Hyper-IgE syndrome: a case report

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The hyper-IgE syndrome (HIES) is a rare disorder characterized by pruritic dermatitis, recurrent Staphylococcus skin abscesses and extremely elevated levels of IgE in serum. In this report, an eleven-year-old-boy with hyper-IgE syndrome is presented. He had a coarse facial appearance, pruritic dermatitis, recurrent skin abscesses, pulmonary infection, a reduced rate of resorption of the roots of primary teeth and an elevated serum IgE concentration. The colonization of Candida albicans, Kiebsiella pneumoniae, Escherichia coli *and* Staphylococcus aureus *were found as; (1x10^2 CFU), (2.2x10^4 CFU), (2.2x10^4 CFU) and (2.6x10^3 CFU) per ml saliva, respectively. Also the pulp of a deciduous molar was investigated with light and transmission electron microscope (TEM). As conclusion, treatment for this condition is lifelong administration of therapeutic doses of a penicillinase-resistant penicillin, with the addition of other antibiotics or anti-fungal agents as required for specific infections.*
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INTRODUCTION

Hyper-IgE syndrome (HIES), also called 'Job Syndrome' and 'hyper-IgE recurrent infection syndrome' was first described as a primary immunodeficiency characterized by recurrent Staphylococcal skin abscesses, recurrent pnuemonia with pneumatocele formation, eczema, pruritic dermatitis, eosinophilia and highly elevated levels of serum IgE.[1-3]

A coarse facial appearance, hyperextensibility of the joints, bone fractures, craniosytosis and prominent triangular mandible have been reported in many cases of HIES.[2,4,5]

Seventy two percent of the patients with the hyper-IgE syndrome, who were older than eight years reported retained primary teeth, non-eruption of permanent teeth, or double rows of teeth where permanent teeth erupted adjacent to primary teeth. Shedding of primary teeth, although delayed, did occur in some patients; however, most patients required extraction of eight or more retained primary teeth. The failure of primary teeth to exfoliate on time had not previously been found to be associated with the hyper-IgE syndrome.[2]

Staphylococcal abscesses involving the skin, lungs, joints and other sites develop first during infancy; persistent pneumatoceles develop as a result of the recurrent *Staphylococcal pneumonias*.[6] In addition, approximately 50% of the patients have monocutaneus Candidiasis. Characteristically, the patients have extreme elevation of serum IgE, particularly against *S. aureus* and *C. albicans*, prompting the name hyperimmunglobulin- E- recurrent-infection syndrome.[7,8]

In patients with HIE there is low or absent serum and salivary anti-S.aureus IgA, slight elevation of IgM, and normal IgD. The low anti-*S. aureus* IgA correlates with sinopulmonary infections. There is a low-grade eosinophilia and prominent eosinophil enrichment at infected foci.[8]

The genetic basis of the hyper-IgE syndrome is unclear, as most cases are sporadic. However, in many kindreds, autosomal dominant transmission, including male to male transmission has been reported.[8]

The following is a dental case report involving an eleven-year-old patient with Hyper-IgE syndrome.

CASE

An eleven-year old boy was referred to Department of Pediatric Dentistry for the treatment of tooth decay.

Physical examination revealed a coarse facial appearance (Figure 1). There were numerous skin abscesses and pruritic dermatitis on his scalp, face, gen-

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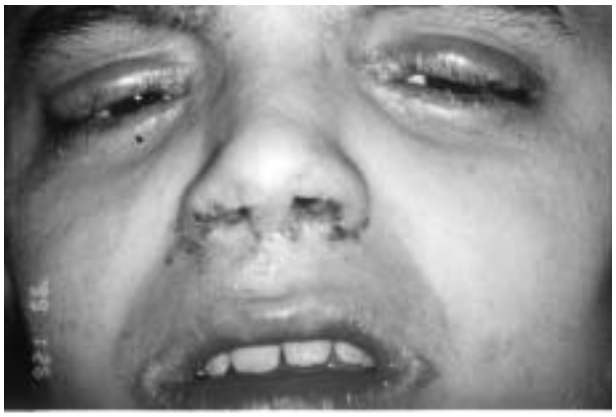
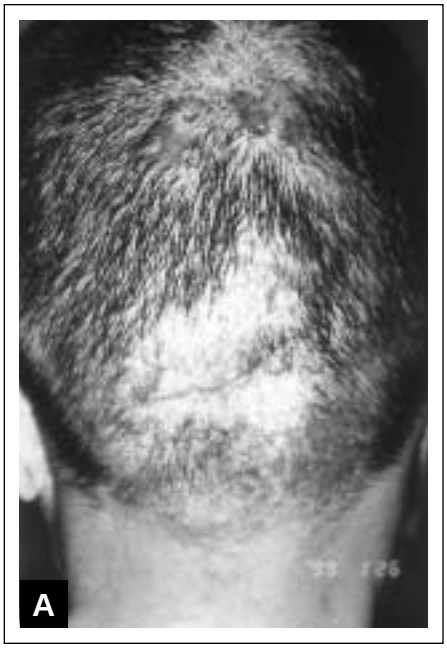
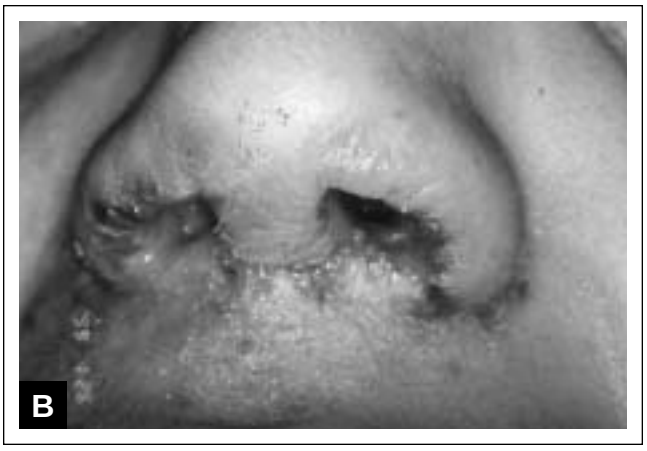


Figure 1. The characteristic facial appearance of patient with a prominent brow and supraorbital ridge, deep-set eyes, increased interalar width, and thick soft tissue of the nose.





Figures 2, A, B. Skin abscesses and pruritic dermatitis on the scalp, and nose in 11-year-old patient.

ital area and buttock, nose and labials (Figures 2, A-D). Cultures of the abscesses yielded *Staphylococcus aureus*.

The patient was first hospitalized at 24 months of age for numerous skin abscesses and fewer. His medical history revealed persistent dermatitis localized on the scalp, face, retroauricular and genital areas, which started at 15 days of age and also recurrent pnuemonia. He had a fracture of the left radius-ulna bone with no history of trauma at 9 years of age. The parents were first degree cousins and healthy.

Intra-oral and radiographic examination revealed delayed exfoliation and a reduced rate of resorption of the roots of primary molars. Retention of these teeth prevented appropriate eruption of the permanent premolars (Figures 3, 4). The carious teeth were restored with amalgam restorations. The upper first primary molars were extracted and investigated with light and transmission electron microscope (Figure 5). No pathological findings were detected under the light microscope (Figure 6). The sections prepared from the pulp of the extracted primary molars revealed a large number of mast cells and eosinophils under transmission electron microscope (Figures 7, A-B). The migration of the granules of mast cells were also observed.

The microbiological investigation revealed the colonization of *Candida albicans, Klebsiella pneumonia, Escherichia coli* and *Staphylococcus aureus* was $1.0x10^2$ cfu, $2.2x10^4$ cfu, $2.2x10^4$ and $2.6x10^3$ cfu per ml saliva, respectively.

The serum IgE level was 1184 IU/ml.

In view of the clinical picture and laboratory findings, the patient was diagnosed as having hyper-IgE syndrome.

DISCUSSION

The hyper-IgE syndrome is a multi-system disorder that effects the dentition, the skeleton, connective tissue and the immune system.[2]

Patients with this syndrome have a striking depression of acute inflammation, as evidenced by cold abscesses despite pronounced local infection. Abnormal neutrophil and monocyte chemotaxis have been documented. Lymphocyte function in HIES is abnormal.[8]

Delayed hypersensitivity responses to a variety of skin-test antigens are impaired in some, but not all, patients. Mitogen-induced and antigen-induced lymphocyte transformation is impaired, especially with regard to Candida antigen and tetanus toxoid, and may be related to the mucocutaneous candidiasis in many patients. Deficient suppressor T-cell numbers may

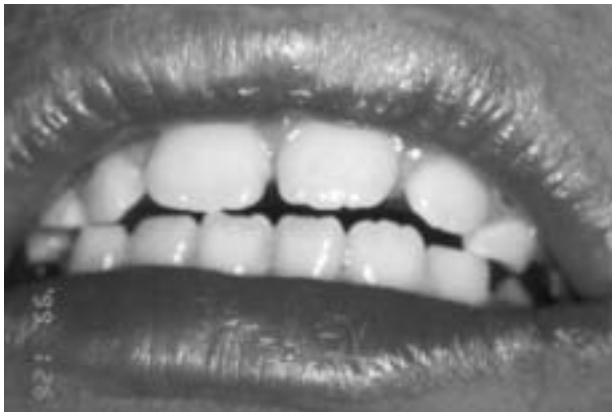


Figure 3. Angular cheilitis was observed in the patient.

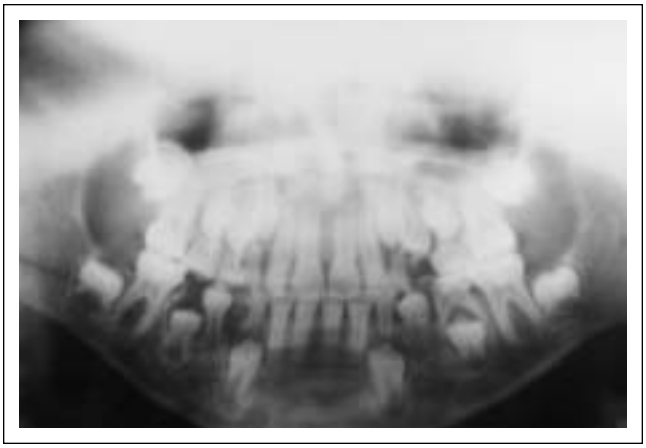


Figure 4. Panoramic radiograph of the patient showing retention of primary molars.

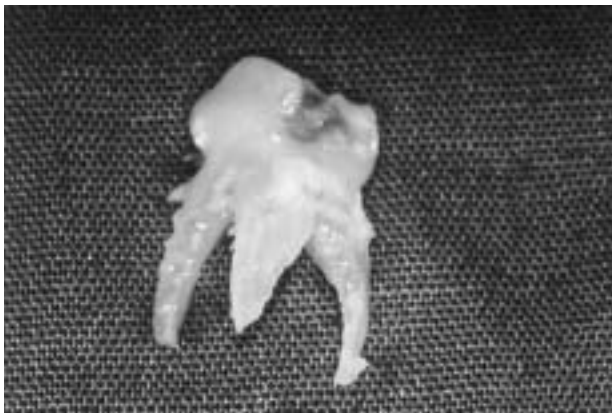


Figure 5. Extracted primary molar revealed delayed root resorption.

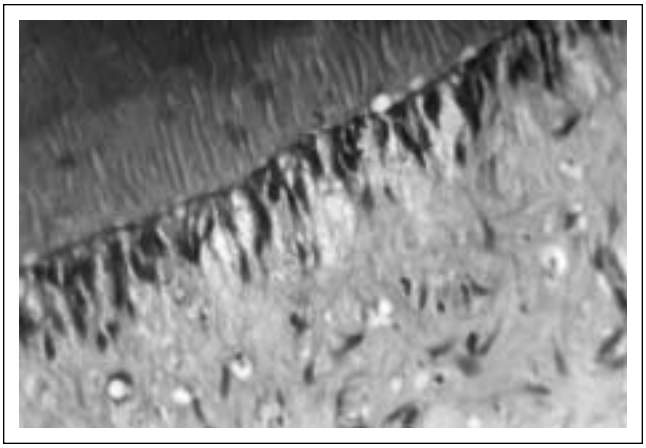


Figure 6. Histological section of upper primary molar showing no pathologic alterations under light microscope (hematoxylin eosin, original magnification)

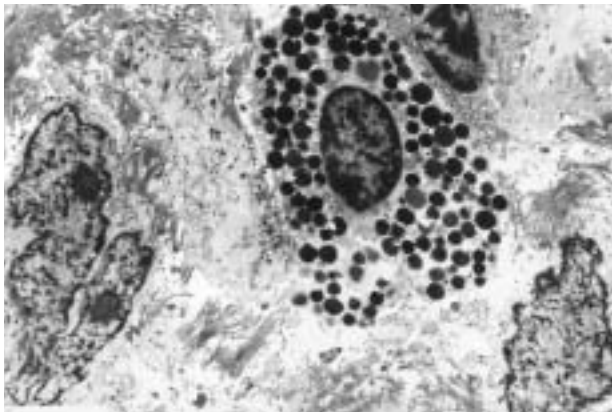


Figure 7, A. Sections prepared from the pulp of the extracted primary molars revealed a large number of mast cells and eosinophils under transmission electron microscope (original magnification)

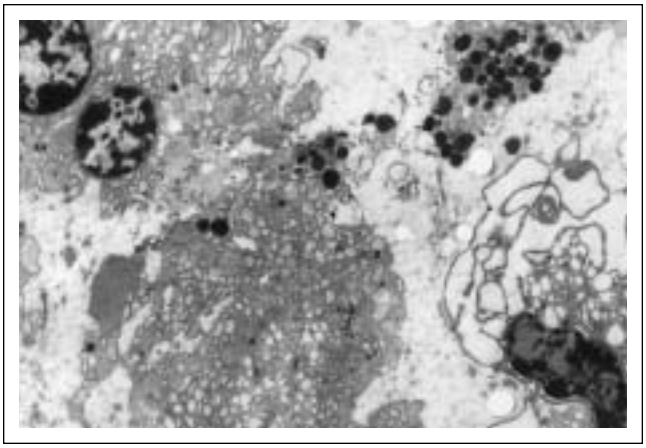


Figure 7, B. Migration of the mast cells were observed and may be interrelated with the high level of IgE in serum.

account for increased IgE. Low or absent salivary and plasma anti-staphylococcal IgA likely contributes to the propensity to mucosal infections.[8]

Children with the HIES are prone to bone fractures and have significantly reduced bone density compared with age and sex-matched controls.[4]

The reduced rate of root resorption contrasts with the early loss of primary teeth as a result of periodontal infection in other disorders of host defense most notably defects in leucocyte adhesion.[2]

The factors that control physiological dental-root resorption are undefined, but may involve the activation of osteoclasts, macrophages, or both by cytokines, which also mediate local inflammation. It is suspected that delayed resorption of the hyper-Ig E syndrome may be defect that results in the ineffective formation of pneumatoceles.[2,8]

O'Connell *et al.*[9] reported that a disorder of tooth eruption is part of the hyper-IgE syndrome and the lack of resorption of the primary teeth may be associated with the persistence of Hertwig's epithelial root sheath.

Oral health maintenance and prompt treatment of dental infections are extremely important for patients with hyper-IgE syndrome because significant morbidity can result from infections of odontogenic origin.

Treatment for this condition is lifelong administration of therapeutic doses of penicillinase-resistant penicillin, with the addition of other antibiotics or anti-fungal agents are required for specific infections.

The dentist plays an important role in the recognition of disorder of eruption. Continuous monitoring of exfoliation and elective extractions of retained primary teeth will allow correct timing and alignment of the succedaneous permanent teeth.

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