

Measles

by Erik Letko, M.D.

Definition

The Centers for Disease Control and Prevention defined "probable measles" as:

1) generalized rash lasting 3 or more days, 2) temperature >101F, and 3) the presence of cough, coryza, or conjunctivitis.

Measles can manifest as a congenital or acquired disease. Subacute sclerosing panencephalitis (SSPE) is a late complication of measles infection.

Congenital measles

In the pre-vaccine era, most people contracted measles in early childhood. For this reason, measles infection in pregnancy was unusual. Gershon et al estimated that four to six pregnancies per 100,000 were complicated by measles in the pre-vaccine era. In the post-vaccine era, a much larger proportion of measles cases has occurred among adults of reproductive age. Measles virus can cross the placental barrier, causing spontaneous abortion or congenital skeletal, cardiac or ocular anomalies.

The congenital, ocular anomalies described in the literature include congenital cataract, dacryostenosis, and two cases of congenital retinopathy are reported as well (**Figure 1**). The visual acuities in both cases were normal.

The diagnosis of congenital measles is made by the history of maternal measles and by the presence of congenital anomalies. Congenital measles is a self limited disease that does not require treatment.

Acquired measles

Epidemiology

Measles vaccine has been available in the United States since 1963. As a consequence, there is a marked decrease of the disease with a shift in the ages of occurrence from children to adolescents and young adults. Vaccination in less developed countries is not widely available, and therefore the course of the disease is more severe and often requires hospitalization. Dabis et al report on measles infection in a partially vaccinated population in an African city. The mortality rate of hospitalized children was 16%.

In spite of vaccine availability, not everyone in the United States receives it, mainly because of parental apathy, contraindications, and religious convictions. The failure of vaccination is present in 5 to 8 percent of population. This population remains susceptible to measles.

Clinical course

Clinical manifestations start with a prodromal phase of the disease 9 to 10 days after exposure, characterized by fever, malaise, lymphadenopathy, and mucosal lesions. The mucosal involvement consists of a catarrhal reaction of the conjunctiva and respiratory tract mucosa, as well as petechial lesions of the palate and pharynx. One to two days before the onset of the rash, Koplik's spots appear on the buccal mucosa. These are small, bluish-white dots surrounded by a red areola typically localized on the buccal mucosa opposite the lower molars. The characteristic skin eruption starts as pink macules behind the ear, on the forehead, and on the neck. The general lymphadenopathy and splenomegaly that arises early in the course of the acute disease may persist for several weeks. The total duration of the rash is approximately 6 days.

Ocular manifestation

Conjunctivitis, along with cough and coryza, is considered as a classical triad in measles. However, it is not always present. The conjunctivitis is usually mild, catarrhal, papillary and nonpurulent. Pseudomembranes may occur, and in debilitated patients, severe, true conjunctival membranes may develop. Koplik's spots (on conjunctiva also called Hirschberg spots) are rarely present in the eye. Epithelial keratitis is even more common than conjunctivitis. It is usually mild and present in both eyes of all infected patients. The keratitis develops in the prodromal phase or at the time of the onset of the skin rash and resolves without scarring several days afterwards. In some patients it may persist as long as 4 months.

Retinitis is, compared to keratitis and conjunctivitis, rarely present. It was described as macular edema, neuroretinitis, macular star formation, the presence of attenuated arterioles, and disc edema.

PATHOGENESIS

The measles virus belongs to the genus Morbillivirus in the Paramyxoviridae family. It has an RNA core and a helical capsid. The size of the virion is 100 to 200 nanometers in diameter. It is highly contagious. The first contact is at the mucous membrane of the respiratory tract. The conjunctiva also might act as a portal of entry for measles. If not inactivated by mucus or specific secretory IgA antibodies, the virus enters the ciliated columnar epithelium. During the primary viremia, two to six days after the infection, the virus is transported intracellularly inside the formed elements of the blood. A second viremia begins 10 days after the infection, with proliferation of the virus inside leukocytes. Neutralizing antibodies appear 14 days after infection, at the time of the appearance of the rash; rash is an expression of immunologic defense. In patients with severely impaired cell-mediated immunity, a measles infection may run its course without the appearance of rash. The measles antibodies cross the placenta and protect the infants against infection for the first six to twelve months of life.

Diagnosis

Diagnosis of measles is made by observing the regular sequence of the prodromal phase, the appearance of Koplik's spots and the generalized rash. The measles virus can be recovered from mucus membranes, urine, and blood for a few days before skin eruption and one or two days afterwards. The virus can be obtained from the urine for an additional few days. Serum antibodies can be detected within one or two days after the onset of the rash. During the prodromal phase and early eruptive phase of measles, multi-nucleated giant cells with eosinophilic inclusions in both the nuclei and cytoplasm can be identified in sputum, nasal secretions, or urine. In electron microscopic studies, inclusion bodies are visible as granular masses, with the characteristic measurements of the RNA helix.

TREATMENT

Uncomplicated measles infection is a self limiting disease. Supportive treatment is usually satisfactory enough. The course of measles infection can be altered by treatment with gamma-globulin as soon as possible after exposure. After six days of exposure, the treatment with gamma globulin may not prevent or modify the disease.

For the ocular manifestations, treatment is also symptomatic. No specific treatment for uveitis is described in the literature.

Complications

The most serious complications of measles are those affecting central nervous system and heart. The incidence of acute encephalitis in measles patients is 0.1%. It usually appears 6 weeks after the onset of the rash. Of these patients, 10 to 25% die, and 20 to 50% of the survivors suffer from permanent neurologic damage. Other central nervous system complications include subacute measles encephalitis, toxic encephalopathy, retrobulbar neuritis, transverse myelitis, and ascending myelitis. SSPE is a late complication of measles affecting the eye discussed later.

The keratitis can become ulcerative in patients with secondary bacterial infections or in debilitated patients with consequent corneal neovascularization, or it may become purulent, with progression to corneal perforation, panophthalmitis, and phthisis bulbi. These severe corneal ulcer complications are most frequent in developing countries as a consequence of malnutrition, vitamin A and protein deficiencies.

Prognosis

The prognosis of measles in vaccinated populations is good. In less developed countries approximately 1% of children with measles end up with permanent ocular damage. The term post measles blindness (PMB) is restricted to the corneal complications of measles, although retinitis and optic neuritis have been also described as a cause of damage to the sight after measles infection. In West Africa, 43 of 193 blind children were blinded by measles.

Interestingly, in one study 10 of 13 patients with uveitis associated with multiple sclerosis had elevated levels of measles IgG antibodies in the anterior chamber fluid.

Subacute sclerosing panencephalitis

Epidemiology

SSPE is a chronic degenerative disease of the central nervous system, first described by Dawson in 1933. Its prevalence has been estimated at 1 to 10 per 10 million cases of measles. The male to female ratio varies from 1.8:1 to 4:1. The onset of SSPE is usually 6 to 7 years after measles. Individuals who had measles before the age of two years are of higher risk of developing SSPE. The majority of patients manifest neurologic signs before the age of 20 years.

Clinical symptoms

A typical clinical picture has three stages. Behavioral changes and intellectual deterioration are present in the first stage. The second stage is characterized by extrapyramidal signs and cortical blindness. Dementia develops in the third stage and the course of the disease is terminated by death within 1 to 3 years.

Ocular symptoms

Thirty to fifty percent of patients with SSPE develop ocular symptoms. These include maculopathy (Figures 2 to 6— *fundus pictures and fluorescein angiogram from one patient taken 18 hours and 11 days apart showing rapid progression of the lesion*), disc edema, papillitis, optic atrophy, retinitis, serous retinal detachment, chorioretinitis, and vasculitis. The measles virus primarily affects the retina with secondary involvement of the retinal pigment epithelium and choroid. The eye involvement starts as a focal area of retinitis in the macula and over time it can spread to the posterior pole and peripheral retina as well. Characteristically, there is little or no vitreous inflammation. Retinitis resolves leaving retinal pigment epithelium mottling and varying degrees of scarring (Figures 6 through 8).

PATHOGENESIS

The classic measles virus replicates by budding and fusion. SSPE is caused by measles virus deficient of certain virion polypeptides, such as matrix (M), hemagglutinin (H), and fusion (F) proteins. These proteins are necessary for alignment of the virus along the host-cell plasma membrane and subsequent budding and release of the virus from the host cell. Defects in these proteins and host's factors may explain the prolonged viral persistence (Figure 9). The disease is a true panencephalitis affecting both gray and white matter.

Diagnosis

The diagnosis is made by the presence of three of these five criteria: 1) clinical course, 2) biopsy or necropsy results, 3) EEG pattern, 4) elevated globulin levels in cerebrospinal fluid, and 5) elevated levels of IgG measles antibodies in serum and cerebrospinal fluid. The negative IgM measles antibodies provide evidence against a new, acute-onset infection.

TREATMENT

There is no definitive treatment for SSPE. However, inosiplex and intracameral or intrathecal interferon may induce remission or stabilize the clinical course. But

SSPE is, generally a lethal disease. A spontaneous remission is reported in 5% of patients. The survival rate differs from 5 to 50% according to various studies. Early diagnosis and treatment are essential to improve the prognosis.

Reading list

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