

LETTER TO THE EDITOR

DERMATOLOGIC
THERAPY

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STAT3-mutated hyperimmunoglobulin E syndrome with perianal skin tags and erosions: A case report

Dear Editor,

STAT3-mutated hyperimmunoglobulin E syndrome (STAT3 HIES) is a rare primary immunodeficiency disease characterized by elevated serum IgE level and recurrent skin and pulmonary infections [1-3].

A sixteen-year-old girl presented to our clinic with complaints of a longstanding history of pruritic lesions on the scalp, skin folds, and perianal regions. At physical examination, diffuse papuloerosive lesions, reminiscent of Sevestre-Jacquet syphiloid were observed on gluteal, genital, and perianal regions, but closer observation revealed also multiple fibromatous skin tags (Figure 1). The patient had been diagnosed atopic dermatitis from the first years of life and prescribed cycles of oral prednisolone and betamethasone lotion. Chronic steroids self-medication for the severe itching on the genital areas could explain the severe erosive dermatitis, with eventual superinfections, but past medical history also revealed recurrent episodes of pneumonia and chest pain, alerting on the possibility of a subjacent immunodeficiency. Blood count revealed a slight anemia (hemoglobin of 11.3 mg/dL, mean corpuscular volume of 78.4 fL) and leukocytosis with eosinophilia (total leukocyte count of 14 000/mm³; neutrophils 47%, lymphocytes 13%, monocytes 1%, eosinophils 39%; platelet 329 000/mm³). Serum IgE was 21.800 g/L (normal range is 0-200 g/L), while serum IgG, IgA, and IgM were within normal limits. Serology for syphilis, herpes simplex virus and HIV infections was negative. In microbiological examinations

from skin swabs, candida infections had been excluded. The liver and renal function tests were normal, as well as stool examination and urine analysis. Chest X-ray revealed mediastinal widening because of aortic arch dilation. Total colonoscopy was normal. Skin biopsy from anal skin tags demonstrated a partially ulcerated and markedly acanthotic epidermis, eosinophilic spongiosis, and abundant neutrophils pustulation, but no granuloma formation, neither koilocytosis nor epidermal dysplasia suggestive of human papilloma virus infection. Besides, Gram-positive cocci superinfection was depicted on skin pathology with specific staining. Based on skin and pulmonary chronic involvement, with hyper-IgE and eosinophilia ascertainment the suspect of Job's syndrome was suspected, and genetic consultation requested, which identified a STAT3 mutation. The patient was asked to use dilute bleach baths for about 10 minutes three times a week with partial improvement of the lesions. Prophylactic antibiotics against Staph with cephalexin 20 mg/kg/dose PO twice daily was started for the patient.

Of all the etiologies identified for HIES, a heterozygous mutations in STAT3 is implicated the defects in JAK/STAT signaling pathway in the pathogenesis of this disease. [4]. Genetic inheritance is associated with different phenotypic expression. Diagnostic guidelines for STAT3 HIES have recently been proposed [5]. Specific criteria include IgE > 1000 IU/mL and a weighted score of five clinical features: pneumonias, newborn papulopustular eruption, pathologic bone fractures,

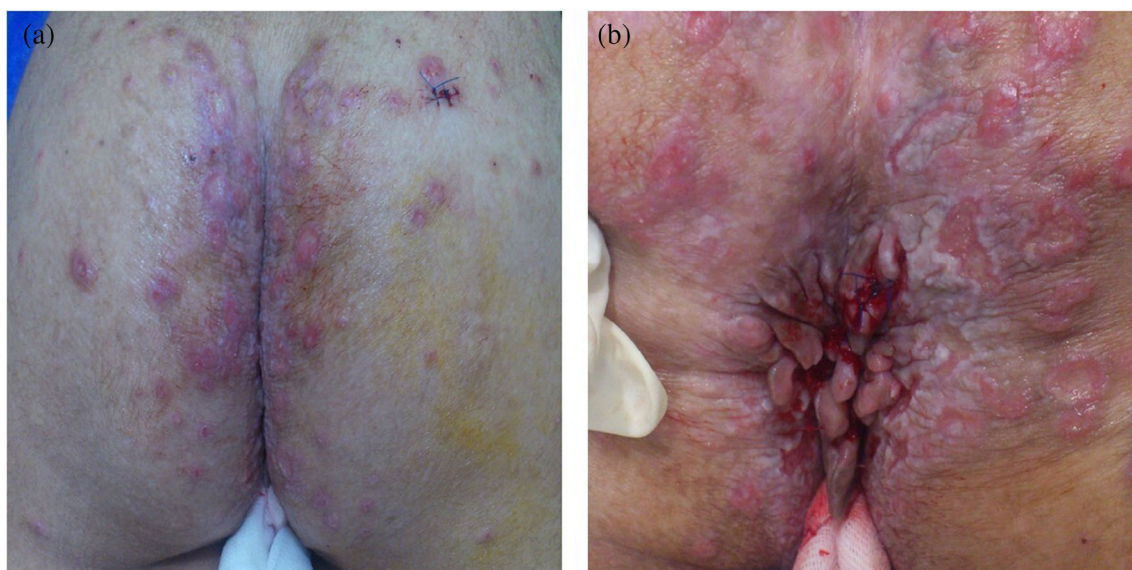


FIGURE 1 (a), Perianal skin erosions; (b), extensive skin tags and erosions

characteristic facies, and high-arched palate. These characteristics plus a lack of Th 17 cells or the detection of a heterozygous STAT3 mutation allow for a probable or definitive diagnosis, respectively [6]. Extensive perianal erosions and skin tags were the unique features of the syndrome, further expanding the spectrum of clinical findings, which should alert the dermatologist to investigate meticulously past medical history, perform the necessary assessment, and point out the diagnosis STAT3 HIES. Early diagnosis is mandatory to limit permanent abnormalities, and establish a multidisciplinary approach, from recurrent infections prevention to local care of cutaneous abscesses, often requiring early surgical drainage. Orthopedists should follow-up skeletal disease and correct scoliosis or severe bone shortening. Treatment with intravenous immunoglobulin reduces the number and severity of recurring infections in some patients. [1].

Regina Fölster-Holst¹
 Armaghan Kazeminejad²
 Ghasem R. Rokni²
 Torello Lotti³ 
 Andy Goren³ 
 Mohamad Goldust^{3,4,5} 

¹Klinik für Dermatologie, Venerologie und Allergologie,
 Universitätsklinikum Schleswig-Holstein, Kiel, Germany

²Department of Dermatology, Mazandaran University of Medical
 Sciences, Sari, Iran

³Department of Dermatology, University of Studies Guglielmo Marconi,
 Rome, Italy

⁴Department of Dermatology, University Medical Center Mainz, Mainz,
 Germany

⁵Department of Dermatology, University Hospital Basel, Basel,
 Switzerland

Correspondence

Mohamad Goldust, Department of Dermatology, University Medical
 Center Mainz, Mainz, Germany.
 Email: mgoldust@uni-mainz.de

ORCID

Torello Lotti  <https://orcid.org/0000-0003-0840-1936>

Andy Goren  <https://orcid.org/0000-0002-8190-2289>

Mohamad Goldust  <https://orcid.org/0000-0002-9615-1246>

REFERENCES

1. Freeman AF, Holland SM. Clinical manifestations, etiology, and pathogenesis of the hyper IgE syndromes. *Pediatr Res*. 2009;65(5 pt 2):32R-37R.
2. Holland SM, DeLeo FR, Elloumi HZ, et al. STAT3 mutations in the hyper-IgE syndrome. *N Engl J Med*. 2007;357(16):1608-1619.
3. Minegishi Y, Saito M, Tsuchiya S, et al. Dominant-negative mutations in the DNA-binding domain of STAT3 cause hyper-IgE syndrome. *Nature*. 2007;448(7157):1058-1062.
4. Sowerwine KJ, Holland SM, Freeman AF. Hyper-IgE syndrome update. *Ann N Y Acad Sci*. 2012;1250:25-32.
5. Woellner C, Gertz EM, Schäffer AA, et al. Mutations in STAT3 and diagnostic guidelines for hyper-IgE syndrome. *J Allergy Clin Immunol*. 2010;125(2):424.e8-432.e8.
6. Milner JD. Learning from job: a rare genetic disease and lessons of biblical proportions. *Rambam Maimonides Med J*. 2018;9(1).