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Short communication

Staphylococcal scalded skin syndrome: An uncommon symptomatology revealing an immune deficiency

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ARTICLE INFO

Article history:

Received 25 March 2017

Accepted 5 November 2017

Available online xxx

Keywords:

Hyper-IgE syndrome

Primary immune deficiency

Childhood SSSS

ABSTRACT

Primary immune deficiencies associated with hyper-IgE syndrome are rare diseases with clinical features dominated by recurring cutaneous and visceral bacterial infections, particularly infections due to *Staphylococcus* species. Most of these infections are associated with milder inflammation compared to normal. We report a primary immune deficiency associated with a hyper-IgE syndrome revealed by a staphylococcal scalded skin syndrome in a 5-year-old girl. The patient presented with a severe staphylococcal infection with extensive skin lesions and disseminated intravascular coagulation. She received intravenous fluids to compensate for fluid losses and anti-staphylococcal antibiotics. Coagulopathy was also corrected. However, the progression was rapidly fatal.

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1. Introduction

Hyper-IgE is a nonspecific biological marker associated with several primary immune deficiencies of various molecular defects and very different clinical presentations and prognosis. The genetic basis for the majority of patients presenting hyper-IgE has now been established and includes mutations in *STAT3*, *DOCK8*, *TYK2*, and most recently *PGM3* genes [1]. In addition to the elevated levels of IgE, patients with primary immune deficiency secondary to *PGM3* mutation display impaired immunity, atopy, autoimmunity, and neurocognitive impairment [1,2]. The infectious complications included recurrent abscesses and pneumonia, most commonly from *Staphylococcus aureus* and chronic mucocutaneous candidiasis [3].

We report an uncommon case of staphylococcal scalded skin syndrome (SSSS) revealing a primary immune deficiency secondary to a *PGM3* mutation in a 5-year-old girl.

2. Case report

A 5-year-old girl was referred to our pediatric intensive care unit for an extensive erythematous rash and blisters. Upon admission, the child was hypothermic at 35 °C and seemed in

intense pain. She was tachycardic (pulse, 130 beats/min), normotensive (blood pressure 116/85 mmHg), and hemoglobin oxygen saturation was at 96%. Cutaneous examination showed erythematous skin eruption with some bullae and erosions located in the mouth area, back, hands, thighs, legs, and perineum (Fig. 1A and B). The Nikolsky sign was positive. The area of damaged skin was estimated at 47%.

Biochemical analysis showed hypoproteinemia (28 g/L) and increased C-reactive protein (141 mg/L). The complete blood count revealed severe anemia (Hb, 7.4 g/dL), leukopenia (white blood cells, 2390/mm³), and thrombopenia (14,000/mm³). The prothrombin time was at 38% and the activated partial thromboplastin time of 44 s.

The patient was placed in a sterile, heated burn injury ward. After insertion of a central vein catheter, she was given sufficient pain relief and intravenous fluids with the Parkland correction for a 47% burn. She also received iterative red blood cell transfusions because of anemia, albumin solutions to compensate hypoproteinemia, and fresh frozen plasma and platelet concentrate to correct her coagulopathy. Intravenous antibiotics were initiated but the patient continued to develop new lesions. The presence of methicillin-sensitive *S. aureus* in the blood culture was confirmed within 2–3 days. A skin biopsy showed an intracorneal and subcorneal cleft with papillary edema and mixed inflammation (Fig. 2A and B). The clinical presentation and findings from the skin biopsy specimen confirmed the diagnosis of SSSS.

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Fig. 1. Erythematous skin eruption with skin peeling and erosions located in the back of the patient (A) and the lower limbs (B).

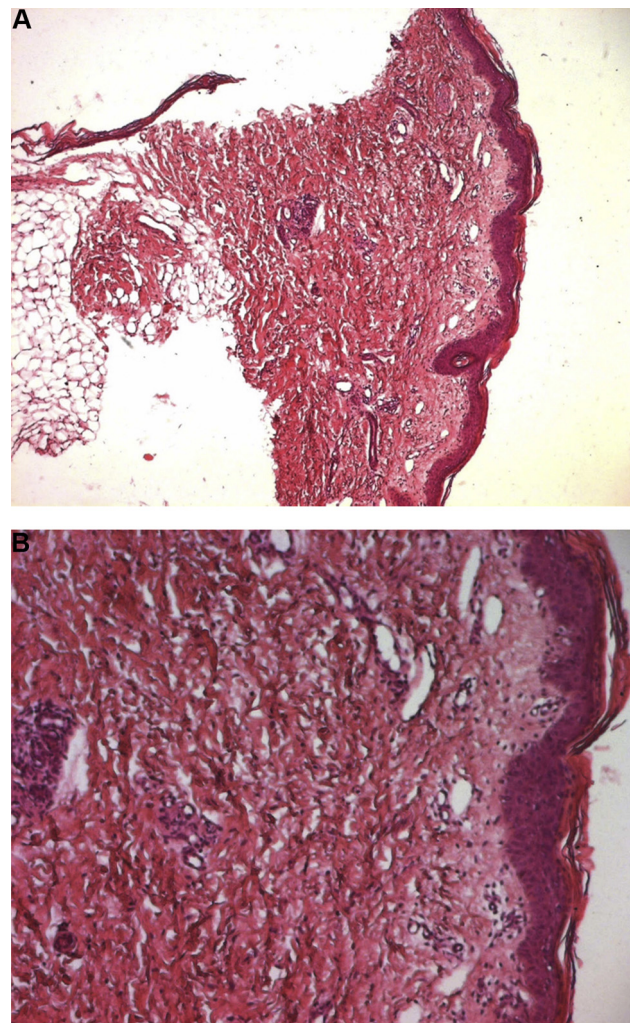


Fig. 2. Histologic skin biopsy specimen findings: intracorneal and subcorneal cleavage with papillary dermal edema and mixed inflammation (hematoxylin-eosin stain: A: $\times 14$; B: $\times 40$).

Anti-staphylococcal antibiotics were continued; however, on day 10 of hospitalization, the patient became hemodynamically unstable and died. Exploration of immunity showed a high IgE level (4390 IU/L) and confirmed the diagnosis of primary immune deficiency. A genetic study identified a mutation in the *PGM3* gene.

3. Discussion

SSSS is a rare toxin-mediated disease caused by *S. aureus*. Most cases of childhood SSSS are caused by phage group II *S. aureus*, mainly serotypes 3A, 3B, 3C, 55, and 71[4], causing blistering and desquamation of the skin. *S. aureus* produces exfoliative toxins A, B, C, and D (ETA-ETD), reducing cell-to-cell adhesion and splitting of the epidermis [4,5]. These exotoxins are secreted into the circulation from the site of primary infection. In children, the gateway is usually a mild infection of the upper respiratory tract [4]. The clinical features presented by our case were in agreement with SSSS as well as toxic epidermal necrolysis. Although it was initially difficult to differentiate between these two diagnoses, we chose to continue the antibiotic therapy. SSSS was then confirmed by the skin biopsy and the blood culture-isolated *S. aureus*. Unlike adult forms of SSSS, in which blood culture is positive in most cases, *S. aureus* can be isolated from blood cultures in only 3% of the childhood cases [6], as it was in our case.

The basic therapeutic approach is based on the administration of intravenous antibiotic therapy, namely Benzylpenicillin and a penicillinase-resistant penicillin at high doses, which should be commenced early in the management of the disease [4]. There is no

utility of topical antibiotics for the skin lesions because this is not the site of primary infection and the blister fluid will be sterile [4]. Fresh frozen plasma should be used in severe forms because it could contain antibodies to the exotoxins. The overall treatment also includes fluid resuscitation, analgesia treatment, nutrition support, and local skin care. Lactulose should be considered in the treatment in order to stop SSSS from progressing [4]. In adults, the immune response against the staphylococcus is an important factor for the development of SSSS. In fact, in most adult cases, renal failure, diabetes mellitus, or human immunodeficiency virus infection were identified as predisposing factors [7]. In children, it seems that the immune response of patients with SSSS was not usually explored. Our patient had an immunodeficiency disease frequently associated with *S. aureus* infection.

In fact, primary immune deficiency associated with hyper-IgE, formerly called hyper-IgE syndrome, is characterized by susceptibility to infections with extracellular bacteria (*S. aureus*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*) and fungal organisms [8]. Although *S. aureus* remains the most common bacterial infection involved in this syndrome, no case of SSSS associated with it has been reported before, and to our knowledge, our patient is the first one. This patient's case is not only original in its clinical presentation, but also by the result of genetic analysis of this immunodeficiency syndrome. Actually, primary immune deficiencies associated with hyper-IgE are rare primary immunodeficiency

diseases that have now been associated with mutations in signal transducer and activator of transcription 3 (STAT3), dedicator of cytokinesis 8 (DOCK8), and tyrosine kinase 2 (TYK2), which encode proteins with pivotal roles in signal transduction pathways in immune cells [2]. Recently, mutations in the gene encoding phosphoglucomutase (PGM3) have been identified in autosomal recessive forms of primary immune deficiencies associated with hyper-IgE [2]. PGM3 catalyzes a central step in the biosynthesis of uridine diphosphate N-acetylglucosamine, which is involved in the synthesis of N-glycans [1]. PGM3 gene mutations result in a partial cell and tissue-specific glycosylation defect that could compromise glycan-mediated processes, such as cell–cell recognition and immune signaling [2,9]. Immunological examination of patients presenting PGM3 generally demonstrates impaired T cell proliferation and differentiation, with an inverted CD4/CD8 ratio, Th2 skewing, and borderline low Th17 cell numbers [2]. Patients also show increased IgE levels and eosinophilia [2,9]. The precise mechanism to explain the link between glycosylation abnormalities and immune dysregulation seen in patients with a PGM3 mutation has not been established yet. The neurological anomalies described in these patients are related to the abnormalities in complex N-glycans, which are considered essential for normal neuronal development and myelination. To distinguish patients with biallelic PGM3 mutations from other patients with primary immune deficiencies associated with hyper-IgE, criteria might include a reversed CD4/CD8 ratio and developmental delay [2].

4. Conclusion

The immunity of each child presenting with SSSS should be explored to identify an early possible immunodeficiency favoring *S. aureus* infections.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Disclosure of interest

The authors declare that they have no competing interest.

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