

Persistency of Bullous Pemphigoid Lesions on a Burn Scar: A Clinically Proven Locoregional Immune Dysregulation

Lo Schiavo A^{1*}, Romano F¹, Alfano R¹ and Ruocco E¹

¹Department of Dermatology, Second University of Naples, Italy

*Corresponding author: Ada Lo Schiavo, MD, Department of Dermatology, 2nd University of Naples, Via Sergio Pansini, 5, 80131 Napoli, Italy, Tel: +39 081 566 68 32; Fax: +39 081 566 68 32; E-mail: ada.loschiavo@unina2.it

Received date: Feb 08, 2015, Accepted date: Mar 13, 2015, Published date: Mar 16, 2015

Copyright: © 2015 Schiavo AL, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

A case of a 75 year old woman with drug-induced bullous pemphigoid is reported. Lesions also involved the site of a burn scar. Systemic steroid therapy proved to be effective on all lesions except for the ones located on the burn scar. In this patient the scarred area acted as a 'vulnerable' site, not only facilitating the localization of bullae on the scar (Koebner phenomenon), but also rendering these lesions resistant to the steroid treatment that proved to be effective elsewhere. The persistency of bullae precisely and solely on the burn scar features another facet of the immunocompromised district.

Keywords Bullous pemphigoid; Burn scars; Immunocompromised district

Persistency of Bullous Pemphigoid Lesions on a Burn Scar: A Clinically Proven Locoregional Immune Dysregulation

Bullous pemphigoid (BP) is a chronic autoimmune subepidermal blistering disease commonly affecting the elderly. Although BP is usually idiopathic, inducing factors may often have a part. Drug intake is the most common precipitating factor [1,2]. Other inducers are physical agents, such as sun exposure [3], UV therapy [4], traumatic events [5] and thermal burns [6,7], which can cause both generalized and localized forms of BP.

Report of a Case

We report the case of a 75 year old woman with a 6-month history of large, tense, serum-filled bullae, developing on itching erythematous

skin areas. The lesions were initially located on the trunk; subsequently, they spread all over her body surface (also on a burn scar of the left forearm that had been caused by boiling water at the age of 8 years), and on the nasal mucosa. The patient had a recent history of coronary artery disease and hypertension on treatment with nitroglycerin transdermal patches, acetylsalicylic acid, valsartan, and amlodipine. The clinical findings led us to suspect the diagnosis of BP. IgG autoantibodies targeting BP180 (117.9 U/ml, n.v. <20 U/ml) and BP230 (26.1 U/ml, n.v. <20 U/ml) were detected by enzyme-linked immunosorbent assays (ELISA), whereas ELISA results for desmoglein 1 and desmoglein 3 were negative. Serum level of total IgE was elevated (484 kU/l, n.v. 240 kU/l). A cytological smear taken from a fresh bulla showed plenty of leukocytes with cytoadherence phenomena ("streptocytes") and absence of acantholytic cells [8]. Taken together, laboratory findings confirmed the clinical diagnosis of BP and allowed ruling out the alternative diagnosis of pemphigus [9].



Figure 1: A. Active bullous lesions on the left forearm at the site of a burn scar (asterisk). Erythematous-pigmentary outcomes on the right forearm. B. Detail of the left forearm.

A possible drug induction by acetylsalicylic acid, valsartan, and amlodipine, all of which are known to be BP-inducing drugs [2,10-13], was taken into account. Therefore, these drugs were immediately withdrawn and replaced with others that were not structurally related. The patient was treated with 45 mg/day oral deflazacort. After a significant clinical improvement was achieved, the steroid dosage was progressively lowered down to zero and replaced with topical 0.05% clobetasol propionate ointment (one tube daily), a treatment which proved to be superior to the systemic one with 1 mg/kg prednisolone daily in a French study [14]. One month later, the patient showed an almost complete clinical remission. All lesions had cleared up leaving erythematous or pigmented areas, except for one crop of bullae, which was still present on the left forearm, exactly on the site of the burn scar (Figure 1). On a recent admission to our clinic, two years after the BP episode, the patient was free of lesions on all her body, except on the burn scar site, where few bullae were still present. She told us that similar eruptions had continuously been appearing on that area since she was discharged two years ago.

Comment

The peculiarity of our case lies in that the burn scar area acted as a 'vulnerable' site, not only facilitating the localization of bullae on the scar site (Koebner phenomenon), but also rendering these lesions resistant to the steroid therapy that proved to be effective on all other lesional sites. Scars, particularly burn scars, like other injuring events (traumas, vaccinations and particularly ionizing radiation), may locally disrupt the regular lymph flow [15-18] and throttle sensory nerve fibres in the skin, as lately shown by some of us [19,20]. These changes, by altering the local neuro-immune network, may destabilize the local immune control, thus paving the way for the local outbreak of immunity-related diseases (infections, tumors and immune disorders). This condition has been termed "immunocompromised district" [21].

The immunocompromised district is a novel, overarching concept encompassing anomalies of the local immune control that are confined to skin areas damaged by heterogeneous injuries [21]. The reason for these circumscribed immune anomalies may reside in locally altered neuromediator signaling (as it occurs in zoster-affected dermatomes), or locally hampered lymph drainage (as it occurs in lymphedema [21]) or concomitance of both conditions (as it occurs in amputation stumps, radiation dermatitis, burn scars) [21]. After the primary injury has disappeared, albeit the affected district may clinically appear normal, its immune behaviour is often compromised for a lifespan. The affected area becomes somehow 'vulnerable' and prone to harbor a secondary disease: infections or tumors if the local immune control has become defective, immune disorders if it has become overactive [22,23]. In our case, the persistency of bullae selectively on the burn scar reveals another facet of the immunocompromised district. In fact, the lack of responsiveness of the scar area to the same steroid therapy that proved to be effective on other lesional areas, might well be explained as a result of local destabilization of the immune control, hampering the healing course.

References

1. Ruocco V, Sacerdoti G (1991) Pemphigus and bullous pemphigoid due to drugs. *Int J Dermatol* 30: 307-312.
2. Stavropoulos PG, Soura E, Antoniou C (2014) Drug-induced pemphigoid: a review of the literature. *J Eur Acad Dermatol Venereol* 28: 1133-1140.
3. Kyriakis KS, Panteleos DN, Tosca AD (1996) Sunlight and air temperature affect autoantibody activity and skin involvement of bullous pemphigoid. *Int J Dermatol* 35: 498-501.
4. Sacher C, König C, Scharffetter-Kochanek K, Krieg T, Hunzelmann N (2001) Bullous pemphigoid in a patient treated with UVA-1 phototherapy for disseminated morphea. *Dermatology* 202: 54-57.
5. Ruocco E, Aurilia A, Simonetti G, Cozzani E, Baroni A, et al. (2002) Bullous pemphigoid: three atypical cases. *Acta Derm Venereol* 82: 222-223.
6. Balato N, Ayala F, Patruno C, Ruocco V (1994) Bullous pemphigoid induced by a thermal burn. *Int J Dermatol* 33: 55-56.
7. Xu HH, Xiao T, He CD, Jin GY, Wang YK, et al. (2008) Bullous pemphigoid triggered by a boiling water burn. *Eur J Dermatol* 18: 466-467.
8. Ruocco E, Brunetti G, Del Vecchio M, Ruocco V (2011) The practical use of cytology for diagnosis in dermatology. *J Eur Acad Dermatol Venereol* 25: 125-129.
9. Lo Schiavo A, Ruocco E, Brancaccio G, Caccavale S, Ruocco V, et al. (2013) Bullous pemphigoid: etiology, pathogenesis and inducing factors. Facts and controversies. *Clin Dermatol* 31: 391-399.
10. Durdu M, Baba M, Seçkin D (2011) A case of bullous pemphigoid induced by aspirin. *J Am Acad Dermatol* 65: 443-444.
11. Femiano F (2003) [Mucocutaneous bullous pemphigoid induced by valsartan. A clinical case]. *Minerva Stomatol* 52: 187-190.
12. Park KY, Kim BJ, Kim MN (2011) Amlodipine-associated bullous pemphigoid with erythema multiforme-like clinical features. *Int J Dermatol* 50: 637-639.
13. Ruocco E, Wolf R, Caccavale S, Brancaccio G, Ruocco V, et al. (2013) Bullous pemphigoid: associations and management guidelines: facts and controversies. *Clin Dermatol* 31: 400-412.
14. Joly P, Roujeau JC, Benichou J, Picard C, Dreno B, et al. (2002) A comparison of oral and topical corticosteroids in patients with bullous pemphigoid. *N Engl J Med* 346: 321-327.
15. Warren AG, Slavin SA (2007) Scar lymphedema: fact or fiction? *Ann Plast Surg* 59: 41-45.
16. Anand S, Lal H, Dhaon BK (1998) Lymphedema of the lower extremity as a complication of local burns. *Burns* 24: 767-769.
17. Lo Schiavo A, Brancaccio G, Romano F, Caccavale S (2014) Lymphangiomas arising on lymphedema: first step of malignant development. *G Ital Dermatol Venereol* 149: 372-374.
18. Anderson JR, Zorbas JS, Phillips JK, Harrison JL, Dawson LF, et al. (2010) Systemic decreases in cutaneous innervation after burn injury. *J Invest Dermatol* 130: 1948-1951.
19. Ruocco E, Di Maio R, Caccavale S, Siano M, Lo Schiavo A (2014) Radiation dermatitis, burns, and recall phenomena: Meaningful instances of immunocompromised district. *Clin Dermatol* 32: 660-669.
20. Pranteda G, Bottoni U, De Simone P, Calvieri S, Grieco T (1999) Bullous keloid: a distinct entity? *Br J Dermatol* 141: 375-377.
21. Ruocco V, Brunetti G, Puca RV, Ruocco E (2009) The immunocompromised district: a unifying concept for lymphoedematous, herpes-infected and otherwise damaged sites. *J Eur Acad Dermatol Venereol* 23: 1364-1373.
22. Ruocco E, Brunetti G, Sangiuliano S, Caccavale S, Lo Schiavo A (2013) Discoid lupus erythematosus at a site of previous injury. *Australas J Dermatol* 54: e16-18.
23. Ruocco V, Ruocco E, Piccolo V, Brunetti G, Guerrera LP, et al. (2014) The immunocompromised district in dermatology: A unifying pathogenic view of the regional immune dysregulation. *Clin Dermatol* 32: 569-576.