Cutaneous Red Cords and Plaques in a Polymedicated Patient

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History, Clinical Findings and Complementary Tests

An 82-year-old female patient with a history of diabetes, hypertension and asthma presented with progressive indurated skin lesions in the upper trunk, armpits and inguinal region that appeared five months ago.

No substantial modifications had been made in her usual medical treatment since the introduction of imidapril four years ago.

On physical examination, indurated linear erythematous cords were observed in the upper third of the back, along with multiple annular erythematous-violaceous plaques in the proximal region of the four extremities and in their intertriginous areas [Figure 1a–c].

Blood tests, including complete blood cell count, biochemistry, proteinogram, autoimmunity markers and serology tests for *Borrelia spp*, were normal.

Histopathological examination of a skin biopsy revealed the presence of a histiocytic interstitial inflammatory infiltrate with eosinophils, degenerated collagen rosettes and histiocyte-rimmed collagen formations with surrounding clefts. There were no signs of vasculitis, mucin deposits or vacuolar interface dermatitis [Figure 3a–c].

What is Your Diagnosis?

Reactive granulomatous dermatitis (RGD).

Evolution

An extensive review of the patient's pharmacological history was performed. Imidapril was identified as a potential trigger of RGD, as it has been previously described[1-3] and was substituted for valsartan. After that, skin lesions disappeared progressively within two months [Figure 2a–c], with no clinical recurrence to this day.

Discussion

Reactive granulomatous dermatitis (RGD) is a term introduced by Rosenbach *et al.*[4] that encompasses three entities with overlapping features: interstitial granulomatous dermatitis (IGD), interstitial granulomatous drug reaction (IGDR) and palisaded neutrophilic and granulomatous dermatitis (PNGD). Differences between them are represented in Table 1.

These four disorders are part of the same spectrum, and they represent different cutaneous reactive patterns to various systemic triggers, including rheumatologic or connective tissue diseases, neoplasms and drugs.[5]

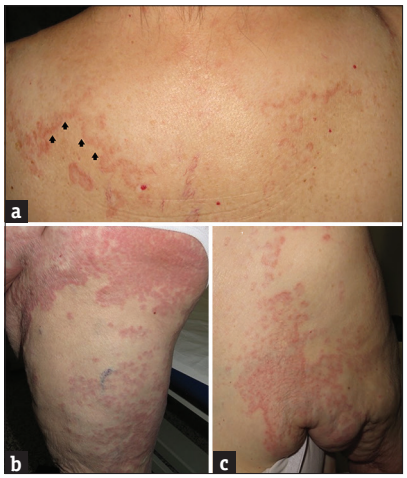

Figure 1: (a). Thick linear erythematous chords known as the 'rope sign' *(arrows)* located in the back of the patient, as a classic manifestation of IGD. (b, c). Erythematous-violaceous plaques affecting armpit and groin. Involvement of intertriginous areas is usually observed in IGDR

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Table 1: Clinicopathological differences between the main forms of reactive granulomatous dermatitis[1-5]

	Clinical appearance of the lesions	Histopathological differential findings	Systemic associations and triggers
IGD	Cord-like linear erythematous plaques located in the trunk	Rosettes of degenerated collagen and 'floating sign'	Rheumatologic and connective-tissue diseases, malignancies, drugs
IGDR	Erythematous-violaceous plaques involving trunk and proximal limb areas	Eosinophils, lymphoid atypia, interface dermatitis	Drugs: β-blockers, angiotensin converting enzyme inhibitors, calcium channel blockers, hydrochlorothiazide, etc.
PNGD	Symmetric papules with an umbilicated or crusty surface located on the elbows	Leukocytoclastic vasculitis and karyorrhexis	Rheumatologic and connective tissue diseases, hematologic disorders

IGD: Interstitial Granulomatous Dermatitis, IGDR: Interstitial Granulomatous Drug Reaction, PNGD: Palisaded Neutrophilic and Granulomatous Dermatitis

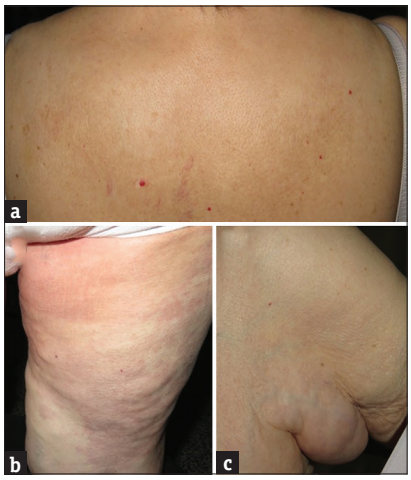

Figure 2: Examination after two months. (a-c). Resolution of the skin lesions after imidapril discontinuation, with post-inflammatory hyperpigmentation and scaling

There are certain clinical and histopathological findings that are more frequently associated with one specific form of the RGD spectrum, although usually, different signs of various entities coexist in the same patient. The presence of erythematous, firm, linear cords in the upper trunk ('rope sign'), as seen in our patient, is more frequently related to IGD, and proximal or intertriginous involvement of the limbs in the form of erythematous-violaceous plaques usually correspond to IGDR.[4] Both conditions were observed in the presented patient as an overlapping phenomenon.

The main clinical feature of PNGD is the onset of umbilicated erythematous papules distributed symmetrically affecting both elbows or knees.[4]

Histopathologically, the common feature in the RGD spectrum is a dermal histiocytic inflammatory infiltrate, but some differences can be observed among its various forms: visible clefts surrounding degenerated collagen which is known as 'floating collagen sign' are more commonly seen in IGD, vasculitis with karyorrhexis in PNGD and atypical lymphocytes with eosinophils within the inflammatory infiltrate in IGDR.[5]

Our case has histopathological features of IGD ('floating collagen sign') and IGDR (eosinophils within the inflammatory infiltrate), as a part of the same spectrum, under the RGD denomination.

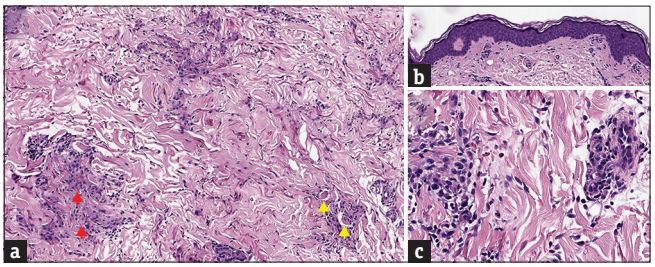

Figure 3: Histopathological findings. (a). Interstitial histiocytic inflammatory infiltrate and degenerated collagen rosettes are observed *(red arrows)*, along with the 'floating collagen sign' surrounded by histiocytes *(yellow arrows)*, a typical sign of IGD. No signs of vasculitis are detected (b). No evidence of interface dermatitis. (c). Eosinophils as a part of the inflammatory infiltrate, common finding in IGDR, and absence of lymphoid atypia

It is mandatory to perform a detailed pharmacological history, providing that such disorders can have a latency period spanning years,[3] as in the presented patient.

Learning Points

- RGD encompasses a spectrum of entities triggered by different systemic or drug-induced conditions. An extensive review of the patient's medication and investigation of underlying diseases must be performed in all cases suspecting an RGD.
- Erythematous, firm, linear cords in the upper trunk (known as 'rope sign') suggest the presence of an IGD.
- The proximal or intertriginous involvement of the limbs in the form of erythematous-violaceous plaques usually corresponds to IGDR.
- The main clinical feature of PNGD is the onset of umbilicated or crusted erythematous papules distributed symmetrically affecting both elbows or knees.
- Those cases in which involvement of drugs is suspected, latency period can span years, and this must be considered when performing a pharmacological history revision.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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