Dermatology Practical & Conceptual

Dermatologic Manifestations of Thymoma-associated Multiorgan Autoimmunity (TAMA) Syndrome: Cutaneous Signs of an Immune Dysregulation

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Introduction

Thymoma-associated multiorgan autoimmunity (TAMA) syndrome is the consequence of auto-reactive T-cells activation developing in the setting of a thymoma, which mediates graft-versus-host-disease (GHVD)-like reactions in several tissues, including skin [1].

Case Presentation

A 61-year-old man was admitted in our Dermatology Department for a skin rash appearing concomitantly to a nodal relapse of a malignant thymoma. Cutaneous examination revealed a confluent erythematous and papulo-squamous eruption involving most of his face, trunk, bilateral upper and lower extremities. His palms and soles presented confluent pink tender papules. Moreover, multiple chronic painful erosions affected the oral mucosa (Figure 1). The patient reported general malaise with deep asthenia and an abundant chronic diarrhea.

A skin biopsy was performed and histologic examination revealed an interface and perivascular dermatitis in the dermis. Epidermis showed psoriasiform hyperplasia, diffuse parakeratosis and spongiosis, hypogranulosis, necrotic keratinocytes with intense eosinophilic cytoplasm (Figure 2). Although several differential diagnoses (including drug reaction, viral exanthema, pityriasis lichenoid, and sub-erytrodermic psoriasis) were considered, relying on

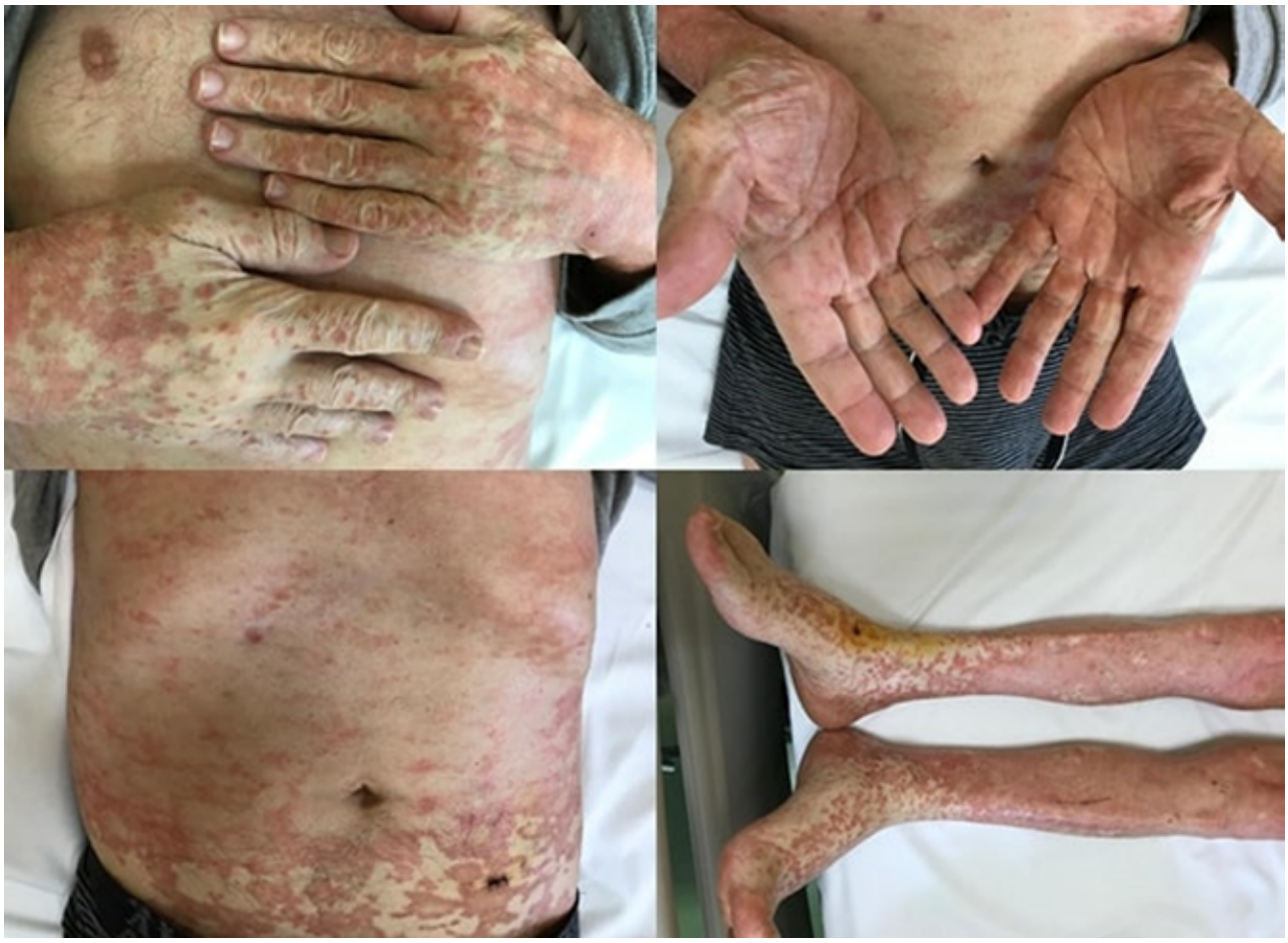

Figure 1. Erythematous and scaly papulosquamous eruption.

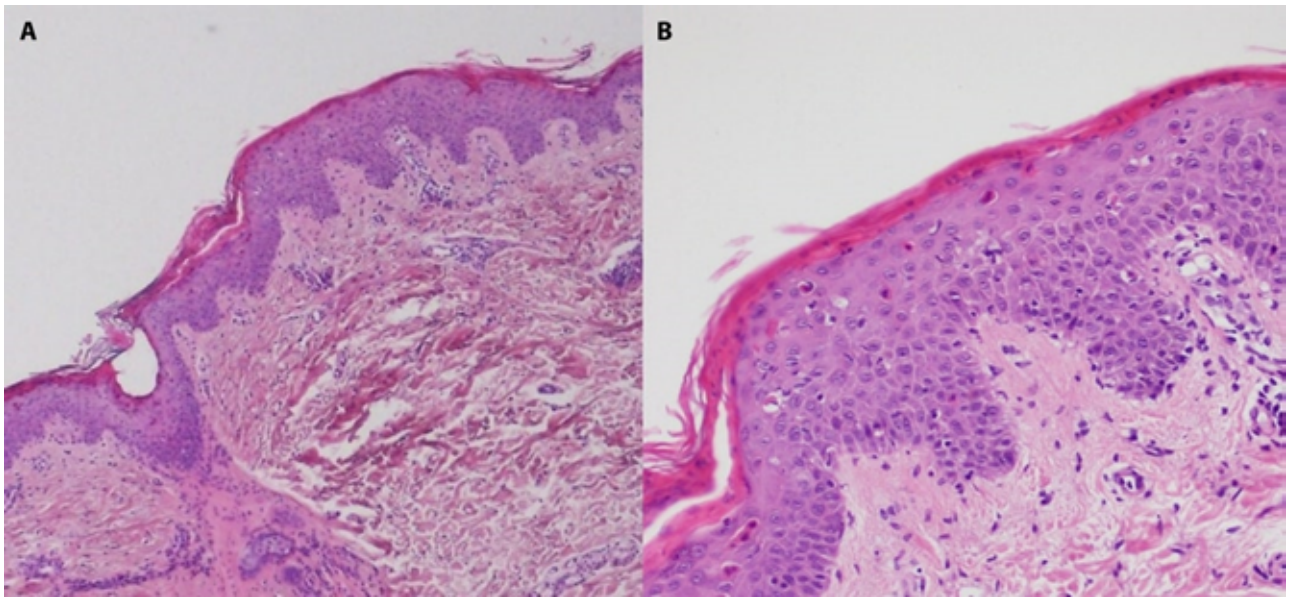

Figure 2. (A) Histology showing epidermal hyperplasia (H&E, 40X). Higher magnification highlights parakeratosis, epidermal spongiosi , hypogranulosis and some apoptotic keratinocytes characterized by intensely eosinophilic cytoplasm. (B) The underlying dermis contains few infiltrates of lymphocytes (H&E, 200X).

anamnesis, histology and literature, a GVHD-like reaction occurring in the setting of a malignant thymoma was finally diagnosed.

In addition, our patient developed a progressive muscle weakness. A thymoma-related myasthenia gravis was diagnosed after the detection of autoantibodies directed against

acetylcholine receptor and electrophysiological evaluation of neuromuscular junctions.

After three months our patient died as a result of the rapidly progressive clinical deterioration and the hypoxemic respiratory failure consequent to a lung infection and myasthenia gravis.

Myasthenia gravis is the most typical paraneoplastic syndrome associated with thymoma; it does not always develop at diagnosis, but it has a high impact of morbidity and mortality [2].

GVHD-like reactions are rare immune response that occur particularly at level of skin, intestine, or liver, which resemble GVHD on histopathology, except for graft lymphocytes [3]. The diagnosis requires the exclusion of the main causes of a real GHVD, such as hematopoietic stem cell transplantation (HSCT) and transfusion of non-irradiated blood. Being not associated to HSCT, Waldhera et al decided to collect the GVHD-like reactions occurred in the setting of a thymoma under the umbrella name of TAMA syndrome [1]. First described cases were characterized by a constant colon involvement; subsequently, TAMA reactions were detected in multiple organs, including not only gastrointestinal tract, but also skin, thyroid and liver [4].

Conclusions

We remark the uniqueness and interest of this case, since TAMA syndrome is a very rare disorder and with few cases reported in literature to date. The dermatologic manifestations of TAMA syndrome consist of diffuse papulo-squamous rash, often involving palms and soles, with possible lesions of oral mucosa. TAMA syndrome should be always kept in mind on a thymoma background when these specific skin signs are associated with systemic manifestations, first of all diarrhea.

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