Case Report

Job's Syndrome (Autosomal Dominant Hyper-IgE Syndrome): A Rare Case Report

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Abstract

Background: Hyper-IgE syndrome (HIES), also known as Job's syndrome, is a rare primary immunodeficiency disorder characterized by markedly elevated serum immunoglobulin E levels, recurrent infections, and chronic eczematous dermatitis. The condition is often associated with distinctive craniofacial features, skeletal abnormalities, and delayed shedding of primary teeth. We report the case of a 22-year-old female who presented with long-standing pruritic skin lesions and recurrent pustular eruptions since childhood, along with persistence of primary dentition. Clinical examination revealed generalized eczematoid dermatitis, retained deciduous teeth, and characteristic facial features. Laboratory investigations showed marked eosinophilia and significantly elevated serum IgE levels (37,760 IU/mL). Radiological assessment demonstrated impacted third molars and the absence of maxillary canines. Considering the typical clinical features and a high score on the diagnostic scoring system, a diagnosis of autosomal dominant Hyper-IgE syndrome was established. The patient was managed with systemic antibiotics, oral corticosteroids, antihistamines, topical immunomodulators, and emollient therapy, leading to notable clinical improvement during follow-up. This case emphasizes the importance of recognizing the characteristic clinical and laboratory findings of Job's syndrome to ensure timely diagnosis and appropriate management.

Keywords: Hyper-IgE syndrome, Job's syndrome, primary immunodeficiency, elevated IgE, recurrent infections, eczema.

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Introduction

Hyper-IgE syndrome (HIES), also known as Job's syndrome, is a rare primary immunodeficiency disorder characterized by markedly elevated serum immunoglobulin E levels, chronic eczematous dermatitis, and recurrent bacterial infections. The condition has an estimated incidence of approximately 1 in 100,000 individuals and is associated with abnormalities affecting the immune system, skin, skeletal structures, and dentition.[1]

The syndrome was first described in 1966 by Davis and colleagues, who reported patients with recurrent "cold" staphylococcal abscesses, eczema, and pulmonary infections resembling the biblical description of Job.[2] Later, Buckley et al. identified markedly elevated serum IgE levels in such patients and described the disorder as Hyper-IgE syndrome.[3]

HIES is broadly classified into two forms: autosomal dominant Hyper-IgE syndrome (AD-HIES), which is most commonly associated with mutations in the STAT3 gene, and autosomal recessive Hyper-IgE syndrome (AR-HIES), which results from defects in other immune regulatory pathways.[4] The classical triad of atopic dermatitis, recurrent staphylococcal skin infections, and recurrent pulmonary infections characterizes the autosomal dominant form. In addition, patients frequently demonstrate characteristic facial features, retained primary teeth, skeletal abnormalities, and immunologic dysfunction.[5]

Because of its rarity and varied clinical manifestations, the diagnosis of Job's syndrome may be challenging. Recognition of the characteristic dermatological, dental, and immunological features is therefore essential for early diagnosis and appropriate management.

Case Report

A 22-year-old female presented to the dermatology outpatient department with complaints of chronic itchy skin lesions and recurrent pustular eruptions.

History

The patient reported itchy, erythematous, and cracked skin lesions predominantly over flexural areas since birth, with worsening episodes over the past 12 years. Over the last 4–5 years, she developed recurrent pus-filled lesions initially involving the arms and legs that gradually spread to the abdomen. She also complained of frequent episodes of sinusitis and pain in the oral cavity while chewing food. The patient reported poor

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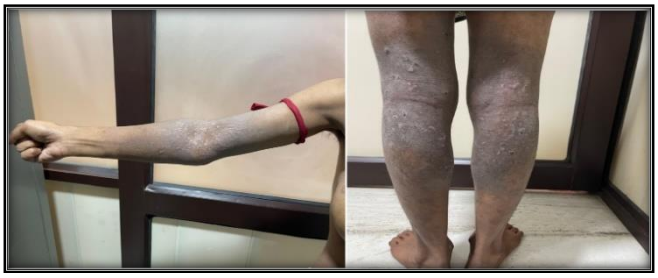
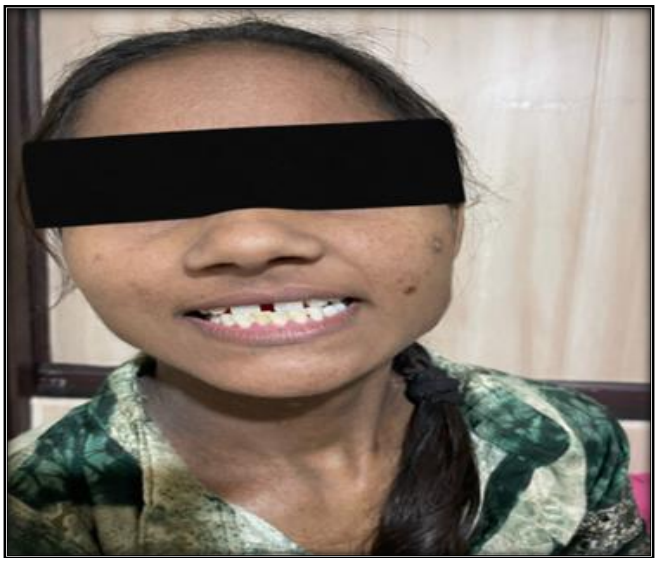
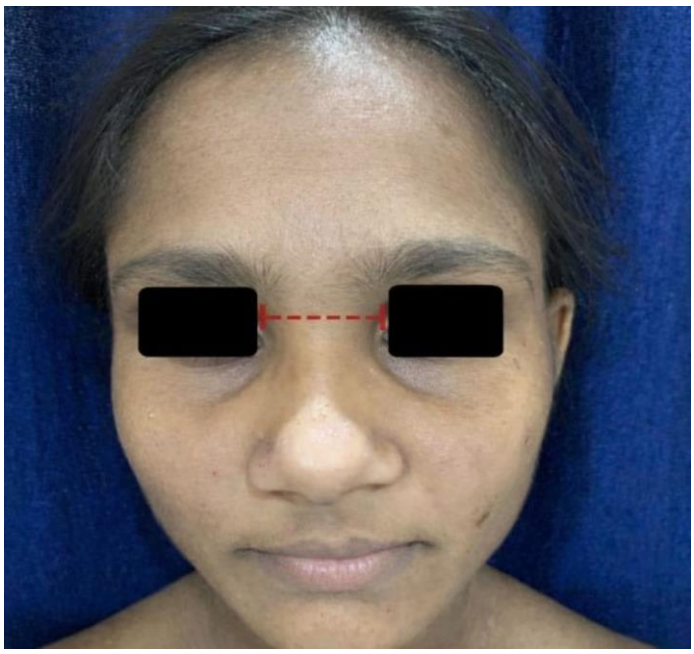
recent memory and persistence of primary teeth since childhood.

Clinical Examination

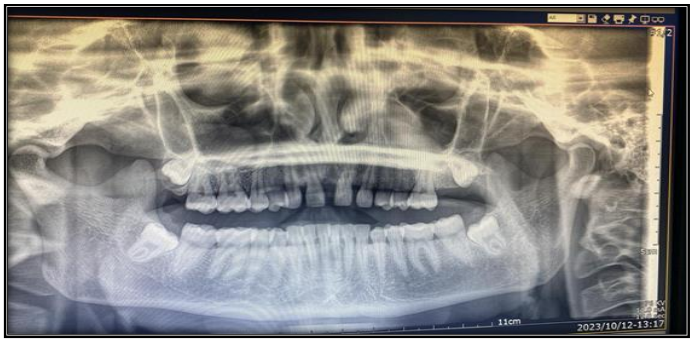
Dermatological examination revealed widespread pruriginous eczematoid rashes over the scalp, neck, arms, and legs. Characteristic facial features were noted, including a broad nasal bridge and mandibular prognathism.







Oral examination demonstrated the presence of 26 retained deciduous teeth along with a high-arched palate, suggesting delayed dental eruption.



Investigations

Laboratory investigations showed:

Eosinophilia with an eosinophil count approximately ten times the normal value

Markedly elevated serum IgE levels of 37,760 IU/mL

Chest radiography was normal.

Orthopantomogram (OPG) revealed missing maxillary canines and impacted third molars.

The NIH clinical scoring system was applied to evaluate the likelihood of Hyper-IgE syndrome.

Table 1: The NIH clinical scoring system

	0	1	2	3	4	5	6	7	8	10
Highest Serum Ig E Level (IU/ml)	<200	200-500			500-1000			1000-2000		✓>2000
Skin Abcess	None		✓1-2		3-4			>4		
Pneumonia	None		1		2		3	>3		
Parenchymal Lung Anomalies	Absent						Bronchiectasis	Pneumatocoele		
Retained Primary Teeth	None	1	2		3			✓>3		
Scoliosis, Max Curvaure	<10 Degree		10- < 14 Degree		15-20 Degree			>20 degree		
Fracture with minor trauma	None				1-2			>2		
Highest eosinophil count	<700			✓700-800			>800			
Characterstic Face	Absent		Mildly			✓Present				

Midline anomaly (cleft palate, Tongue, other vertebral anomaly	Absent		Present			Present				
Newborn Rash	Absent				Present					
Eczema (worst stage)	Absent	Mild	Moderate		✓Severe					
Upper Respiratory tract infection per year	1-2	3	4-6		>6					
Candidiasis	None	Oral	Finger nails		Systemic					
Other Serious infection	None				Present					
Fatal Infection	Absent				Present					
Hyperextensibility	Absent				Present					
Lymphoma	Absent				Present					
Increase Nasal width	<1 SD	1-2 SD		✓>2 SD						
High Palate	Absent		✓Present							
Young-age Correction	> 5 year		2-3 year		1-2 year			</= 1 year		

The total calculated score = 36, which strongly supports the diagnosis of Autosomal Dominant Hyper-IgE Syndrome.

Management

The patient was treated with a combination of systemic and topical therapies, including:

Capsule Doxycycline 100 mg twice daily

Oral methylprednisolone in tapering doses during acute flares

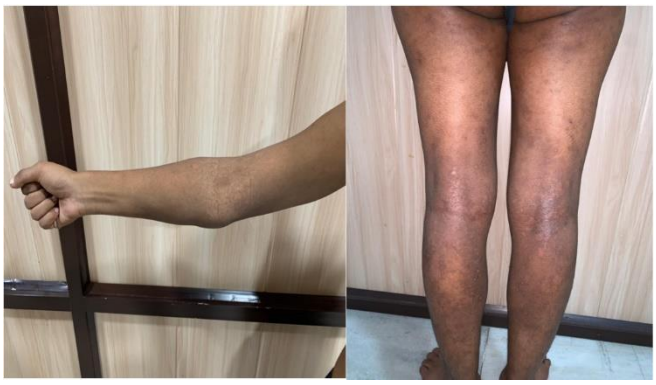
Tablet Bilastine 20 mg once daily

Tacrolimus 0.1% topical ointment

Liquid paraffin-based emollient cream

Clobetasol propionate topical ointment

The patient was followed up for eight months and received intermittent oral antibiotics for recurrent infections. Symptomatic improvement was observed with treatment.



Discussion

Job's syndrome is primarily caused by mutations in the STAT3 gene, which plays a critical role in immune regulation and tissue repair mechanisms. These mutations result in impaired immune responses, leading to recurrent infections and elevated IgE levels.[6]

The abnormal STAT3 signaling pathway results in excessive IgE production by B lymphocytes and defective neutrophil chemotaxis. Additionally, impaired signaling of cytokines such as IL-6, IL-10, and interferon-gamma contributes to immune dysfunction.

One of the key immunological abnormalities in HIES is the deficiency of Th17 cells, which are essential for protection against extracellular bacterial and fungal infections.[7] The lack of these cells increases susceptibility to recurrent infections.

A major diagnostic hallmark of this disorder is a serum IgE level exceeding 2000 IU/mL. When elevated IgE levels are accompanied by a diagnostic score greater than 30, the likelihood of autosomal dominant Hyper-IgE syndrome is high. Genetic confirmation typically reveals a dominant-negative mutation in the STAT3 gene.[8]

- Patients with Job's syndrome may also develop serious complications, including:
- Malignancies such as non-Hodgkin lymphoma
- Autoimmune disorders including systemic lupus erythematosus
- Cerebral aneurysm rupture leading to lacunar infarcts
- Coronary aneurysm rupture causing myocardial infarction

Early diagnosis and multidisciplinary management are essential to reduce morbidity and improve patient outcomes.

Conclusion

Job's syndrome is a rare immunodeficiency disorder characterized by elevated IgE levels, recurrent infections, and distinctive skeletal and dental abnormalities. Recognition of its clinical features, supported by laboratory findings and scoring systems, is essential for timely diagnosis. Appropriate medical management, including infection control and dermatological treatment, can significantly improve patients' quality of life.

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Conflicts of interest

There are no conflicts of interest.

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