Don't Miss Pediatric Progressive Histoplasmosis

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ASPEN, COLO. — Pediatric progressive disseminated histoplasmosis is a disease whose recognition is critical, Dr. Matthew Zahn said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver, and the University of Colorado.

"An awful lot of histoplasmosis will go away without treatment. This is not one of those. This is one that you have to identify and you have to treat," stressed Dr. Zahn, medical director of the Louisville (Ky.) Metro Department of Health and Wellness.

Pediatric progressive disseminated histoplasmosis (PDH) has a 15% mortality, occurring mainly in children in whom the disease wasn't recognized. Indeed, pediatric PDH is typically fatal if it is left untreated.

Pediatric PDH is said to occur in children less than 2 years of age, although Dr. Zahn said that in his experience the affected population is mostly 8 months old or less.

PDH will not go away without treatment as is often the case with histoplasmosis—it must be identified and treated.

DR. ZAHN

The pathophysiology is thought to involve inhalation of the pathogen, followed by its passage from the lungs into the bloodstream and from there to the reticuloendothelial system, where the fungus overwhelms the young child's still-developing immune system.

The classic symptoms of pediatric PDH include prolonged fever, malaise, and failure to thrive. Without treatment the child typically develops disseminated intravascular coagulation. Other common manifestations include respiratory distress, hepatomegaly with a granulomatous hepatitis, and pancytopenia.

Serologic testing using both a complement fixation assay and immunodiffusion assay is generally the best way to diagnosis histoplasmosis.

The immunodiffusion assay is more specific, whereas complement fixation is more sensitive. But cross-reactivity to tuberculosis and fungal antigens can occur with both tests. And both tests are slow. A complement fixation assay may not show positive results until 2-6 weeks after onset of acute illness, and an immunodiffusion assay often lags further behind.

Faster results are obtained with a urine histoplasmosis antigen test. It's not a terribly sensitive test, and a negative result doesn't exclude infection, but its reliability is greater in cases of disseminated histoplasmosis, said Dr. Zahn, a pediatrician at the University of Louisville (Ky).

Histoplasmosis culture has traditionally been considered the gold standard of diagnosis. It's only positive in about 15% of cases, although this rate is higher in PDH because the laboratory is likely to be working with biopsy specimens from the liver or other infected organs. A downside of culture is that results can take 2-4 weeks.

The histoplasmin skin test is the oldest form of diagnostic testing for histoplasmosis. Today it's most useful for epidemiologic studies. The test can have negative results in disseminated disease. Moreover, once positive the test stays positive for life. In Louisville and the rest of the Ohio River Valley, where 80% of the population has been infected by *Histoplasma capsulatum* var. *capsulatum* by age 18 years and 95% of those infections are asymptomatic, the skin test has little clinical utility.

The treatment of choice for PDH or severe disease is intravenous amphotericin B. It cures disease more rapidly than the azoles. The standard regimen for PDH is 4-6 weeks of therapy. Alternatively, 2-3 weeks of amphotericin B can be followed by 3-6 months of oral itraconazole.

Fluconazole is less effective than itraconazole and is generally reserved for itraconazole-intolerant patients and those with CNS disease.

Liposomal amphotericin has shown considerable promise in adult studies. It is better tolerated and yields a faster response than the traditional formulation, Dr. Zahn said. ■