Mimicking urticaria: a Schnitzler syndrome case☆

Dear Editor,

Schnitzler Syndrome (SchS) is a rare disorder, with ∼350 cases reported in the literature, characterized by a neutrophilic urticarial dermatosis and monoclonal gammopathy (IgM in more than 90% of the cases), associated with clinical and biological signs of inflammation.[1–3] In 2013, Lipsker, Schnitzler, and other experts met and proposed the Strasbourg diagnostic criteria, which are widely used today to diagnose SchS (Table 1).[1,4] We report a case of a man with a clinical and laboratory diagnosis of SchS in Brazil.

A 67-year-old man presented to our department with recurrent pruritic, not painful, urticaria-like lesions on the extremities and the trunk (Fig. 1). The lesions resolved within 24 hours without leaving behind dusky hyperpigmentation. He had intermittent fever of up to 39 °C, generalized arthralgia, and fatigue. The inflammatory episodes lasted for 2–5 days with severe general impairment. The patient suffered outbreaks with variable intensity on almost a monthly basis over the past fifteen years. Histopathology of lesional skin showed a perivascular and interstitial polymorphonuclear infiltrate, described as consistent with the diagnosis of urticarial lesions and compatible with SchS (Fig. 2).

Laboratory investigations revealed leucocytosis (up to 21.000 mm^3, ref 4000–11600 mm^3), an elevated ESR (120 mm/hr; 0∼20 mm/hr), and increased IgM levels (2550 mg/dL; 46∼260 mg/dL) in serum protein electrophoresis (Fig. 3). In the bone scan, there is a slight asymmetry of uptake in the tibias, slightly greater on the left. Bone marrow biopsy was performed with a negative cytogenetic study for lymphoproliferative diseases. Based on these clinical and laboratory findings, he was diagnosed with Schnitzler Syndrome.

He was started on a high-dose corticosteroid, NSAIDs, and antihistamines with partial remission of his symptoms.

There are a few cases reported in Latin America and in general, it is underdiagnosed despite the well-established diagnostic criteria, but the pathogenesis is unknown.[5]

The major complication is hematological malignancy, with lymphoproliferative disorder occurring in about 10%–20% of patients.[5,6] In addition to chronic spontaneous urticaria, other differential diagnoses should be considered (Table 2).[7]

At present, for patients with CRP < 3 mg/dL, treatment options include, colchicine, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), and hydroxychloroquine.[1,2] Corticosteroids has a moderate effect and antihistamine therapy has no effect.[8] According to Simon et al., the efficacy of colchicine is only 25%, but based on the benefit/risk ratio, colchicine is recommended as the first choice of treatment.[9] Experts recommend the use of anakinra (IL-1 block) in more symptomatic patients, such as Erythrocyte Sedimentation Rate (ESR) and CRP above the upper limit of normal (CRP > 3 mg/dL).[1]

Treatment with corticosteroids, NSAIDs, and antihistamines is symptomatic and unsatisfactory.[9] Anakinra (IL-1-neutralizing) is the choice drug. The effect of inhibition of IL-1 has led to new expectations, but there is currently unavailable in Brazil. An alternative drug could

Table 1 Strasbourg diagnostic criteria of Schnitzler syndrome.

Obligate criteria
- Chronic urticarial rash and
- Monoclonal IgM or IgG
Minor Criteria
- Recurrent fever[a]
- Objective findings of abnormal bone remodeling with or without bone pain[b]
- A neutrophilic dermal infiltrate on skin biopsy[c]
- Leukocytosis and/or elevated CRP[d]
Definite diagnosis if
- Two obligate criteria AND at least two minor criteria if IgM and three minor criteria if IgG
Probable diagnosis if
- Two obligate criteria AND at least one minor criteria if IgM and two minor criteria if IgG

[a] Must be >38 °C and otherwise unexplained. Occurs usually – but not obligatory – together with the skin rash.
[b] As assessed by bone scintigraphy, MRI, or elevation of bone alkaline phosphatase.
[c] Corresponds usually to the entity described as ''neutrophilic urticarial dermatosis''; absence of fibrinoid necrosis and significant dermal edema.
[d] Neutrophils >10,000 mm^3 and/or CRP > 3 mg/dL.

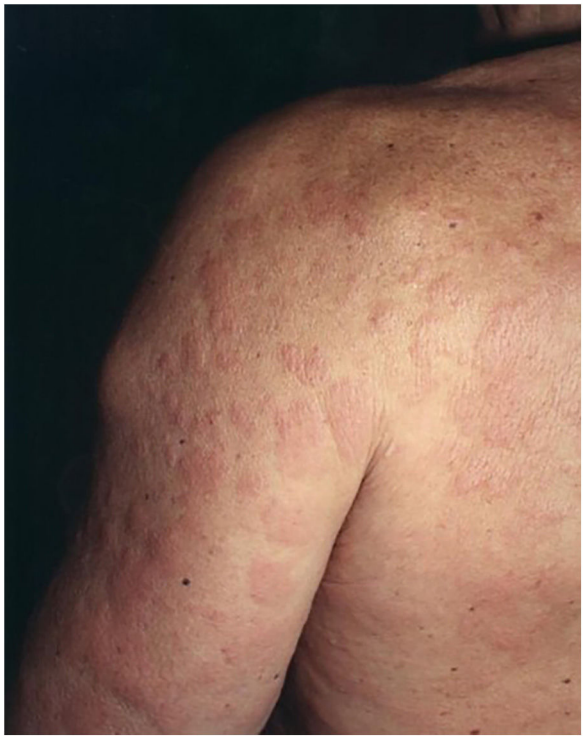

Fig. 1 Urticarial lesions on the trunk and left arm.

☆ Study conducted at the Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

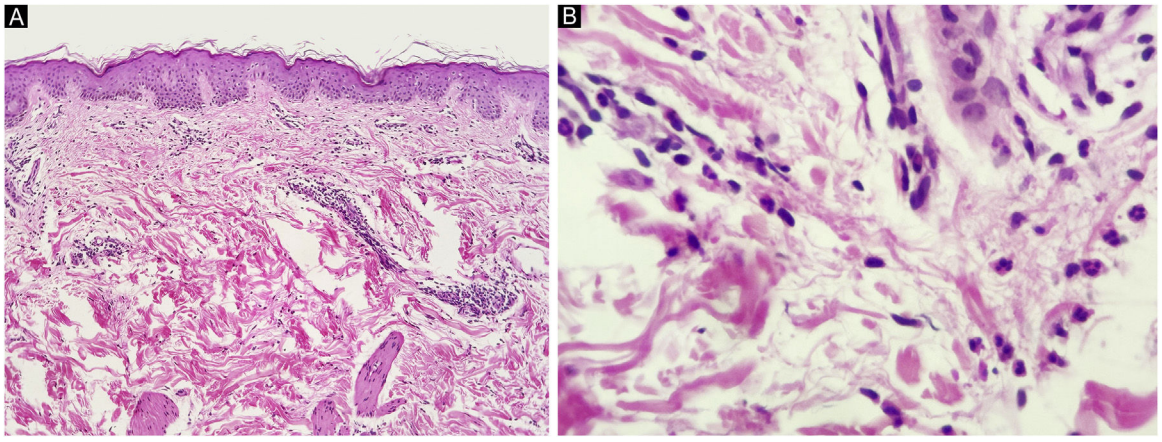

Fig. 2 Inflammatory cells around superficial dermal vessels with neutrophils (A, Hematoxylin & eosin, ×100) also observed in the interstitial space among collagen fibers (B, Hematoxylin & eosin, ×400).

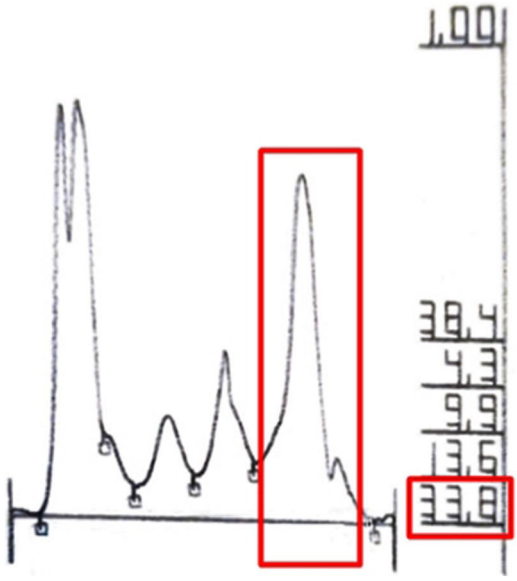

Fig. 3 Increased IgM levels in serum protein electrophoresis test.

be canakinumab, a human anti-IL-1β monoclonal antibody aiming at the neutralization of 1β signaling.[10]

In patients presenting with chronic urticaria associated with signs of systemic inflammation, this rare and debilitating syndrome should be considered. Early treatment can improve patient's quality of life and disease prognosis.

Table 2 Differential diagnoses of Schnitzler syndrome.

Autoimmune diseases
Adult Onset Still Disease (AOSD)
Systemic Lupus erythematosus
Acquired C1-esterase inhibitor deficiency
Hematologic diseases
Monoclonal gammopathy of undetermined significance (MGUS)
POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, mono-clonal gammopathy and skin changes)
Waldenström macroglobulinemia
Lymphomas
Multiple myeloma
Hereditary autoinflammatory syndromes
Cryopyrin-associated syndromes (CAPS):
Familial cold urticaria
Muckle-Wells syndrome
Chronic infantile neurologic cutaneous and articular syndrome (CINCA)
Infectious diseases
Hepatitis B and C
Chronic meningococcemia
Other
Chronic Spontaneous Urticaria
Hypocomplementemic urticarial vasculitis
Delayed pressure urticaria
Cryoglobulinemia
Behçet syndrome
Mastocytosis

Financial support

None declared.

Authors' contributions

Kelielson Cardoso de Macêdo Cruz: Preparation and writing of the manuscript; intellectual participation in propaedeutic and/or therapeutic management of studied cases; approval of the final version of the manuscript; critical literature review.

Daniela de Abreu e Silva Martinez: Preparation and writing of the manuscript; approval of the final version of the manuscript.

Danielle Carvalho Quintella: Preparation and writing of the manuscript; approval of the final version of the manuscript.

Tullia Cuzzi: Preparation and writing of the manuscript; approval of the final version of the manuscript.

Sergio Duarte Dortas Junior: Preparation and writing of the manuscript; intellectual participation in propaedeutic

and/or therapeutic management of studied cases; approval of the final version of the manuscript.

Solange Oliveira Rodrigues Valle: Preparation and writing of the manuscript; intellectual participation in propaedeutic and/or therapeutic management of studied cases; approval of the final version of the manuscript.

Conflicts of interest

None declared.

References

1. Matsuda T, Takimoto-Ito R, Lipsker D, Kambe N. Similarities and differences in autoinflammatory diseases with urticarial rash, cryopyrin-associated periodic syndrome and Schnitzler syndrome. Allergol Int. 2023;72:385–93.
2. Bonnekoh H, Krause K, Kolkhir P. Chronic recurrent wheals - if not chronic spontaneous urticaria, what else? Allergol Select. 2023;7:8–16.
3. Sá DC, Neto Festa C. Inflammasomes and dermatology. An Bras Dermatol. 2016;91:566–78.
4. Gusdorf L, Lipsker D. Schnitzler syndrome: a review. Curr Rheumatol Rep. 2017;19:46.
5. Aceituno Caño AM, Vogt Sánchez EA, León Ruiz L. Schnitzler's syndrome: a case report. Med Clin (Barc). 2021;157:301–2.
6. Tinoco G, Kanji R, Moola D. Schnitzler's syndrome: a case report. Case Rep Med. 2013;2013:956464.
7. Eiling E, Schröder JO, Gross WL, Kreiselmaier I, Mrowietz U, Schwarz T. The Schnitzler syndrome: chronic urticaria and monoclonal gammopathy – an autoinflammatory syndrome? J Dtsch Dermatol Ges. 2008:626–31.
8. Chu CQ. Schnitzler syndrome and Schnitzler-like syndromes. Chin Med J (Engl). 2022;135:1190–202.
9. Simon A, Asli B, Braun-Falco M, De Koning H, Fermand JP, Grattan C, et al. Schnitzler's syndrome: diagnosis, treatment, and follow-up. Allergy. 2013;68:562–8.
10. Fujita Y, Asano T, Sakai A, Norikawa N, Yamamoto T, Matsumoto H, et al. A case of Schnitzler's syndrome without monoclonal gammopathy successfully treated with canakinumab. BMC Musculoskelet Disord. 2021;22:257.

Kelielson Cardoso de Macêdo Cruz [a,*], Daniela de Abreu e Silva Martinez [a], Danielle Carvalho Quintella [b], Tullia Cuzzi [b], Sergio Duarte Dortas Junior [a], Solange Oliveira Rodrigues Valle [a]

[a] *Department of Immunology, Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil*
[b] *Department of Pathology, Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil*

* Corresponding author.
E-mail: kelielsoncma@gmail.com (K.C. Cruz).

Received 21 September 2023; accepted 11 October 2023
Available online 26 August 2024

https://doi.org/10.1016/j.abd.2023.10.004

Pyoderma gangrenosum triggered by secukinumab in a patient with palmoplantar pustulosis☆

Dear Editor,

A 35-year-old female patient presented with recurrent multiple pustules involving her palms and soles for more than one year (Fig. 1A). No acne, keratotic plaques, or bone-joint manifestations were reported. A skin biopsy taken from her palm showed a collection of neutrophils within the spongiform epidermis (Fig. 1B–C). Thus, a diagnosis of palmoplantar pustulosis (PPP) was made. As she could not tolerate the side effects of conventional systemic drugs, secukinumab was chosen as an alternative therapy. Her pustular lesions on the palms and soles almost healed after 3 months of treatment (secukinumab 300 mg per week for 5 weeks, followed by secukinumab 300 mg per month, Fig. 1D). However, several painful eruptions started on her lower legs after 6 doses of secukinumab. The lesions rapidly ulcerated and enlarged after the 7th dose of secukinumab. Fever or other systemic symptoms were absent. She had a history of rheumatic heart disease with normal cardiac function for 10 years, controlled by 4 mg methylprednisolone every day. No history of inflammatory bowel disease was reported.

On physical examination, multiple tender wide ulcers with irregular elevated violaceus borders surrounded by infiltrated erythema were found on her lower extremities (Fig. 2A). The largest ulcer was approximately 6 cm in diameter (Fig. 2B). Repeated swab cultures for bacteria, fungi, and mycobacteria from these ulcers were all negative. Hematoxylin-eosin staining of skin biopsy revealed a predominantly neutrophilic infiltrate in the dermis (Fig. 3A–B). In addition, laboratory examinations revealed normal complete blood count and moderately elevated levels of erythrocyte sedimentation rate (56 mm/h, normal range 0–20 mm/h), C-reactive protein (37.6 mg/L, normal range <10 mg/L), and anti-streptolysin O (438 IU/mL, normal range <200 IU/mL). A blood test for HLA-B51 was positive. Based on the clinicopathological findings, this patient was diagnosed with secukinumab-induced pyoderma gangrenosum (PG). Then, we discontinued her anti-IL17A treatment and started oral methylprednisolone (24 mg/day), oral sulfasalazine (3 g/day), and a careful ulcer care. Lesions ulcers improved substantially after 8 weeks (Fig. 4A–B).

☆ Study conducted at the Peking University First Hospital, Beijing, China.