

Rapid Transition of Facial Features from Early to Mid - Adolescence in Autosomal Dominant Hyper IgE Syndrome with a *STAT3* Variation

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To the Editor: A fifteen-year-old boy of non-consanguineous parentage was admitted with ‘cold abscesses’ over his forehead and neck (Fig. 1). He had a history of recurrent pustules, multiple abscesses, lower respiratory tract infections, diarrhea, oral thrush, otitis media and empyema. He had a neonatal pustular rash and atopic dermatitis from infancy. He had lost only 6–7 primary teeth.

Examination revealed a characteristic facies, barrel shaped chest, severe kyphoscoliosis, grade four clubbing with onychomycosis, hypermobile joints and pes cavus. He had several scars and pits on his face and deep set eyes with bushy eyebrows. He had a bulbous nasal tip, prominent chin, thin upper lip and a high arched palate. His facial features took on the typical ‘old man’ facies from the age of twelve.

Chest X-ray showed bilateral pneumatoceles apart from bronchiectatic changes. Dental X-ray showed several retained primary teeth. IgE level was 10,000 IU/ml and peripheral smear showed eosinophilia. *Staphylococcus aureus* was isolated on several occasions. He had been on prophylaxis with cotrimoxazole for the last three years.

Whole exome sequencing was done using Nextera rapid capture expanded exome kit and a variation c.1145G > A (p.R382Q) in exon number 13 of *STAT3* gene was identified on the DNA binding domain.

There are few reports of Hyper IgE syndrome from India and the changing phenotype over time has not been described [1]. Characteristic features include recurrent *Staphylococcal* pneumonia, skeletal abnormalities

Fig 1 Evolution of facial features in AD hyper IgE syndrome



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and a distinctive facies, 'cold' abscesses and elevated levels of IgE with eosinophilia [2].

Inheritance may be autosomal dominant (AD) with associated skeletal abnormalities or autosomal recessive with viral infections and neurological involvement; *STAT 3* mutations are found in autosomal dominant hyper IgE syndrome (AD HIES) while other reported mutations include those in *DOCK8* and *TYK2* genes [3].

A lack of Th17 cells has been reported to be a useful predictive marker for heterozygous mutations in *STAT3* [4]. Management includes prophylactic antibiotics and emergent treatment of infections. Recently, intravenous immunoglobulin has been found to be useful and stem cell transplant has been recommended when all other treatment options have failed [5].

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Contributions GMG designed the study and collected the data. VS did the whole exome sequencing and helped in writing the paper. AR and CK helped in diagnosis and management of the case. GMG will act as guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

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