed right atrium (Reprint with permission from Acar Z, et al. *J Am Coll Cardiol*, 2012, 59 (1): e1)

Case Study 18

A male patient aged 34 years experienced dyspnea and palpitation. By serological test for syphilis, TPHA was strongly positive and VDRL was strongly positive (Fig. 23.12).

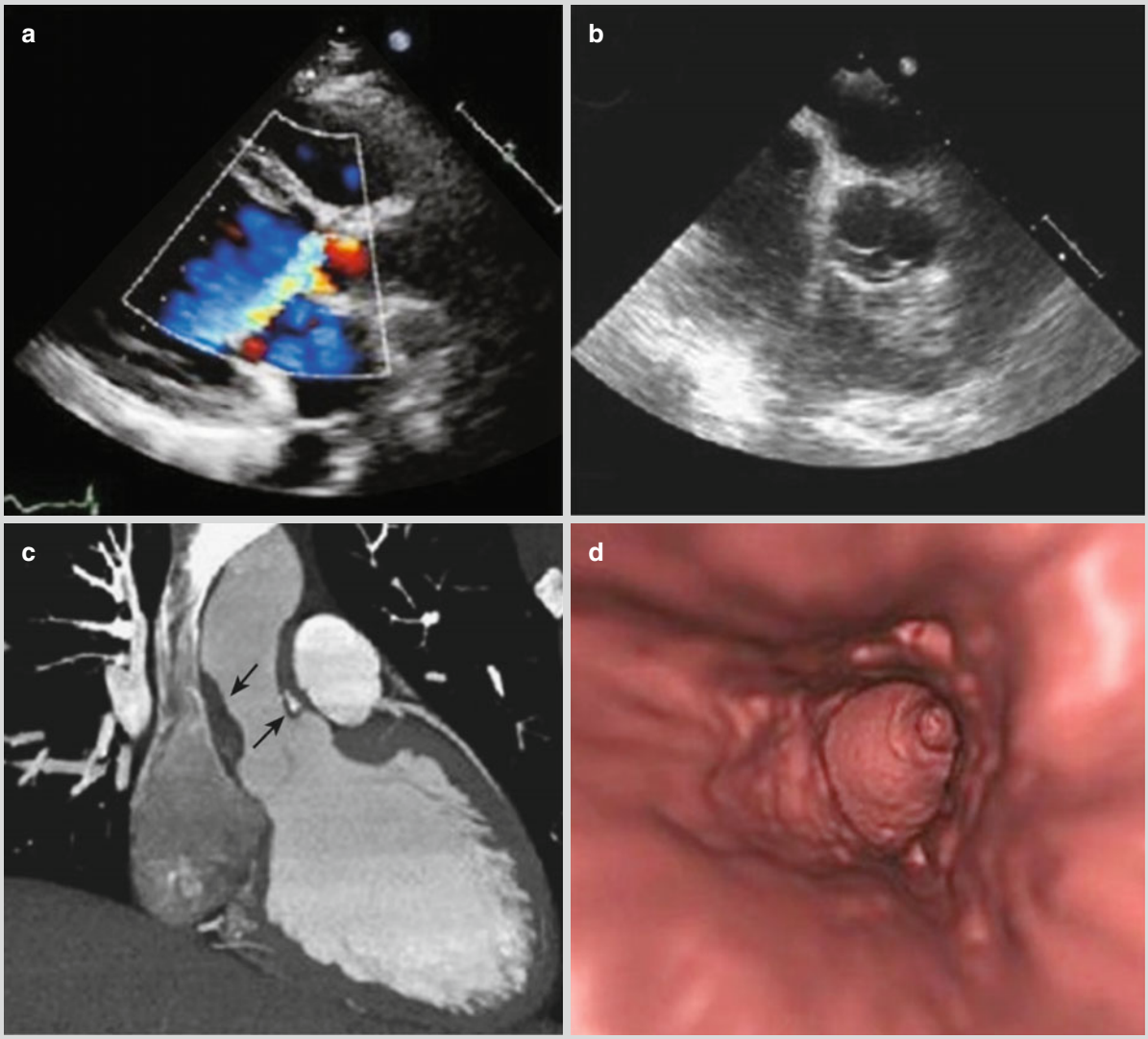


Fig. 23.12 Syphilitic inflammatory gumma. (**a**, **b**) Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) demonstrate serious aortic regurgitation. (**c**) CT scanning demonstrates ring-shaped thickening of the aortic wall, with a thickness of about 8 mm (indicated by an *arrow*). (**d**) It is demonstrated that calcification of partial vascular wall causes stenosis of major artery lumen, with a diameter of 16 mm (Reprinted with permission from Bouvier E, et al. *J Am Coll Cardiol*, 2011, 57 (24): e375)

23.7.4 Ocular Syphilis

Case Study 19

A female patient aged 42 years complained of blurry vision of both eyes for 4 months. By examinations, the light sense of right naked eye was within 1 m, the vision of left naked eye was 0.08, both ciliary bodies were congested, the cornea was transparent, a small quantity of flocculent exudates from the right eye, PHA was (+), and RPR titer was 1:64.

For case detail and figures, please refer to Zhao Q et al. *Ophthalmologic Research*, 2009, 27 (4): 268 (In Chinese).

Case Study 20

A male patient aged 59 years had a history of unhealthy sexual life. He complained of painless blurry vision for 10 days. By examinations, the binocular vision was 0.5, there was no congestion of the bulbar conjunctiva, cornea was transparent, KP and vitreous opacity were positive, and crystalline lens was transparent. Primary screening test for syphilis was positive (++); antibody test for syphilis was positive (++) (Fig. 23.13).

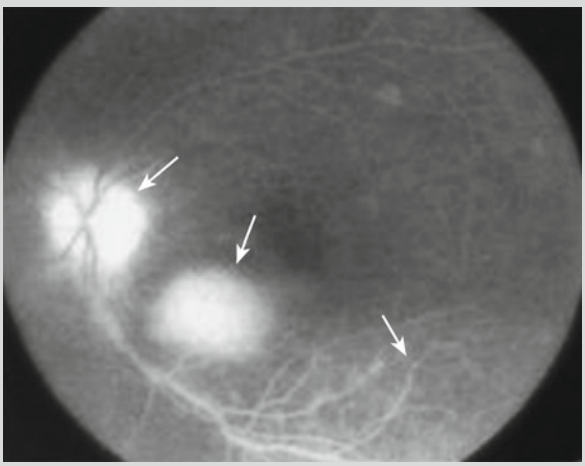


Fig. 23.13 Syphilitic neuroretinitis and uveitis. FFA of the left eye fundus demonstrates focal leakage of fluorescein at the retina, leakage at the venous wall, and leakage at the optic disk (indicated by *arrows*)

Case Study 21

A male patient aged 42 years had a past history of unhealthy sexual life. He complained of sudden decline of the right eye vision for 5 days. By examinations, the vision of right eye for counting fingers was 30 cm, and the vision of left naked eye was 1.0. By laboratory tests, the primary screening test for syphilis was positive (++), and the antibody test for syphilis was positive (++).

For case detail and figures, please refer to Cai QH et al. *Ophthalmologic Research*, 2005, 23 (6): 631. (In Chinese)

23.8 Diagnostic Basis

The definitive diagnosis of syphilis should be based on comprehensive analysis of the medical history, clinical manifestations, physical examination findings, and laboratory test findings.

23.8.1 Diagnosis of Syphilis

23.8.1.1 Primary Syphilis

Epidemiological History

The patients usually have multiple sexual partners and high-risk sexual behaviors. Otherwise, his/her sexual partner has a case history of syphilis infection.

Clinical Manifestations

The patients usually have singular painless caries callosa, which has an incubation period of 2–4 weeks, and has cartilage like hardness. The caries callosa is commonly found at the external genitals, with inguinal lymphadenectasis or lymphadenectasis around the lesion.

Laboratory Tests

By dark-field microscopy, patients with syphilis usually have lesions at the skin and mucosa. Otherwise, by puncture of lymph node, TP can be detected in the collected fluid.

After occurrence of caries callosa for 2–3 weeks, serological test for TP antigen turns to be positive.

23.8.1.2 Secondary Syphilis

Epidemiological History
The patients usually have multiple sexual partners and high-risk sexual behaviors. Otherwise, his/her sexual partner has a history of syphilis infection or the patient has a history of blood transfusion.

Clinical Manifestations
The patients may have a history of primary syphilis that lasted for less than 2 years. The patients with syphilis usually have various skin rashes, accompanying general upset and systemic superficial lymphadenectasis.

Laboratory Tests
The serological test for TP antigen is positive.

23.8.1.3 Tertiary Syphilis

Epidemiological History
The patients usually have multiple sexual partners and high-risk sexual behaviors. Otherwise, his/her partner has a history of syphilis infection.

Clinical Manifestations
The patients may have a history of primary or secondary syphilis that lasted for above 2 years. The typical manifestations include nodular syphilid, syphilitic gumma, perforation of palate and nasal septum caused by syphilitic gumma, saddle nose, bone syphilis, ocular syphilis, and other organ syphilis. Tertiary syphilis may involve respiratory tract, gastrointestinal tract, liver and spleen, urogenital system, endocrine glands, and skeletal muscles. Neurosyphilis and cardiovascular syphilis may also occur.

Laboratory Tests
(1) Serological test for non-TP antigen is positive, and serological test for TP antigen is also positive. (2) By examination of cerebrospinal fluid, the WBC count in the cases of neurosyphilis $\geq 10 \times 10^6$/L, the protein level >500 mg/L, and VDRL test was positive.

23.8.1.4 Latent Syphilis

Epidemiological History
The patients usually have multiple sexual partners and high-risk sexual behaviors. Otherwise, his/her sexual partner has a history of syphilis infection.

Clinical Manifestation
The patients usually have no symptoms and signs of syphilis.

Laboratory Test
Serological test for non-TP antigen is positive for at least twice. Otherwise, serological test for TP antigen is positive, with biologically false positive excluded.

Cerebrospinal Fluid Examination
By examination of the cerebrospinal fluid, the results are negative.

23.8.1.5 Congenital Syphilis

Epidemiological History
The biological mother is a patient with syphilis or TP infection.

Clinical Manifestation
The patients usually have typical symptoms and signs of syphilis.

Laboratory Test
By dark-field microscopy, TP is found at the lesions of skin and mucosa or at the placenta in baby patients. Serological test for non-TP antigen is positive and serological test for TP antigen is positive.

23.8.2 Diagnosis of Syphilis-Related Complications

23.8.2.1 Bone Syphilis

The diagnosis of bone syphilis should be comprehensively based on medical history, clinical manifestation, laboratory test findings, and radiological findings. Congenital bone syphilis is common in children, and the mother usually has a history of syphilis infection. X-ray commonly demonstrates metaphysitis, periostitis, and diaphysitis. The characteristic manifestation is multiple symmetric lesions, commonly at long bones of all four limbs, such as femur and tibia. Metaphysitis is manifested as concurrent osteoproliferation and bone destruction, in typical signs of hamburger sign, cat-bite sign, and Wimberger sign. And the lesions usually do not involve metaphysis. Periostitis is common in the cases of bone syphilis, with X-ray demonstrations of thickening of diaphysis and periosteum in various morphologies. In some serious cases, X-ray demonstrates sarcophagus-like sign. In the cases with lesions of periostitis at the tibia, the periosteum is demonstrated with laminar or lacelike proliferation, and the diaphysis is demonstrated to be thickened, with an appearance of a curved knife, which is typically saber tibia sign. Osteomyelitis is common at long bones, which is manifested as worm-bitten-like bone destruction, and accompanying osteoproliferation and osteosclerosis. By X-ray,

diaphysis is demonstrated with transparent areas in different sizes. Based on the above characteristic demonstrations of bone syphilis by X-ray as well as the case history and positive finding by serologic test, the diagnosis can be defined.

23.8.2.2 Neurosyphilis

Currently, the diagnosis of neurosyphilis still has no golden standard. Therefore, its diagnosis is commonly based on comprehensive analysis of the case history, clinical manifestations, laboratory test findings, and radiological demonstrations.

The diagnostic criteria for syphilis implemented by CDC of the United States are (1) having evidence supporting TP-induced infection of the central nervous system; (2) a serological test for syphilis is positive and VDRL test of CSF for TP is positive; (3) suspected cases with syphilis at any stage having VDRL test of CSF negative plus the following two conditions, the increase of CSF protein and cells counts with no other known causes and symptoms and signs in consistency with neurosyphilis with no other known causes; and (4) definite cases with syphilis at any stage having laboratory findings in consistency with neurosyphilis.

The diagnostic criteria for syphilis are feasible and practicable, but with no criteria to exclude neurosyphilis. FTA-ABS test of cerebrospinal fluid has high specificity to neurosyphilis, and the cases with negative result can be excluded as non-neurosyphilis.

The radiological demonstrations of neurosyphilis are nonspecific. Contrast CT scanning and MR imaging demonstrate meningeal syphilis with linear enhancement of the meninges, swollen adjacent brain tissue, as well as widened cistern and sulcus. Contrast MR imaging demonstrates meningovascular syphilis with patches of enhancement of the lesion and gyrus-like enhancement of the cortex. CT scanning and MR imaging commonly demonstrate brain parenchymal syphilis with atrophy of brain parenchyma and dilated lateral ventricle, which are more common at the frontal and temporal lobes with accompanying edema of different degrees. Gumma neurosyphilis is commonly demonstrated with round-like lesions in the brain, which are surrounded by accompanying edema. By contrast scanning or imaging, the lesions may be demonstrated with irregular ring-shaped enhancement and adjacent meningeal enhancement. The adjacent meningeal enhancement indicates meningeal involvement.

23.8.2.3 Cardiovascular Syphilis

Syphilitic aortitis is usually manifested as dilated aorta, aortic valve regurgitation, and enlarged left ventricle. Syphilitic incomplete closure of aortic valve is manifested as enlarged aortic ring, dilated ascending aorta, and aortic valve regurgitation of various degrees. X-ray demonstrates syphilitic aortic aneurysm with mediastinal mass shadow, while CT scanning and MR imaging usually demonstrate cystiform or spindle-shaped aortic aneurysm shadow. Syphilitic stenosis of coronary orifice can be examined by coronary angiography to define the morphology of coronary artery as well as the location, severity, and range of the obstructive lesions.

23.9 Differential Diagnosis

23.9.1 Primary Syphilis

Caries callosa should be differentiated from soft chancre, fixed drug eruption, genital herpes, tuberculous ulcer, and Behçet disease.

23.9.2 Secondary Syphilis

The skin rashes are morphologically various, which may resemble to skin rashes of various skin diseases. The differential diagnosis should be comprehensively based on case history, clinical manifestations, and laboratory findings. Macular syphilis rash should be differentiated from pityriasis rosea. Other skin rashes should be differentiated from drug rash, lichen planus, pustule sore, and psoriasis.

23.9.3 Tertiary Syphilis

Nodular syphilitic rash should be differentiated from lupus vulgaris, rheumatic nodule, lepra lepromatosa, scrofuloderma, sporotrichosis, and chronic leg ulcer. Syphilitic gumma should be differentiated from lupus vulgaris, lepra lepromatosa, erythema induratum, and ulcers.

23.9.4 Neurosyphilis

23.9.4.1 Differential Diagnosis of Meningeal Syphilis

Meningeal syphilis should be differentiated from diseases with meningeal enhancement. The meningeal lesion at the skull base in the cases of meningeal syphilis is more serious than that in the cases of other diseases. By contrast imaging, meninges is demonstrated to be thickened with obvious enhancement, which are more obvious at the hypothalamus, brainstem, suprasellar cistern, and around the sylvian cistern.

23.9.4.2 Differential Diagnosis of Meningovascular Syphilis

Meningovascular syphilis should be differentiated from cerebral infarction. Generally, meningovascular syphilis has multiple asymmetric infarction lesions at the cerebral hemispheres, mainly located at the subcortex and deep cerebral white matter. CT scanning demonstrates patches of low-density areas. In some serious cases, the middle cerebral artery can be occluded. In addition, meningovascular neurosyphilis should also be differentiated from herpes simplex virus encephalitis. Meningovascular neurosyphilis has chronic onset, which is commonly manifested as slight atrophy of the temporal lobe and slight dilation of the temporal horns of cerebral ventricles. However, herpes simplex virus encephalitis has an acute onset, commonly with space-occupying effect.

23.9.4.3 Differential Diagnosis of Brain Parenchymal Syphilis

Paralytic dementia in the cases of brain parenchymal syphilis is often manifested as diffuse cerebral atrophy of different degrees, which is commonly located as the frontal lobe and temporal lobe. In addition, most cases have asymmetric cerebral atrophy of bilateral hemispheres and accompanying symmetric dilation of bilateral ventricles. In the cases of Alzheimer's disease, cerebral atrophy is commonly symmetric, with accompanying hippocampal atrophy.

23.9.4.4 Differential Diagnosis of Gumma Neurosyphilis

Gumma neurosyphilis should be differentiated from brain neoplasm, parasitic granuloma, and tuberculoma. Gumma neurosyphilis may be manifested as ring-shaped enhancement of the lesions adjacent to the meninges, with thickened adjacent meninges that can be observed with enhancement.

23.9.5 Cardiovascular Syphilis

23.9.5.1 Differential Diagnosis of Syphilitic Aortitis

Syphilitic aortitis should be differentiated from atherosclerosis. Syphilitic aortitis commonly occurs at the ascending aorta, with common complications of syphilitic aortic aneurysm, incomplete disclosure of aortic valve, and stenosis of coronary orifice. By X-ray, it is demonstrated with dilated ascending aorta, linear calcification, and irregular edge of vascular lumen. However, atherosclerosis usually does not involve the ascending aorta, which commonly involves the descending aorta with masses of calcification.

23.9.5.2 Differential Diagnosis of Syphilitic Aortic Aneurysm

Syphilitic aortic aneurysm should be differentiated from the diseases with intramediastinal lump, such as central lung carcinoma, lymphoma, and retrosternal thyroid. These diseases are usually not accompanied by shift of aorta. Aortic angiography can facilitate to define the diagnosis. Syphilitic aortic aneurysm usually occurs at the thoracic aorta, which is singular and commonly found at the ascending aorta and aortic arch.

23.9.6 Congenital Bone Syphilis

Congenital bone syphilis should be differentiated from late-onset congenital bone syphilis, congenital rickets, and pyogenic osteomyelitis. Late-onset congenital bone syphilis occurs at an elderly age, and periostitis commonly occurs at the tibia, which is usually confined at the anterior tibia in saber tibia sign. Pyogenic osteomyelitis is manifested as systemic toxic symptoms, confined bone destruction, obvious sequestration and osteoproliferation, rare simultaneous involvements of multiple bones, and even rarer occurrence of symmetric lesions. Congenital rickets is manifested as common osteoporosis of diaphysis, cup-shaped metaphysic, and serration-shaped metaphysis due to bone destruction. In addition, laboratory tests demonstrate abnormalities of calcium and phosphate concentrations in the blood. By physical examinations, typical signs of rickets, such as rachitic beads, cephalus quadratus, and hand-foot bracelets, can be found. However, bone changes are not definitely demonstrated by X-ray in the cases of neonatal congenital syphilis, especially those experiencing premature delivery and baby patients. In such cases, the metaphysis can be demonstrated normal by X-ray.

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