CLINICAL FINDINGS LEADING TO THE DIAGNOSIS OF X-LINKED AGAMMAGLOBULINEMIA


**Purposes of the Studies.** Hyper-immunoglobulin E (HIE) syndrome is an immunodeficiency disorder characterized by recurrent skin abscesses, pneumonia, elevated serum IgE, and increased incidence of dental abnormalities (retained primary teeth), bone fractures and scoliosis. X-linked agammaglobulinemia (XLA) attributable to a mutation in the gene for Bruton’s tyrosine kinase (BTK) typically results in recurrent bacterial infections in the first few years of life. These studies reviewed the clinical features of patients with these diagnoses and report clinical features that could lead to earlier diagnosis.

**Study Populations.** Eight children with hyper-IgE syndrome were identified from 5 pediatric dermatology practices through a retrospective chart review. Eighty-two patients with clinical features leading to the diagnosis of XLA, and proven mutations in the BTK gene culled from 53 institutions were evaluated.

**Methods.** The clinical history, laboratory results and clinical photographs were obtained from chart review (hyper-IgE) or from structured survey forms completed by referring physicians or genetic counselors (XLA).

**Results.** The 8 children recruited from dermatology practices had been evaluated for a papulopustular eruption on the face and scalp in the first year of life and were not diagnosed with HIE until an average of 18 months later. Six developed the rash by 1 month of age and most also developed lesions in the axillae, upper trunk, extremities and diaper area. Five children later developed ecematous dermatitis, but the initial rash was not consistent with atopic dermatitis and among 6 who underwent skin biopsy; an eosinophilic spongiform dermatitis was observed. At the time of the eruption, 6 patients had otitis media, pneumonia or unexplained fevers, 2 had fractures and 7 had persistent peripheral blood eosinophilia. The mean age of diagnosis for sporadic XLA was 35 months. Fewer that 10% of patients with sporadic XLA were diagnosed before a hospitalization for infection and 36% were not diagnosed until after >1 hospitalization. Patients with more dramatic infections were diagnosed earlier. Most patients had recurrent otitis media before diagnosis.

**Conclusions.** A papulopustular eruption with the described features and distribution, along with additional findings such as early infections, fractures, and/or eosinophilia, should prompt an evaluation for HIE. Children with 3 or more episodes of otitis media or sinusitis should be examined closely and if the tonsils or cervical lymph nodes are unusually small or absent, serum immunoglobulin levels should be screened with appropriate referral for additional studies if they are abnormal.

*Reviewer’s Comments.* Prompt diagnosis of immunodeficiency disorders allows for earlier treatment and can prevent sequela. Knowing the results of these 2 studies will allow pediatricians to increase the chance for early diagnosis. It must be kept in mind, however, that the presentations emphasized here are not the only ones that are possible with these disorders. Vigilance in keeping primary immunodeficiency disorders on the differential diagnosis of recurrent, recalcitrant, and unusual infections is key.

**Reviewer’s Comments.** This is a wonderful study that will lead many people to revise their diagnostic work-up of