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COMMENT. Pediatric-onset MS has a slower rate of progression than adult-onset disease, according to several reports. The discrepancy between higher relapse rate and slower long-term progression of pediatric-onset MS is unexplained.

FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS TYPE 3 WITH DEMYELINATING CNS DISEASE

A case of familial hemophagocytic lymphohistiocytosis type 3 (FHLH3) presenting in a 3-year-old boy with fulminant demyelinating neurological disease is reported by researchers at Kravis Children's Hospital at Mount Sinai Medical Center, New York. Clinical examination 4 days after onset of neurological symptoms revealed an alert, active child with massive splenomegaly, and broad-based gait. MRI showed diffuse small demyelinating foci in subcortical and perivascular white matter. CSF protein was 55 mg/dL, and myelin basic protein was elevated (7.2 ng/mL, normal 0-4). EEG showed bilateral slowing. He had presented 6 weeks earlier at another hospital with irritability, abdominal pain, head tilt, neck and back pain, and inability to walk. Laboratory tests showed anemia, neutropenia and thrombocytopenia; serum ferritin was normal. Having recently returned from a trip to Honduras, he had received a course of amphotericin B for clinical suspicion of visceral leishmaniasis, later confirmed negative.

His neurological status deteriorated in hospital, with fever, progressive loss of head control, side-to-side head movements, right hemiparesis with tremor, and generalized hypotonia. MRI showed progressive demyelination. On suspicion of ADEM, he was treated with methylprednisolone without benefit. He developed seizures refractory to anticonvulsants. At 40 days after onset, typical diagnostic criteria for HLH were absent. Brain biopsy was consistent with ADEM. At 50 days after onset, soluble interleukin-2-receptor antibody levels were elevated, with increased expression of perforin-granzyme B. Sequence DNA analysis of blood showed a mutation in intron 10 of the Munc13-4 gene, diagnostic of FHLH3. The disease was too advanced for standard treatment with chemotherapy and stem cell transplantation; the patient continued to have seizures and died of sepsis 173 days after initial presentation. The family was offered genetic screening. (Weisfeld-Adams JD, Frank Y, Havalad V, et al. Diagnostic challenges in a child with familial hemophagocytic lymphohistiocytosis type 3 (FHLH3) presenting with fulminant neurological disease. **Childs Nerv Syst** February 2009;25:153-159). (Dr JD Weisfeld-Adams, Division of Medical Genetics, Mount Sinai School of Medicine, One Gustave L Levy Place, PO Box 1497, New York NY 10029. E-mail:james.weisfeld-adams@mssm.edu).

COMMENT. Familial HLH is an autosomal recessive multisystem disease characterized by fever, rash, splenomegaly, cytopenias, hyperferritinemia, and variable CNS manifestations with demyelination. This case report illustrates the difficulties encountered in diagnosis of HLH, and the need for a high index of suspicion and early molecular testing in cases of undiagnosed inflammatory CNS disease presenting as ADEM or pediatric MS. Leishmaniasis, considered as a possible cause of the symptoms in this case, shares similar features and is reported in 12% of HLH cases.