Case 36

The patient was a 9-year-old female who was brought to her pediatrician in February because of fever and rash for 2 days. She also had a headache, sore throat, and mild cough. There were no gastrointestinal symptoms. No one else in the household was ill, but she had a classmate with a similar illness.

On examination she was alert and in mild distress. Her temperature was 38.3°C, pulse rate was 110 beats per min, blood pressure was 90/60 mm Hg, and respiratory rate was 40/min. She had a mild conjunctivitis. Her posterior pharynx was injected, and petechiae were present on her soft palate. The buccal mucosa was injected with scattered raised papular lesions. She had a macular rash on her trunk, face, and arms (see Fig. 1). Her chest radiograph was normal. A throat swab was sent for culture, and blood was drawn for viral serologic examination. Subsequently, the throat culture was read as negative for group A beta-hemolytic streptococci. Acute- and convalescent-phase (obtained 2 weeks later) serum specimens confirmed the clinical diagnosis, and the school nurse was notified.

Figure 1

1. What is the differential diagnosis in an individual who presents with the symptoms cited in this case, with specific emphasis on the skin rash? What is the agent of this patient's infection?

2. How is the diagnosis of this infection usually made?

3. Describe the typical clinical course of this infection, and name three complications which can occur.

4. How can infection with this virus be prevented? What is the current epidemiologic status of this disease in the United States? Worldwide?

5. How would you manage her case? Are specific treatments available?

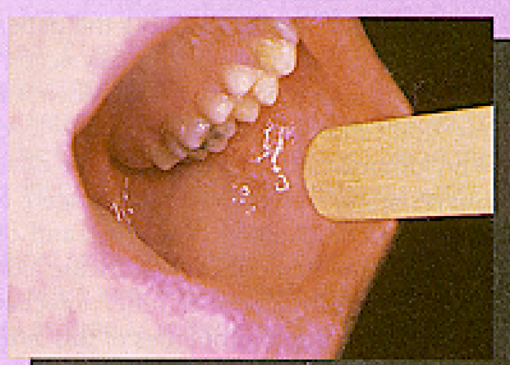

Figure 2

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Case Discussion

1. In general, the differential diagnosis is quite large in patients with fever and rash, so it is important to focus on the specific type of rash. In this patient the rash was diffuse and macular (see Fig. 1). Macular or maculopapular rashes are seen with viruses such as measles virus, rubella virus, roseola virus, enteroviruses, Epstein-Barr virus, cytomegalovirus, and parvovirus B19. Other types of infections associated with this type of rash include meningococcal infection, salmonellosis, mycoplasma infection, Rocky Mountain spotted fever, secondary syphilis, and subacute bacterial endocarditis. Coexisting enanthemas (involvement of mucous membranes) can help to narrow down the differential diagnosis. This patient had a rash that was readily recognizable (i.e., measles) from its specific appearance and accompanying findings of coryza, conjunctivitis, pharyngitis, and palatal petechiae. The measles virus is a paramyxovirus (a single-stranded RNA virus). Humans are the only natural host.

2. The diagnosis of measles is usually made on clinical grounds, with laboratory diagnostic procedures playing a secondary role. A nasopharyngeal aspirate stained with fluorescein-labeled antibody detects the measles virus directly in clinical specimens, allowing same-day confirmatory laboratory diagnosis of infection.

Immunoglobulin M (IgM)-based tests are also available for the rapid diagnosis of measles. Serum samples for IgM antibody should be collected after day 3 of the rash since IgM antibody may not be detectable before this time. The virus can be isolated in tissue culture, but isolation is difficult and unreliable for the diagnosis of measles.

3. The measles virus, which is spread by the respiratory route, is the most easily transmitted human infectious agent. After exposure, the incubation period of measles is 10 to 14 days. Typically, patients initially develop fever, cough, coryza, conjunctivitis, sore throat, and headaches. Several days later a generalized morbilliform rash appears. Koplik spots, which are pathognomonic for measles, may be seen. These are small bluish-gray lesions on a red base, which appear on the buccal mucosa (Fig. 2).

The virus multiplies in the upper respiratory tract and conjunctiva. Viremia then develops, and after this viremia the patient experiences fever, constitutional symptoms, and rash. Leukopenia usually accompanies acute infection.

In the upper respiratory tract, edema and loss of cilia as a result of the measles infection can predispose to secondary bacterial invasion, which can lead to bacterial pneumonia and otitis media. In the developing world, secondary diarrheal disease and respiratory infections are often seen, especially in malnourished infants and children. The combination of measles and other infectious agents has a much higher mortality rate than does either disease alone. The mechanism by which measles predisposes to acquisition of other infectious agents is believed to be due to the immunosuppressive properties of this virus. This period of immunosuppression may last for weeks to months, during which time these children will continue to be at increased risk for other infectious agents.

The most severe complication is encephalitis, which develops in 1 of every 1,000 to 2,000 cases. This develops 1 to 14 days after the rash. A high proportion of patients with encephalitis are left with neurologic sequelae. Subacute sclerosing panencephalitis (SSPE) is an extremely rare complication of early infection and usually is seen in patients less than 2 years old. SSPE is a persistent encephalitic infection which is distinct from the encephalitis that may complicate acute measles infection. The virus which causes SSPE may be a defective measles virus or another measles virus variant. SSPE has an insidious onset, usually manifested by behavior problems. The disease progresses over a period of weeks to months, resulting in severe neurologic dysfunction including seizure activity, loss of motor function, coma, and eventually death.

4. Measles can be prevented with live, attenuated vaccine. This vaccine is administered after maternally acquired immunity wanes, usually at 9 months (in the developing world) to 12 to 15 months (in developed countries). In addition to vaccination, infection may be prevented by the use of passive immunity (immunoglobulin). This is usually administered to persons at significant risk of severe measles following specific exposure. Immunoglobulin can be used in babies less than 1 year old and in children with cancer and/or specific defects in cell-mediated immunity in whom vaccination with a live, attenuated vaccine would be contraindicated. In 1995, 300 cases of measles were reported in the United States, a remarkable decline from the over 50,000 cases of measles seen in the United States between 1989 and 1991. Unvaccinated children in day care centers are particularly at risk for measles infection and contribute a significant number of these cases. Some of the 300 cases had received vaccine, as did the child described in this case, and must be considered vaccine failures. Antibody levels may wane in college-aged individuals, making them vulnerable to this disease. A little more than 10% of the United States cases were imported, most coming from industrialized countries.

Measles continues to be a major childhood health problem in much of the world. It is estimated by the World Health Organization (WHO) that 1 million children die each year from measles and its complications. Although these numbers are indeed grim, vaccination programs have reduced yearly worldwide measles-related mortality by two-thirds over the past 15 years. It is estimated that approximately 80% of children worldwide are vaccinated. Current WHO goals call for 90% reduction in measles cases and 95% reduction in measles-related deaths worldwide compared to prevaccination levels. In certain areas of the world such as the United States, many countries in Latin America, and the Caribbean, these goals are being met. Not surprisingly, in those countries over 90% of the eligible population is vaccinated.

5. This patient should be managed with supportive therapy. No specific antiviral treatment is available. The school nurse and local health department should be notified about this case (as was done) as soon as possible so that necessary control measures can be implemented.

References

1. **Centers for Disease Control and Prevention.** 1996. Measles—United States, 1995. *Morbid. Mortal. Weekly Rep.* **45:**305–307.

2. **De Quadros, C. A., J. M. Olivé, B. S. Hensh, M. A. Strassburg, D. A. Henderson, D. Brandling-Bennett, and G. A. Alleyne.** 1996. Measles elimination in the Americas: evolving strategies. *JAMA* **275:**224–229.

3. **Gellin, B. A., and S. L. Katz.** 1994. Measles: state of the art and future directions. *J. Infect. Dis.* **170**(Suppl. 1):S3–S14.