Hyper-IgE syndrome: Diagnosis of a 3-year-old with 10-year follow-up

By Karen R. Kessler, RN, AE-C

This is the clinical presentation of a child diagnosed with hyper IgE syndrome (HIES) at age 3 years, 4 months after repeated episodes of severe eczema, herpetic infections, wheezing, pneumonia, and failure to thrive since infancy when the patient was first hospitalized for severe dehydration, sepsis, and bronchospasm. Throughout childhood and into adolescence, the patient continued to exhibit these conditions and required multiple hospitalizations for acute wheezing and recurrent skin infections. At age 13 years, 9 months, the patient continues to display the features of an individual with HIES and has recurrent episodes of pneumonia, herpetic skin infections, and eczema. He also has many of the characteristic facial features and remains short in stature with consistently poor weight gain.

Physical exam revealed a height of 35.5 inches (90.2 cm), 10th percentile; weight 28.5 lb (12.9 kg), 10th-25th percentile; BMI 15.5, 25th percentile; HR 96; and RR 24. He had severe chronic eczema with new and crusted lesions. Underlying skin was lichenified. Head, eyes, ears, nose, and throat was normal and the neck was supple. The chest exam revealed no gross deformity. Air entry was good bilaterally with no crackles or wheezes. Cardiac exam revealed normal first and second heart sounds without murmurs, heaves, or thrills. Abdominal exam showed soft, nontender abdomen; no organomegaly. Inguinal lymphadenopathy was noted. Neurological and musculoskeletal exams were normal.

Lab evaluation was initiated. Complete blood cell count showed a normal white blood cell count and differential with 0% bands, 46% lymphocytes, 37% neutrophils, and 10% eosinophils. The immunoglobulin, IgG was 1,010 mg/dL (reference range 458-1,193 mg/dL), IgA 42.1 mg/dL (22.0-122 mg/dL), IgM 110.0 mg/dL (36.0-138 mg/dL), and IgE 7,156 IU/mL (0-230 IU/mL).

Follow-up

This patient receives coordinated care from a family medicine medical home with consultations in pediatric pulmonology, dermatology, and infectious disease. He has been hospitalized on multiple occasions—the first for severe dehydration, sepsis, and bronchospasm followed by multiple admissions for acute wheezing and recurrent skin infections. His primary teeth required extraction. He has had multiple episodes of oral candidiasis and herpetic infections.

While his characteristic facial features were not identified in early life, the phenotype of deep-set eyes, coarse facial features such as prominent pores and a wide nasal bridge were recognized as he matured to adolescence. Despite aggressive nutritional management, he has short stature and consistently poor weight gain. At age 13 years, 9 months, he has radiographic evidence of degenerative joint disease. There is no history of HIES on either side of the child's family. While no genetic testing was ever performed, the conclusion is that the HIES is autosomal recessive.

Important considerations for NPs

HIES is a rare primary immunodeficiency.[1] Although there are no exact data regarding the prevalence, it is listed by the National Organization of Rare Disorders indicating an incidence of less than 200,000 individuals in the United States. Clinical diagnostic clues were first described by Buckley et al.[2] in 1972, as a constellation of recurrent skin and lung infections, eczema, and elevated serum IgE with a characteristic phenotype, which included the following craniofacial characteristics: prominent forehead, deep-set eyes, broad nasal bridge, prognathism, and facial asymmetry. Typically, children with HIES present in infancy.

Two distinct forms of HIES have been reported—autosomal dominant HIES (AD HIES) and autosomal recessive HIES (AR HIES).[3] Mutations in signal transducer and activator of transcription 3 (STAT 3), which is a transcription factor gene, are responsible for most cases of AD HIES. The etiology of most cases of AR HIES is unknown.[3] There is a lack of connective tissue and skeletal findings and neurologic abnormalities occur with greater frequency in AR HIES.[3]

In childhood, the patient was treated with a regimen of antistaphylococcal

Short Communications enables clinicians to trade practice tips, experiences, information, and research findings. Short Communication articles are not reviewed by the editorial review board; the goal is to allow a free dialogue among journal readers.

Copyright © 2011 Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

therapies with antimicrobials or antiseptics in conjunction with topical corticosteroids.

Beginining in infancy and lasting throughout childhood, the patient had multiple hospitalizations for pneumonia, which were treated aggressively. Pneumonias in the HIES are frequently caused by *Staphylococcus aureus* and *Haemophilus influenzae*, which can be associated with abscess formation.[1] Pneumonias secondary to opportunistic infections have been reported.

To promptly identify comorbidities, clinicians should be aware of findings that are associated with HIES. Vascular anomalies are common as children with HIES become adults, with coronary artery dilatation, aneurysms, and tortuosity being most common. Arnold-Chiari malformations are reported in approximately 20% of patients.[1] HIES has been associated with increased incidence of malignancy, particularly Hodgkin's and non-Hodgkin's lymphoma, although leukemia, liver, lung, and vulvar cancers have also been reported in patients with AD HIES.[1]

Currently, clinical management focuses on prevention of eczema flare-ups, control of infection, and monitoring for known comorbidities. NPs need to be alert for signs of worsening eczema and skin infection. Respiratory infections should be addressed promptly.

HIES, like other disfiguring conditions, can lead to educational underachievement, lowered self-esteem, depression, and social isolation.[4,5] Clinicians should assess for signs and symptoms and refer to appropriate specialties. NP

REFERENCES

1. Freeman AF, Holland SM. Clinical manifestations, etiology, and pathogenesis of the hyper-IgE syndromes. *Pediatr Res*. 2009;65(5):32R-37R.
2. Buckley RH, Wray BB, Belmaker EZ. Extreme hyperimmunoglobulinemia E and undue susceptibility to infection. *Pediatrics*. 1972;49(1):59-70.
3. O'Gormon MR. Recent developments related to the laboratory diagnosis of primary immunodeficiency diseases. *Curr Opin Pediatr*. 2008;20(6):688-697.
4. Hearst D. Can't they like me as I am? Psychological interventions for children and young people with congenital visible disfigurement. *Dev Neurorehabil*. 2007;10(2):105-112.
5. Thies KM. Identifying the educational implications of chronic illness in school children. *J Sch Health*. 1999;69(10):392-397.

Karen Kessler is the asthma coordinator for the Suffolk County Department of Health Services, Hauppauge, NY.

The author has disclosed no financial relationships pertaining to this article.

DOI-10.1097/01.NPR.0000405152.07772.9e

Copyright © 2011 Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.