Epidermotropic B-cell lymphoma. A peculiar histopathological presentation often associated with extranodal (splenic) marginal zone B-cell lymphoma

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INTRODUCTION

Primary and secondary cutaneous B-cell lymphomas can rarely present with intense epidermotropic malignant lymphoid infiltrates resembling those observed in mycosis fungoides and other cutaneous T-cell lymphomas.

CASE REPORT

An 84-year-old woman presented with a 3-months history of multiple erythematous papules and plaques on her trunk, abdomen, back and nipples (Figure 1A, 1B and 1C). Past medical history was unremarkable. No mucosal lesions, hepatomegaly, splenomegaly or lymphadenopathy were noted. Histopathological exam from a skin biopsy revealed a deep and band-like dermal infiltrate (Figure 2A) with extension of atypical lymphocytes to the dermoepidermal junction with intense epidermotropism and folliculotropism features (Figure 2B and 2C). The infiltrate was composed predominantly of small to medium-sized lymphocytes with a monocytoid or plasmacytoid appearance (Figure 2D). Neoplastic cells expressed B-cell markers (CD20) and were positive for bcl-2 (Figure 2E and 2F) showing negativity for CD10, CD23, Bcl-6 and CD30 antigens. The accompanying T-lymphocytes consisted of mixed CD4+ and CD8+ mature T-cells without loss of pan-T-cell antigens (CD7, CD5, CD2). A monoclonal B-cell population was detected. Fluorescence in situ hybridization assays did not detected abnormalities for IgH/Bcl2, IgH/MALT1, IgH/CCND1 translocations and MYD88, tp53, 3q and 7q mutations.
A staging work up disclosed mild splenic enlargement, bone marrow (Figure 3A and 3B) and gastrointestinal tract involvement (Figure 3C and 3D) by a monoclonal B-cell population. Peripheral blood study with complete blood cell count, peripheral smear and flow citometry revealed no abnormalities in white blood cell count, platelet count and hemoglobin, and detected aberrant villous lymphocytes expressing B-cell markers (CD19, CD20, CD22, CD79a) and CD5 antigen (36%) as well. Monotypical expression of lambda chain was also detected. Serological studies for Borrelia burgdorferi and hepatitis virus were negative. An splenic marginal B-cell lymphoma (MZL) with epidermotropic cutaneous involvement was diagnosed. A conservative approach in management was considered. Lesions disappeared spontaneously few weeks later and new ones appeared on the eyelid showing a diffuse dermal infiltration by marginal B-cell lymphoma.

Figure 1. A) and B) Multiple erythematous papules and plaques on the trunk, breasts and nipples. C) Multiple lesions on the back.

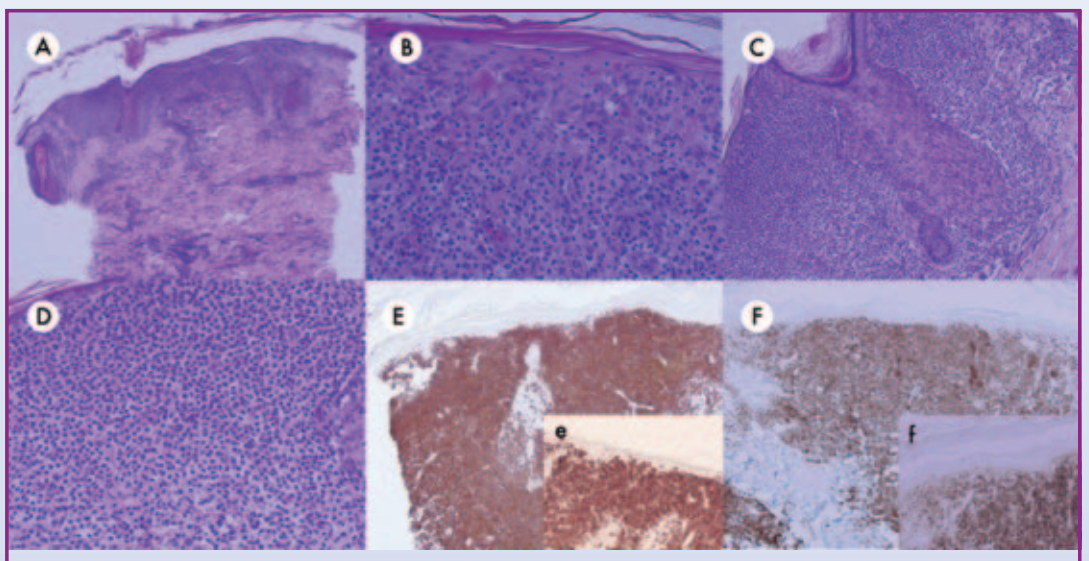

Figure 2. A) Skin biopsy specimen from the trunk with dense bandlike infiltrate in papillary dermis and deep interstitial infiltrate in reticular dermis (HE stain, x40). B) and C). Epidermotropism and follicutropism of atypical lymphocytes with concomitant vacuolar interface changes (HE stain, x200 and x100). D) The infiltrate was mainly composed by small-to-medium monomorphic lymphocytes with monocytoid and plasmacytoid cells (HE stain, x200). E) and F) CD20 and Bcl-2 (respectively) immunostaining showing a predominant B-cell population in the epidermal and dermal lymphocytic infiltrates (E) and F) x40, e) and f) x100).

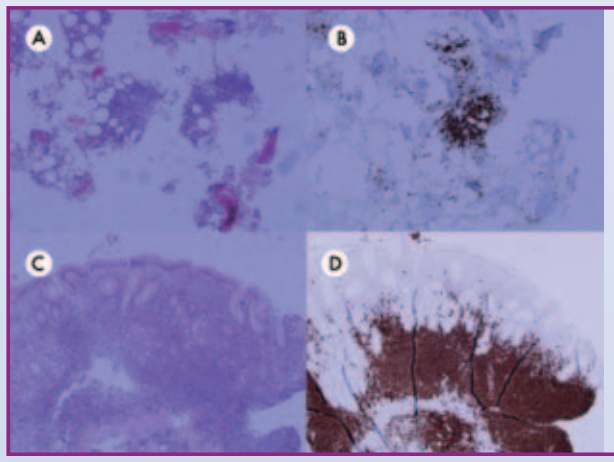

Figure 3. A) Bone marrow biopsy showed lymphocytic micronodular infiltrates (HE stain, x200). B) CD20 staining highlighted the neoplastic B-cells (x200). C) Gastric biopsy showed superficial and deep subepithelial lymphocytic aggregates (HE stain, x100). D) The infiltrating cells stained positively for CD20 (x100).

DISCUSSION

Epidermotropism is a typical characteristic feature of T-cell cutaneous malignancies, that could also be observed in cutaneous infiltrates from Langerhans cell histiocytosis and some reactive benign lymphoid hyperplasias. However, it is not a common phenomenon associated with cutaneous B-cell neoplasms.
As far as we are concerned, only 11 cases of epidermotropic MZL have been previously reported and mostly described in elderly patients as the initial clinical symptoms of splenic marginal zone lymphoma with secondary cutaneous involvement. Clinically it often presents as non-specific patches, plaques and/or nodules with variable pruritus involving the trunk and proximal extremities. Some cases of primary epidermotropic cutaneous marginal zone lymphomas have been reported as well with no distinctive cutaneous clinical aspects regarding those without epidermotropic features (Table 1).
Secondary cutaneous involvement has been described in nodal, splenic and extranodal marginal zone lymphoma of the MALT type. Histopathology and immunohistochemical features may not be distinctive enough to distinguish between a primary cutaneous MZL or a secondary cutaneous involvement and full staging work-up is necessary.
Histologically, in MZL, dense dermal nodular or diffuse centrocyte-like cells, monocytoid cells, lymphoplasmacytic cells and mature plasma cells infiltrates, often involving the adnexa, are usually observed. In most cases, the histopathologic features of epidermotropic MZL are characterized by a band-like infiltrate of small-to- medium, centrocyte-like and monocytoid lymphocytes in the papillary dermis with extension of atypical lymphocytes to the dermal-epidermal junction. Immunophenotypic profile displays positive staining for CD20, CD79a, CD19, Bcl-2, and negative Bcl-6, CD10, CD23 and cyclin D1. Many cases showed an accompanying subpopulation of small CD3+ T cells showing normal CD4/CD8 ratio.
To conclude, epidermotropism is an exceedingly rare phenomenon in cutaneous B-cell lymphomas. The observation of epidermotropism in cases of cutaneous B-cell lymphomas should point to the possibility of a secondary cutaneous involvement from an extracutaneous marginal zone lymphoma mostly from an splenic origin.

Reference (Year)	Age/ Sex	Skin Manifestations	Extracutaneous Involvement	Diagnosis	Therapy	Outcome
Chui et al (1999)	70/M	Red-brown scaly pruritic patches and atrophic plaques Trunk and proximal extremities	Bone Marrow	Extranodal MZL	CHOP	Alive
Pavlovic et al (2008)	56/M	Erythematous pruritic papules Trunk and arms	-	PCMZBCL	Doxycycline, systemic PUVA, subcutaneous interferon alpha	Alive
Chiang et al (2010)	57/M	Erythematous pruritic papules Trunk and proximal extremities	Bone marrow Peripheral blood Splenomegaly	Extranodal MZL	Narrowband UVB phototherapy	Alive
Gómez de la Fuente et al (2012)	68/M	Erythematous plaques and nodules Trunk and proximal extremities	Bone marrow Peripheral blood Splenomegaly	SZML	Splenectomy and R-CHOP	Deceased because of latent hepatitis reactivation
Lee et al (2013)	80/M	Pink papules and golden brown patches Trunk and lower proximal extremities	Unknown	Non classifiable	Unknown	Unknown
Magro et al (2016)	51/M 74/W	Salmon-colored papulosquamous eruption Trunk Two erythematous nodules Abdomen and cheek	Bone marrow (6 months after) Non specified	PCMZBCL PCMZBCL	Chemotherapy Unknown	Alive Alive
Baykal et al (2017)	65/W	Salmon-colored papules and nodules Trunk and arms	Splenomegaly (4 years before cutaneous symptoms) Bone Marrow	SZML	CHOP	Alive with disease
Magro et al (2017)	69/M	Red-to-brown papules and plaques Trunk and buttocks	Splenic infiltration (PET) Bone Marrow	SZML	Rituximab	Alive with disease
Hedayat (2018)	66/W	Orange to salmon-colored papules and plaques Trunk, lower proximal extremities	Splenomegaly Bone marrow Peripheral Blood	SZML	Narrowband UVB phototherapy	Alive with disease
Magro et al (2019)	89/M	Pytiriasis rosea-like skin rash Trunk, extremities, face	Bone Marrow (flow cytometry analysis)	PCMZBCL	Rituximab	Alive with disease
Present case	84/W	Non pruritic erythematous papules and plaques trunk	Splenomegaly Gastrointestinal disease Peripheral Blood Bone Marrow	SZML	No treatment	Alive with disease Skin lesions resolved and reappeared later

Table 1. Cases of epidermotropic cutaneous marginal B-cell lymphoma. PCMZBCL: primary cutaneous marginal zone B-cell lymphoma. MZL: marginal cell lymphoma. SZML: splenic marginal cell lymphoma.

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