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What Pediatricians Should Know About Lassa Virus

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After the 2014–2015 Ebola outbreak, viruses causing hemorrhagic fever have garnered increasing international attention. Infection with Lassa virus is an important cause of fever in children in West Africa. Exact figures are unknown, but a study showed 6% of febrile admissions in Nigeria were due to Lassa fever.¹ Considering ever-increasing global migration, pediatricians should be aware of Lassa virus risk factors and treatment standards. The diagnosis should be considered by pediatricians in the United States treating children newly arrived from endemic areas, as Lassa virus may be an under recognized source of infection in this population.

Virology and Epidemiology

Lassa fever is caused by an RNA virus from the *Arenaviridae* family. The virus was first discovered in the village of Lassa, Nigeria, in 1969 when 2 missionary nurses contracted infection and died. Its most severe form causes hemorrhagic fever and shock. Most cases are reported in the “Lassa belt” of western Africa. In Guinea, Liberia, Nigeria, and Sierra Leone, cases are considered to be hyperendemic, and cases have been reported in Benin, Ghana, Mali, and Togo. Eight imported cases of Lassa virus in the United States have been reported since 1969.² Imported cases have also been reported in Japan, the United Kingdom, Germany, the Netherlands, and Israel. Outbreaks in Africa occur primarily in the dry season (November to April), and 338 suspected cases were reported in the first half of 2017 in Nigeria.³ The estimated yearly incidence in West Africa is 100 000 to 300 000 cases and approximately 5000 deaths. Children under age 10 years are considered most vulnerable, with 1 study showing 15% seropositivity for Lassa virus in that population in West Africa.⁴

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The Lassa virus reservoir is *Mastomys natalensis* or the multimammate rat. These rats are primarily found in west and central Africa and are attracted to houses in rural areas where they seek out accessible food sources. The virus is shed in the rodents' urine and feces and then can be transmitted from rats to humans through contact with these materials via inhalation of the virus or direct contact with open cuts or sores on humans. Butchering and preparation of rats for cooking are believed to be another route of transmission. The virus is spread from human to human by direct contact with body fluids from symptomatically infected individuals or corpses. Nosocomial outbreaks have been reported.¹

Recent case reports detected viral nucleic acid in semen up to 103 days after onset, suggesting sexual transmission is possible.⁵ No studies have investigated virus presence in breast milk, but high level of viremia implies that the virus may be present in the milk of an infected mother and therefore could be passed on to her child. Risk of transmission also exists from close contact between mother and child.

Clinical Manifestations and Prognosis

Lassa fever is not well studied in children, but disease manifestations range from asymptomatic to viral hemorrhagic fever (VHF) leading to death. The incubation period is 7 to 21 days, and the most common signs and symptoms (studied in adults) are nonspecific and include fever, general malaise, cough, sorethroat, retrosternal pain, and myalgia. More severe cases result in vomiting, hemorrhage, shock, encephalitis, and death. Similar findings are seen in children. Lassa fever can present with acute abdomen, although rare, and patients have wrongly received abdominal surgery when infected with the virus. Acute hearing impairment has been noted in up to one-third of adult hospitalized patients, with two-thirds of those patients suffering from permanent hearing loss.⁶ Common laboratory findings associated with Lassa fever include leukopenia, thrombocytopenia, elevated transaminases, and coagulation abnormalities.

Up to 80% of cases are believed to be mild or asymptomatic, but when fulminant the disease is deadly. A study in Nigeria showed that up to 23% of hospitalized children with the disease died.¹ In epidemics, the case fatality ratio in patients with Lassa fever can approach 50% among hospitalized patients.

Pregnant women and neonates are thought to be particularly susceptible to severe disease. Swollen baby syndrome is the severe form of Lassa virus infection described in a case series from a Liberian hospital.⁷ This syndrome presents mostly in neonates, who likely contract Lassa virus from their infected mothers, but can also be seen in infants and toddlers. It causes widespread tense-pitting edema, abdominal distention, and hemorrhage. One study showed an 87% fatality rate in neonates born to infected mothers.⁸

Diagnosis and Treatment

Multiple modalities are available to detect Lassa virus infection. Enzyme-linked immunosorbent serologic assays, which detect IgG and IgM antibodies as well as Lassa antigen, and reverse transcriptase-polymerase chain reaction are most commonly used to detect virus RNA in the early stage of disease. More than 1 reverse transcriptase-polymerase

chain reaction assay may be required to confirm infection because of the high virus genetic diversity across West Africa. Because specimens from patients with Lassa fever can be infectious, special handling conditions are required and testing usually is only performed in reference laboratories. In the United States, the Centers for Disease Control and Prevention provides testing and confirmation for Lassa virus.

Supportive treatment is the mainstay of therapy in Lassa fever. This includes aggressive management of hypovolemia, supportive treatment for fever, and management of electrolyte imbalances. In severe cases, coagulation factors should be monitored. The patient should also be monitored for superimposed bacterial infection. The antiviral ribavirin has been shown to be effective in lowering the mortality for adult patients if given early (less than 6 days after onset) in the disease course, but no studies show its effectiveness against the disease in children. Ribavirin has, however, been used to treat chronic hepatitis C and respiratory syncytial viruses in the pediatric population. In the United States and Germany, 2 recent cases were successfully treated with ribavirin and favipiravir, suggesting combination therapy may have utility against Lassa virus.⁵ Currently, no effective vaccine against the virus exists.

Contact Precautions

To minimize the risk of person-to-person and nosocomial spread, standard precautions should be used for all patient encounters, regardless of suspected pathogen. When a case of Lassa virus infection is suspected, VHF precautions should be instituted, which include the isolation of the patient and the use of protective eye wear, mask, head cover, rubber boots, 2 pairs of gloves, and a protective gown with plastic apron. Respirator use is indicated if any aerosol-generating procedures (eg, ventilation and suction) are performed. Any equipment that contacts the patient or bodily fluids must be sanitized and then bleached or otherwise sterilized. If a patient dies, VHF precautions must continue until burial or cremation.

Importance for Pediatricians

Pediatricians should consider Lassa virus with a consistent clinical picture in any febrile child arriving from rural areas of endemic countries where more common tropical diseases (eg, malaria, dengue, and typhoid fever) have been ruled out, especially between November and April. Lassa fever can concomitantly present with malaria and, although Lassa fever is less common, should be considered in children with proven malaria infection that is not responding to treatment. Ebola, Marburg virus disease, and Crimean-Congo hemorrhagic fever can also produce similar clinical presentation. In the United States, Lassa virus infection is nationally notifiable as a VHF. When Lassa fever is suspected, patients should be placed on VHF contact precautions and immediately reported to local and state health departments. When the diagnosis is confirmed, treatment with ribavirin should be initiated.

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