Rubella

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Rubella is an acute respiratory infectious disease caused by rubella virus (RV). The acquired infection of rubella has clinical manifestations of mild respiratory tract inflammation, fever, red maculopapules, retroauricular, and occipitoposterior lymphadenectasis. Its infection in early pregnancy may cause fetal malformation or fetal death.

27.1 Etiology

Rubella virus is a positive single-stranded RNA virus, which is categorized into the family of Togaviridae. The viruses of this family are enveloped by a lipoprotein layer to maintain its activity. Electron microscopy demonstrates rubella virus in irregular sphericity with a diameter of 60–70 nm. Its two major components are an envelope and an inner nucleocapsid. On the surface of the envelope, there are protuberances in length of 5–6 nm containing prothrombin. The nucleocapsid is about 30 nm in diameter, with helical protein and a single-stranded RNA. Rubella virus contains 3–8 kinds of structural proteins, with envelope protein E1, envelope protein E2, and capsid protein C as its most important components. Both envelope protein E1 and envelope protein E2 are the transmembrane glycoprotein, while capsid protein C is a capsid protein surrounding viral RNA. The envelope protein E1 contains antigenic determinants that are related to hemagglutination activity (HA) and hemolytic activity (HL) of rubella virus. In addition, these antigenic determinants also play a role in inducing neutralizing antibody response, and the envelope protein E1 plays an important role in RV immunity. The antigenic structure of RV is quite stable, with only one serotype. Human is the most common host of RV, with survival and reproduction in placenta or fetus. RV may even survive and reproduce for several months or even several years in the body of neonatals to produce chronic progressive infection involving multiple body systems. RV is sensitive to ultraviolet rays, ether, chloroform, and formaldehyde. A slim chance of survival is found at conditions of pH < 6.8 or pH >8.1. And RV can be inactivated at the condition of pH < 3. RV is not heat resistant and can be inactivated at the temperature of 56 °C for 30 min. It can be preserved for 9 months at freezing and dry places.

27.2 Epidemiology

27.2.1 Source of Infection

Patients with rubella are the only source of infection, including asymptomatic patients and patients with subclinical infection. Rubella is transmissible from 7 days prior to the onset of rashes to 5 days after the onset of rashes, and its infectivity is the strongest from 1 day prior to the onset of rashes to the day of rashes onset. Rubella virus can be isolated from secretions of the mouth, nose, and pharynx as well as blood, stool, and urine of the patients. For neonatals with congenital rubella, viruses can be discharged via the nose, pharynx, stool, and urine after delivery, and the discharge of viruses may last for several weeks or even several months.

27.2.2 Route of Transmission

The virus can be found in respiratory secretions of patients or asymptomatic patients. And it commonly spreads via airborne droplets after patients or asymptomatic patients cough or sneeze. The virus can also spread via contacts to contaminated utensils, clothes, and daily necessities. Breast milk and placenta are also carriers of the virus for its spreading.

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27.2.3 Susceptible Population

Populations are generally susceptible to rubella, especially fetus and babies aged above 6 months. Due to the increasingly strong immunity along with age, children aged 1–9 years are susceptible to rubella whose occurrence is more common in young children aged 1–5 years. Rubella is also found in adults, with more male patients than female patients. Persistent immunity against rubella can be acquired after its infection.

27.2.4 Epidemic Features

The cases of rubella can be found worldwide all year round. In temperate regions, the peak incidence is in winters and springs. Before the wide use of rubella vaccines, the prevalence of rubella is periodic in most countries, with an interval of about 3–4 years. After infection of rubella virus, about one third of infected people are symptomatic.

27.3 Pathogenesis and Pathologic Changes

27.3.1 Pathogenesis

The rubella virus firstly replicates in local mucosa after its invasion into the upper respiratory tract, with following spreading into cervical, submaxillary, and retroauricular lymph nodes to cause lymphadenectasis. After that, the virus gains its access into the blood flow to cause viremia. The virus then reaches the mononuclear cell system along with leukocytes for replication and returns back into the blood flow to induce viremia again. Rashes may occur when the virus invades the skin via blood flow, mild conjunctivitis when it invades conjunctiva, and arthritis when it invades joints. Occasionally, encephalitis may also occur when it invades the brain tissues. Currently, it is believed that the direct effects are caused by virus underlying the pathogenic mechanism of rubella. Meanwhile, the impairments induced by immune responses to rubella also contribute to the occurrence of the disease.

Regardless of symptoms, after primary RV infection by pregnant women, the virus can invade the placenta during the phases of viremia and further involves the fetus. In patients suffering from rubella during the first 11 weeks of gestation, about 90 % has neonatals with congenital defect. In patients suffering from rubella after the first 16 weeks of gestation, fetus infection and congenital rubella syndrome (CRS) can be found. The pathogenesis underlying the occurrence of congenital rubella syndrome remains elusive. Currently, it has been believed that (1) RV directly causes necrosis and apoptosis of specific cells; (2) RV suppresses cell mitosis and causes chromosome breakage, leading to impaired differentiation and development of organs and tissues; (3) RV impairs vascular endothelium to cause insufficient blood supply to fetus; (4) the formation of specific immune complex and autoantibodies results in autoimmunological injuries; and (5) persistent RV infection causes delayed occurrence of diseases.

Embryonic development of the heart occurs from week 3 to week 8 of gestation, during which the infection of RV by pregnancies increases the risk of congenital heart disease (CHD) in fetus. Its teratogenic mechanisms mainly include:

1. *The interfering effects of the pathogen on division and differentiation of cardiovascular cells*. Rubella virus can suppress mitosis by affecting actin filaments to impair chromosomes (breakage and increased quantity) after its infection of cells. Therefore, the division and differentiation of cells are interfered. RV can also cause changes of cellular receptors of specific growth factors to limit multiplication of cells. Therefore, the cell proliferation decreases to cause insufficient accumulation of cell masses, leading to negative impacts on the formation and development of embryonic tissues.
2. *The effects of immune complex*. Specifically, after congenital RV infection of fetus, the pathogen commonly fails to be eliminated but survives for a long period of time. These pathogens and the abnormal substances produced by destructed cells act as antigens to bind to their corresponding antibodies to form immune complex. The immune complex then triggers a series of immunocompromising events. The immunocompromising effects on cardiovascular tissues, in combination with the direct negative effects exerted by the pathogens, increase the risk of CHD.

27.3.2 Pathologic Changes

The pathological changes of organs caused by acquired rubella are relatively mild, including capillary inflammatory exudates in the upper dermis of the skin with rash, intradermal mononuclear cell infiltration, lymphatic edema, follicular hyperplasia, and absence of characteristic structures. The pathological changes of rubella viral encephalitis include cerebral tissues edema, perivascular lymphocyte infiltration, nerve cell degeneration, mild meningeal responses, and demyelination in the cerebrum, brainstem, cerebellum, and spinal white matter. In the cases complicated by arthritis, there are pathological changes of sporadic fibrin exudation, synovial cell hyperplasia, lymphocytic infiltration, and vascular hyperplasia in synovium.

In the cases of congenital rubella syndrome, the symptoms of the nervous system include microcephaly and meningitis. Eye disorders include cataract, microphthalmia, amphiblestritis, and other eye disorders. Cardiac symptoms include myocardial necrosis, interventricular septal defect, pulmonary stenosis, and patent ductus arteriosus. The symptoms of other systems include hepatitis, pancreatitis, thyroiditis, skeletal malformation, and deafness. By autopsy of children with CRS, RV can be isolated from the organ and tissues. RV can also be isolated from the skin rashes of patients with acquired rubella.

The neurological pathology of congenital rubella encephalitis is characterized by cerebral vasculitis, which causes angionecrosis and multiple focal infarctions of cerebral tissues. The lesions are found only in the cerebrum, basal ganglia, spinal white matter, and the gray matter of brainstem. In the vascular walls of old lesions, amorphous sediments in small vessels can be found. There are also disseminated astral cell proliferations in white matters.

27.4 Clinical Symptoms and Signs

Clinically, rubella can be divided into two types, acquired rubella and congenital rubella syndrome, with more common occurrence of acquired rubella.

27.4.1 Acquired Rubella

The disease has an incubation period of 14–21 days, with a mean of 18 days. The clinical manifestations include fever, skin rashes, and enlarged lymph nodes.

27.4.1.1 Prodromal Stage

Prodromal stage has no obvious characteristic symptoms in children with rubella, and the earliest symptom is skin rashes. In young adults and adults, rubella usually has a prodromal stage of 1–5 days, with upper respiratory tract symptoms of fever, conjunctival congestion, headache, sore throat, cough, and runny nose. Some other symptoms can be rarely found, including vomiting, diarrhea, nasal bleeding, and gingival swelling.

27.4.1.2 Eruption Stage

The skin rashes erupt within two days after the onset of fever, firstly in the face and then quickly spreading to the trunk and limbs. The skin rashes can be found all over the body within 1 day after the onset of fever, which are absent in the palm and sole. The skin rashes are morphologically various, and congestive maculopapules are the most common. Occasionally, the skin rashes are hemorrhagic with tendency of systemic bleeding, which is caused by thrombopenia and increased capillary permeability. The skin rashes of rubella resemble the symptom of measles, and the fused skin rashes of rubella resemble the symptom of scarlet fever. In addition, the skin rashes generally persist for 3 days. Therefore, rubella is also known as 3-day measles. No pigment remains with no desquamation after the skin rashes vanish. During the eruption stage, the commonly found symptoms include low-grade fever, mild inflammation of upper respiratory tract, splenomegaly, and systemic superficial lymphadenectasis. Particularly, the symptoms of retroauricular, occipital, and posterior cervical lymphadenectasis are obvious. Swelling rapidly vanishes after rubella is cured. In some cases, swelling may persist for several weeks after the disease is cured.

The absence of skin rashes in the cases of rubella is common in elder children and adults, with only symptoms of mild fever, pharyngeal congestion, and lymphadenectasis. Cases of rubella with no symptoms and signs are also found but with findings of rubella antibodies by serological tests, which are known as asymptomatic infection or subclinical cases. Therefore, during the prevalence of rubella, persons with no skin rashes are still possible to be patients with rubella.

27.4.2 Congenital Rubella Syndrome (CRS)

Infection of RV during the first 3 months of pregnancy may cause congenital defects of multiple systems, which is known as congenital rubella syndrome (CRS). The earlier infection by pregnant woman causes more severe damages to the fetus. After the fetus is infected, fetus death, abortion, and premature birth may occur in some serious cases, and fetal growth retardation may occur in some mild cases. Sometimes, the whole body systems can be involved to cause multiple malformations. In most cases of CRS, clinical symptoms can be found at delivery, with common manifestations of CRS triad including congenital cataract, deafness, and congenital heart disease. No progressive symptoms or new malformations can be found in months or years after birth. CRS has common manifestations of the following:

27.4.2.1 Low Birth Weight

The newborn commonly has a body weight of less than 2.5 kg, with a small body and malnutrition.

27.4.2.2 Deafness

CRS is commonly presented with bilateral sensorineural hearing loss or accompanying conductive hearing loss to cause secondary language impairments. The hearing is impaired progressively or suddenly lost in the first year after birth. Deafness is the result of poor development secondary to the degenerations of cochlea and the organ of Corti.

27.4.2.3 Eye Defects

The incidence of cataract may reach as high as 54.5–66 %. It is commonly bilateral and often complicated by microphthalmia. The lens is spherical with nucleoid necrosis at the center. The eyesight is affected by focal retinal lesions and retinal neovascularization.

27.4.2.4 Cardiovascular Malformation

At least half of the fetuses with CRS in the first 2 months of pregnancy have cardiac damages. The most common conditions include patent ductus arteriosis, atrioventricular septal defect, tetralogy of Fallot, and advanced manifestations of renal artery stenosis and aortic stenosis secondary to hypertension.

27.4.2.5 Central Nervous System Diseases

The dominant manifestations of central nervous system diseases are delayed neural development or autism with severe motor nerve impairments and characteristic spastic diplegia. Progressive rubella panencephalitis (PRP) is a chronic progressive disease of the central nervous system, with higher incidence in the population aged 10–30 years. Its incubation period commonly lasts for 12 years. Patents with a past history of congenital rubella develop into progressive encephalopathy with manifestations of intellectual deterioration, ataxia, epilepsy, tonic spasm, dysarthria, and nystagmus, with occurrence of death due to progression of the conditions.

27.4.2.6 Metabolism and Endocrine Diseases

Diabetes is the most common manifestation at the advanced stage of CRS, with more common occurrence in the population aged 10–30 years. All the patients have deafness and other impairments. Hypothyroidism or hyperthyroidism and thyroiditis are the manifestations of advanced CRS. Chronic or progressive hypothalamic dysfunction may lead to growth hormone deficiency, which has a rare incidence.

27.4.2.7 Others

Other manifestations including interstitial pneumonia, hepatosplenomegaly, meningitis, thrombocytopenic purpura, hemolytic anemia, and bone damage are also common.

27.5 Rubella-Related Complications

The symptoms of rubella are generally mild with rare complications. Only a small quantity of patients may suffer from complications of otitis, pharyngitis, bronchitis, pneumonia, pancreatitis, hepatitis, gastrointestinal bleeding, thrombocytopenic purpura, hemolytic anemia, nephrotic syndrome, acute or chronic nephritis, and other complications. Some serious complications are listed as the following:

27.5.1 Encephalitis

The incidence of the disease is about 1/6,000, with more common occurrence in children. The symptoms in patients of school-aged children are more serious, which is probably related to stronger virulence of RV in infected elderly children. The onset of symptoms is common at days 1–7 after occurrence of skin rashes, including headache, lethargy, cervical rigidity, convulsion, and acroparalysis. The disease runs a short course, and its recovery usually requires 3–7 days, with sequelae in a few cases. Its mortality rate is about 20 %, and death commonly occurs due to coma and respiratory failure in several days after the onset of encephalitic symptoms.

27.5.2 Myocarditis

The patients suffer from symptoms of chest distress, heart palpitation, and dizziness with changes of electrocardiogram and myocardial zymogram. Its recovery commonly requires 1–2 weeks, and it may concur with encephalitis or other complications.

27.5.3 Arthritis

The disease usually presents in females aged 20–40 years, also with occurrence in children. Its pathogenesis remains elusive, which is most likely to be related to direct invasion of the virus to the joint cavity or immune responses. It is common after the onset of skin rashes, with occasional occurrence before the onset of skin rashes. It is also believed that the disease occurs at the regression of skin rashes. Proximal phalangeal joints and metacarpophalangeal joints are commonly involved, with occasional involvements of the ankle, knee, wrist, and elbow joints. Although multiple joints are involved, it is bilaterally symmetric or migratory. The symptoms commonly persist for 3–13 days, with manifestations of joint pain and stiffness, limited range of movement, slight swelling, and spindle-shaped swelling in proximal phalangeal joints. Carpal tunnel syndrome may be found in a few cases, and sometimes the pain may persist for 1 year. Articular effusion is defined as inflammatory exudates, from which the pathogenic virus can be isolated.

27.5.4 The Tendency of Bleeding

It has a rare occurrence, which is the result of thrombopenia and increased capillary permeability. Sudden bleeding occurs in 3–4 days after the onset of skin rashes, with petechiae, ecchymosis, hematemesis, hematochezia, and hematuria. In most cases, the symptoms spontaneously relieve within 1–2 weeks, with rare occurrence of death due to cerebral hemorrhage.

27.6 Diagnostic Examinations

27.6.1 Laboratory Test

27.6.1.1 Routine Blood Test

By routine blood test, there are decreased WBC count and increased lymphocyte count, with findings of heteromorphic lymphocytes and plasmacytes.

27.6.1.2 Virus Isolation

Rubella virus can be isolated by cultures of nasopharyngeal secretion and amniotic fluid from patients on RK13, Vero, or SIRC for cell subculture. Otherwise, for neonatals with rubella, blood, bone marrow, and urine should be subcultured to isolate the virus. Further identification should be performed by using immunofluorescence assay or ELISA.

27.6.1.3 Serologic Test

Specific antibody can be detected by complement fixation test, hemagglutination inhibition test, and neutralization test, whose findings of at least 4 times increase of antibody titers in paired sera have the diagnostic value. Hemagglutination inhibition test is the optimal choice, with the advantages of simple operations and reliable results within a short period of time, which can be widely applied. Specific IgM antibody of rubella in serum and saliva can be detected by ELISA, with a positive rate of 100 % at days 5–14 after the onset of skin rashes. The positive finding by ELISA indicates a recent infection of rubella. For neonatals, positive finding of specific IgM antibody by ELISA which persists for more than 6 months, along with increased titer can define the diagnosis of CRS.

27.6.1.4 Rubella Virus Antigen Test

Rubella virus RNA in oropharynx swab specimen can be detected by RT-PCR, with favorable sensitivity and specificity.

27.6.1.5 Electron Microscopy

The morphology of virus can be observed directly by an electron microscope. In addition, the virus particles can be detected directly from specimens collected at the early stage of infection. By immunoelectron microscopy, various antigens can be precisely located.

27.6.2 Diagnostic Imaging

27.6.2.1 Ultrasonography

Prenatal Ultrasonography

Prenatal ultrasonography is a diagnostic radiology of choice for fetus with CNS malformation. Especially, 3-dimensional ultrasound can display 3-dimensional spatial relationship of CNS malformation and its subtle structures, which improves prenatal diagnostic accuracy of fetus CNS malformation.

Echocardiography

Echocardiography is currently recognized as the most effective examination for the diagnosis of CHD in fetus and infants by demonstrating cardiac structure as well as hemodynamics in cardiac chambers and major vessels. The application of real-time 3-dimensional echocardiography can precisely demonstrate 3-dimensional morphology of cardiac structures, with multiple sectional imaging for observations from any perspective. It has been widely applied in diagnosing cardiovascular disorders, guiding surgical procedures, assessing cardiac functions, and assessing therapeutic efficacy and prognosis.

27.6.2.2 X-Ray Radiology

X-ray radiology is a basic examination for the diagnosis of CHD in children, which can favorably demonstrate the shape and location of the heart and aortic arch and the changes of pulmonary blood and facilitate in calculating cardiothoracic ratio. However, it fails to demonstrate intracardiac malformations.

27.6.2.3 CT Scanning

MSCT fast volume scan can harvest high-quality reconstructed images that render favorable demonstrations of the spatial location of the lesion from various levels and perspectives. It is operated noninvasively and simply, which is an optimal choice for the diagnosis of CHD. Dual-source CT (DSCT) further improves time and space resolutions, which can favorably display the anatomical structure of the heart and major vessels. Particularly, in terms of demonstrating extracardiac major vascular malformations, DSCT is superior to echocardiography. However, DSCT fails to provide information about hemodynamics and blood oxygen content.

27.6.2.4 MR Imaging

MR imaging provides images of multiple perspectives, sequences, and parameters, which can achieve arbitrary sectional reconstruction to completely demonstrate the anatomic abnormalities in children with CHD. Meanwhile, it provides anatomic and functional information. However, MR imaging requires a longer period of time, and moving shadows may be produced. The heart rate of children is relatively fast, which, therefore, results in the limitations in displaying coronary artery, peripheral pulmonary artery, and vein.

Fetus MR imaging is currently recognized as the optimal imaging examination for the diagnosis of fetal nervous system malformations. It can directly show the process of fetal brain development and myelination, therefore, facilitates in

defining various abnormalities. In combination to prenatal ultrasonography, it can greatly improve the diagnostic accuracy of fetal nervous system malformations.

27.7 Imaging Demonstrations

27.7.1 Rubella Viral Encephalitis

The imaging demonstrations of rubella viral encephalitis resemble to imaging demonstrations of other encephalitic lesions, which lack specificity.

27.7.1.1 CT Scanning

Calcification is the most common finding by CT scanning which can be found in the cerebral cortex and basal ganglia with manifestations of nodular, strip-like or spot-like calcifications. Subependymal strip-like calcification is the typical manifestation of rubella viral encephalitis. There are also demonstrations of decreased density of limbic system and deep whiter matter, cerebellar cortical atrophy, widened sulci and cistern as well as enlarged ventricles. The lateral ventricle, trigone, and the 4th ventricle commonly have the most prominent enlargement.

Case Study 1
A neonatal girl aged 4 days was diagnosed as having congenital rubella syndrome.

(For case detail and figures, please refer to Numazaki K, et al. J Child Neurol, 2003, 18(4): 296.)

27.7.1.2 MR Imaging

MR imaging can demonstrate deep cerebral white matter degeneration and subcortical white matter degeneration induced by cerebrovascular lesions and ischemic necrosis. The demonstrations include multiple linear and patches of high signals in bilateral white matter, which are commonly found in the white matters of frontal lobe and parietal lobe. Periventricular subcortical high signal in infants and children indicates delayed myelination. In addition, dilated ventricles are also common.

Case Study 2
A neonatal baby aged 7 days was found with systemic purpura, which is multiple purpura in diameters of 3–10 mm. By laboratory test, PLT 33×10^9/L and RV-specific IgM antibody positive.

For case detail and figures, please refer to Takano T, et al. J Perinat Med, 2006, 34(3): 254.

Case Study 3
For case detail and figures, please refer to Lane B, et al. AJNR, 1996, 17(1): 99.

27.7.2 Congenital Heart Disease

27.7.2.1 Atrial Septal Defect (ASD)

Doppler echocardiography demonstrates that the blood crosses the septum from the left atrium into right atrium. By X-ray radiology, the demonstrations include increased pulmonary blood flow, widened hilum artery in different degrees, small aortic knob, and protruding pulmonary artery segment. The heart is characterized by a mitral-like shape, pear-liked shape, dilated right ventricle and atrium that is more obvious in right atrium. Contrast CT scanning and MR imaging can demonstrate the continuity of the interatrial septum for the diagnosis of ASD. In addition, contrast CT scanning and MR imaging can also favorably demonstrate indirect signs of ASD, including dilated right ventricle and atrium as well as dilation of pulmonary artery.

27.7.2.2 Patent Ductus Arteriosus (PDA)

Doppler echocardiography demonstrates abnormal red-colored blood flow from aortic artery to pulmonary artery via arterial ducts. By Doppler spectrum analysis, a dual-phase continuous turbulence flow can be found. X-ray radiology demonstrates increased pulmonary blood flow, normal sized or slightly enlarged left atrium, enlarged left ventricle, and enlarged aortic knob, sometimes with the presence of funnel sign. CT scanning and MR imaging can favorably demonstrate PDA for its diagnosis. Contrast CT scanning and MRI SE sequence can demonstrate PDA as high-density vascular shadow connecting superior end of descending aorta and the beginning of left pulmonary artery and flow void vessel shadow in low signal. CT scanning and MR imaging can also favorably demonstrate the indirect signs of PDA, including enlarge left ventricle and atrium, dilated pulmonary artery, and dilated ascending aorta, which facilitate the diagnosis of PDA.

27.7.2.3 Tetralogy of Fallot (TOF)

Doppler echocardiography demonstrates blood flow from the right and left ventricles into the aorta. At the ventricular level, there is bidirectional blood flow, from left to right during diastoles and ventricular pressure discrepancy-dependent blood flow direction during systoles. High velocity turbulent flow spectrum can be found at the site of right ventricular outflow tract stenosis or pulmonary artery stenosis, with multicolored CDFI. X-ray radiology has demonstrations of decreased pulmonary blood flow, depression in pulmonary artery, enlarged right ventricle, and visible aortic knob in

right superior mediastinum due to complicated right migration aortic arch. In addition, X-ray radiology also demonstrates typical boot-like heart shadow, which is induced by enlarged right ventricle and relatively small left ventricle, upturned cardiac apex, and right spinning of the heart. MSCT can show aortic translocation, the size of cardiac chambers, and various intracardiac malformations. MR imaging can show obviously thickened right ventricular wall and dilated and anterior migrated ascending aorta across the interventricular septum. Sagittal MR imaging demonstrates enlarged and anterior migrated aorta, narrow pulmonary artery ring, infundibular stenosis, and ventricular septal defect.

27.7.3 Rubella Arthritis

X-ray radiology demonstrates swollen soft tissues and intact osteoarticular surface, with no chronic joint disorders resembling rheumatoid arthritis. In some rare cases, there is slightly widened interarticular space. In some case reports, there is also interphalangeal joint surface involvement, and in some serious cases, defective interphalangeal joint surface and carpal joint surface occur, with narrowed interarticular space.

27.7.4 The Changes of Skeleton

Changes of skeleton may also be found in the cases of CRS. Roche reported 1 case of infant CRS complicated by skeleton changes.

Case Study 4
Rubella complicated by skeleton changes
For case detail and figures, please refer to Roche CJ, et al. Radiographics, 2002, 22(6): 1369.

27.8 Diagnostic Basis

27.8.1 Acquired Rubella and Congenital Rubella Syndrome

27.8.1.1 Acquired Rubella

Typical Clinical Manifestations
The symptoms are mild, with retroauricular and retro-occipital lymphadenectasis and tenderness and quick occurrence of skin rashes that persist for a short period of time.

Epidemiologic Data
The epidemiologic data includes age, season of occurrence, and exposure history to rubella.

Specific Laboratory Tests
The definitive diagnosis should be based on specific laboratory tests.

27.8.1.2 Congenital Rubella Syndrome

History
The mother has a suspected history of rubella during pregnancy.

Laboratory Test
The laboratory tests for diagnosis include the isolation of rubella virus and RV-IgM-specific antibody positive in blood from neonate umbilical cord, neonatal, or infant.

Diagnosis
High titer IgG antibody in infants aged 6 months is also the basis for the definitive diagnosis of congenital rubella syndrome.

27.8.2 Rubella-Related Complications

27.8.2.1 Rubella Viral Encephalitis

1. A history of rubella occurs within 1 week before the onset of CNS symptoms, or CNS symptoms occur in children with CRS.
2. Electroencephalography and cerebrospinal fluid examination.
3. Diagnostic imaging demonstrates basal ganglia and subependymal calcifications, enlarged cerebral ventricle, and cerebral atrophy.

27.8.2.2 Congenital Heart Disease

1. A history of rubella
2. Clinical manifestations
3. Typical imaging findings such as typical heart shadow and patent ductus arteriosus

27.8.2.3 Rubella Arthritis

1. Clinical manifestations include characteristic skin rashes and enlarged lymph nodes and obvious joint symptoms around the onset of skin symptoms.
2. X-ray radiology demonstrates swollen articular soft tissues, no osteoarticular lesions and short course of joint symptoms.
3. CT scanning demonstrates shadows with water-like even density, which facilitates the diagnosis of articular cavity effusion.

27.9 Differential Diagnosis

27.9.1 Acquired Rubella

Acquired rubella should be differentiated from other diseases such as measles, scarlet fever, and exanthema subitum. Laboratory tests and clinical manifestations facilitate the differential diagnosis.

27.9.2 Rubella Viral Encephalitis

Rubella viral encephalitis should be differentiated from other diseases, such as congenital cerebral toxoplasmosis, tuberous sclerosis, hypoparathyroidism, and cytomegalovirus (CMV) encephalitis.

27.9.2.1 Congenital Cerebral Toxoplasmosis

Typical CT findings include intracerebral calcification, low density of cerebral parenchyma, and hydrocephaly. Diagnosis can be defined by detecting anti-toxoplasmosis-specific IgM or IgG antibodies.

27.9.2.2 Tuberous Sclerosis

Tuberous sclerosis is more common in teenagers and young adults with clinical triad symptoms including epilepsy, steatoadenoma, and mental retardation. CT scanning shows multiple subependymal and periventricular nodules and calcifications. In some cases, CT scanning demonstrates dilated ventricles and encephalatrophy. In combination with clinical manifestations and laboratory tests findings, it can be differentiated from CRS.

27.9.2.3 Hypoparathyroidism

Clinically, hypothyroidism is characterized by hands and foots spasm, epilepsy, and convulsion. And the imaging findings include calcification in the basal ganglia, thalamus, and corticomedullary junction. By biochemical assays, hypocalcemia and hyperphosphatemia can be found.

27.9.2.4 Cytomegalovirus (CMV) Encephalitis

Microcephaly is common in children with congenial cytomegalovirus encephalitis with clinical manifestations of fever, sensory abnormalities, convulsions, loss of vision, drowsiness, and coma. Plain CT scanning demonstrates encephalatrophy, dilated ventricles, and brain parenchymal calcification that is more common in the periventricular region of the brain. MR imaging can also show ectopic deformity of neuron, encephalomalacia, and delayed myelination. The diagnosis can be defined based on positive findings of CMV-IgM antibody and CMV antigen in blood and cerebrospinal fluid.

27.9.3 Rubella Arthritis

Rubella arthritis should be differentiated from other diseases such as rheumatic arthritis, pyogenic arthritis, and rheumatoid arthritis.

27.9.3.1 Rheumatic Arthritis

Rheumatic arthritis is common in joints of the knee, shoulder, elbow, and wrist of adults. Its occurrence usually follows upper respiratory tract infection with symptoms of migratory arthralgia, swelling, fever, and other rheumatic fever symptoms.

27.9.3.2 Pyogenic Arthritis

Pyogenic arthritis is commonly caused by invasion of bacteria into the articular cavity. It commonly involves the hip joint of teenagers and children, with an acute onset. Clinically, the toxic symptoms and signs are obvious. Within short period of time, extensive damages in articular cartilage and subchondral bone occur.

27.9.3.3 Rheumatoid Arthritis

Its typical clinical manifestations include symmetrical lesions, involvement of minor joints with arthralgia and swelling, as well as morning stiffness of the involved joints. By X-ray radiology, it can be demonstrated as having early and even narrowness of the articular space. Based on these clinical and radiological findings, along with positive finding of rheumatoid factor, it can be differentiated from rubella arthritis.

Further Reading

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