

Correspondence

Cartilage-hair hypoplasia and severe allergy

To the Editor:

A recent review on primary immune deficiencies with aberrant IgE production by Ozcan et al¹ discussed 5 disorders: hyper-IgE syndrome; immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome; Wiskott-Aldrich syndrome; Omenn syndrome; and atypical complete DiGeorge syndrome. These disorders are associated with increased IgE levels and eosinophilia, but the occurrence of atopy was not specifically discussed in the review. Of particular interest are mutations involving the RNA component of the mitochondrial RNA-processing endoribonuclease gene (*RMRP*) that can lead to the presentation of Omenn syndrome with skeletal dysplasia akin to cartilage-hair hypoplasia (CHH).² CHH is an autosomal recessive disorder frequently caused by a homozygous *RMRP* g.70A>G mutation.³ It results in metaphyseal chondrodysplasia, short-limb dwarfism, and light-colored hypoplastic hair. It is variably associated with T-cell immunodeficiency and sometimes with immunoglobulin deficiency.⁴ Despite the presence of *RMRP* gene mutations in patients with CHH, as in a few cases of Omenn syndrome, increased IgE levels or atopic phenotype in CHH has not been described, although an association with autoimmunity has been found.⁵

We present a patient with CHH who had an anaphylactic reaction to an insect sting. This patient had recurrent sinopulmonary infections since birth, a protracted course of varicella infection, disproportionate short stature, and skeletal dysplasia. She was lost to follow-up at 9 years of age and returned at 17 years of age to be seen at our skeletal dysplasia clinic. Genetic testing documented that she was homozygous for the *RMRP* g.70A>G mutation and was given a diagnosis of CHH. Four months before being seen by us, she had oral pharyngeal angioedema and an anaphylactic reaction to an insect sting and was hospitalized for 2 days. She had a normal white blood cell count and eosinophilia of 7.2% (normal range, 0% to 3%), with a count of 457 cells/ μ L (normal range, 0–190 cells/ μ L). Her IgG level was 1090 mg/dL, IgA level was 271 mg/dL, IgM level was 132 mg/dL, and IgE level was 56.5 IU/mL (all values within the normal range). RASTs for venoms revealed 0.47 kU/L to honeybee (class 1), 1.4 kU/L to white-faced hornet (class 2), 2.92 kU/L to wasp (class 2), and 1.42 kU/L to yellow jacket (class 2). She had tetanus and diphtheria antibody titers of greater than 10 IU/mL; weak prevaccination pneumococcal titers (postvaccination titers pending); a

strong delayed hypersensitivity skin reaction to tuberculin, *Candida*, and tetanus antigens; a normal lymphocyte phenotype, as determined by means of flow cytometry; normal proliferation with mitogen stimulation; a slightly decreased proliferation response to *Candida* antigen; and no proliferation response to streptokinase and tetanus antigens.

Overall, this patient with CHH showed little evidence of serious immunodeficiency but had an allergic phenotype and eosinophilia without an increased IgE level. The authors of the review article gave an excellent summary of the 5 primary immune deficiencies associated with increased IgE production.¹ We would like them to comment on the occurrence of atopy in these disorders and also of allergic phenotype and IgE levels in patients with CHH, especially in the context of *RMRP* gene mutations, some of which can be associated with Omenn syndrome.

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