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Case Studies

Neutrophilic Dermatoses in Autoimmune Diseases: Report of Two Cases Associated with Autoimmune Thyroiditis

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Keywords
Neutrophilic dermatoses · Autoimmune diseases · Autoimmune thyroiditis

Abstract
The term "neutrophilic dermatoses" includes a rare inflammatory pattern characterized by neutrophil-rich cutaneous infiltrate. Both innate and adaptive immune pathways may be involved in neutrophil recruitment. Occasionally, neutrophilic dermatoses may occur in association with autoimmune thyroiditis. Pathogenetic aspects of this autoimmune disorder may elucidate their possible connection. Two exemplificative cases are taken as a pretext for a short review of this topic.

Introduction

Neutrophilic dermatoses include a rare inflammatory pattern characterized by neutrophil-rich cutaneous infiltrate. The histologic diagnosis of neutrophilic dermatoses is based on the clinical picture combined with the distribution of neutrophils in cutaneous compartments. Neutrophil recruitment may involve both innate and adaptive immune system pathways that typically define respectively autoinflammatory and autoimmune diseases. Autoimmune thyroiditis (AT) used to be considered pathogenetically a typical consequence of impaired adaptive immune mechanisms. Some information about less known mechanisms underlying this condition may help to understand how a noninfective neutrophilic inflammation may occasionally be triggered.

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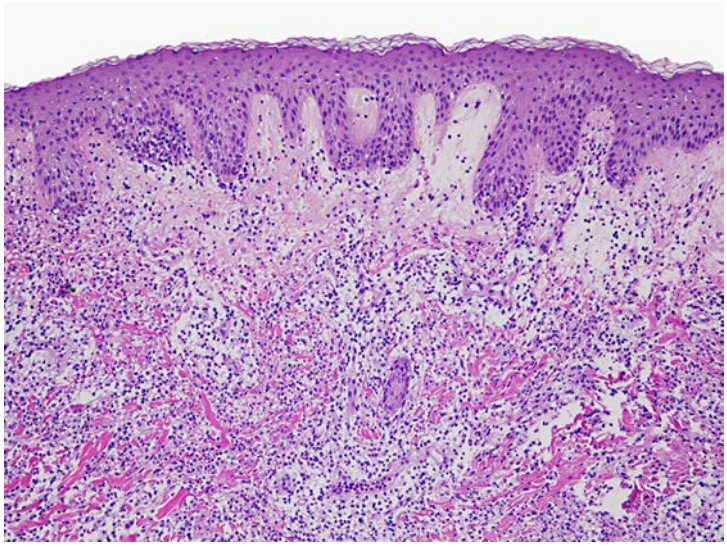

Fig. 1. Diffuse dense infiltrate of mature neutrophils and marked edema of the superficial dermis. Leukocytoclastic fragments are present in absence of vasculitic changes.

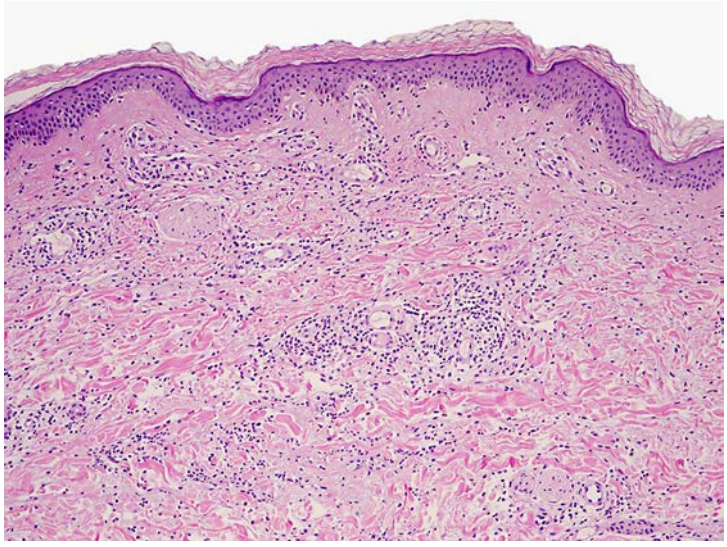

Fig. 2. Superficial and deep dermal interstitial neutrophilic infiltrate; the epidermis is unaffected.

Case Presentation

Case 1

A 44-year-old female with a history of AT presented to us with high fever, arthralgia, and elevated erythematous plaques on the trunk and limbs. Histologic examination revealed a diffuse dermal infiltrate of mature neutrophils associated with marked superficial edema. Some interstitial leukocytoclastic fragments were also present in the absence of vasculitic changes (Fig. 1). A diagnosis of Sweet syndrome was made.

Case 2

A 60-year-old woman presented with recurrent slightly raised, nonpruritic, large patches on the lower abdomen and the inner aspect of the thighs disappearing within a short time without leaving any sequelae. At the time of biopsy only one large evolving patch with raised borders was present on the inner aspect of the right thigh and proximal leg. Workup showed

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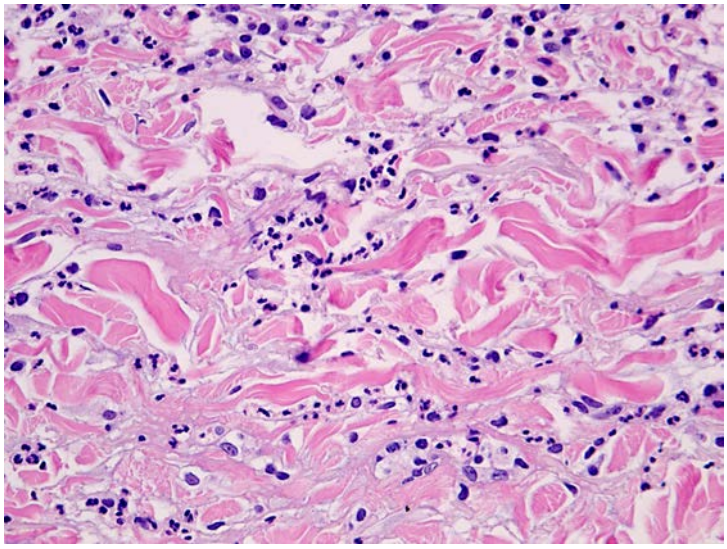

Fig. 3. Neutrophils are distributed along the collagen bundles associated with some leukocytoclastic fragment. No vasculitic changes can be seen.

a high TSH level and antibodies to thyroid peroxidase and antithyreoglobulin in high titers consistent with a diagnosis of AT. Further data included a transitory elevation in ANA (>1/160), a slight elevation in anti-TSH-R antibodies, and a light exophthalmos. Further back in time, the patient had been treated for hepatitis B and subsequently considered clinically healed. Histology showed a superficial and deep dermal interstitial neutrophilic infiltrate (Fig. 2). Neutrophils appeared distributed along the collagen bundles associated with some hints of leukocytoclasia (Fig. 3). Eosinophils were absent. The epidermis was unaffected. A diagnosis of neutrophilic urticarial dermatitis was made.

Discussion

Both cases represent examples of neutrophilic dermatoses associated with AT. Relying on the clinical history, we can suppose that AT may be considered the main triggering condition in both cases. An association of Sweet syndrome with AT has been previously reported [1, 2]. Neutrophilic urticarial dermatosis on the other hand has been described in association with autoinflammatory diseases, Schnitzler syndrome, adult-onset Still disease, and systemic lupus erythematosus [3].

In AT the adaptive immune system produces antibodies against thyroid antigens, resulting in two related disorders, Graves disease and Hashimoto thyroiditis. Nonspecific autoantibodies, although not clinically significant, are also variably present in AT. They include ANCA, anti-lactoferrin, and anti-myeloperoxidase, and all of them can directly impair neutrophil activation and homeostasis [4]. TSH-R on the membrane of granulocytes can be directly triggered by TSH and anti-TSH-R autoantibodies, resulting in hyperpolarization and enhancement of their locomotor, secretory, and phagocytic functions [5]. TSH and T4 may impair neutrophilic functions influencing their Ca^{2+} homeostasis [6]. Thyroid hormones can exert responses in various immune cells, influencing chemotaxis and other immune responses [7]. Mutation of the *NLRP1* gene, a key regulator of the innate immunity, has been reported as a predisposing factor to AT [8], testifying the merging between innate and adaptive immunity.

Conclusions

It is important to recognize neutrophilic dermatoses as possible expression of autoimmune diseases. Occasionally they can be the first manifestation of such diseases, so patients must be carefully investigated, including serologic evaluation for autoantibodies. The complex mechanisms underlying AT explain the variability in clinical presentation and associated disorders. A better understanding of the relationship between innate and adaptive immune mechanisms may help to uncover the complex and dynamic inflammatory pathways sustaining autoimmune diseases and related cutaneous manifestations. New therapeutic options are also expected to be formulated.

Statement of Ethics

This study was approved by the institutional review board of the C. Poma Hospital of Mantua in accordance with the Helsinki Declaration of 1975. All the personal data collected from the cases were anonymized and cannot be traced to named individuals.

Disclosure Statement

The author declares no conflict of interest.

Funding Sources

Internal founding of the Pathology Unit, C. Poma Hospital of Mantua was used in part for study-related facilities.

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