Case Report

Dermatology

Dermatology 2007;215:229–232
DOI: 10.1159/000106580

Received: January 12, 2007
Accepted: February 20, 2007

Borrelia burgdorferi-Associated Primary Cutaneous Marginal-Zone B-Cell Lymphoma: A Case Report

P. Monari C. Farisoglio P.G. Calzavara Pinton

Department of Dermatology, University of Brescia, Azienda Spedali Civili, Brescia, Italy

Key Words
Borrelia burgdorferi · Cutaneous B-cell lymphoma · Antibiotic therapy

Abstract
An association between *Borrelia burgdorferi* with primary cutaneous B-cell lymphoma (PCBCL) has long been suspected but just recently, thanks to a polymerase chain reaction technique, it had been possible to demonstrate *B. burgdorferi*-specific DNA in skin lesions of patients with different PCBCL subtypes. Locating cases of PCBCL that are related to *B. burgdorferi* infection could be really important for therapeutic implications; in fact, there are several reports of PCBCL responding to antibiotic therapy against *B. burgdorferi*. We report a case of *B. burgdorferi*-associated primary cutaneous marginal-zone B-cell lymphoma that, after specific antimicrobial therapy, did not show any clinical regression. We can conclude that additional studies are necessary in order to establish the use of antimicrobial therapy in *B. burgdorferi*-associated PCBCL.

Copyright © 2007 S. Karger AG, Basel

Introduction

The spirochete *Borrelia burgdorferi* has been identified as the aetiological agent of Lyme disease and of several skin manifestations of that, including erythema chronicum migrans, lymphocytoma cutis and acrodermatitis chronica atrophicans [1–5]. An association between *B. burgdorferi* with primary cutaneous B-cell lymphoma (PCBCL) has long been suspected but just recently, thanks to a polymerase chain reaction (PCR) technique, it had been possible to demonstrate *B. burgdorferi*-specific DNA in skin lesions of patients with different primary cutaneous B-cell lymphoma subtypes [6–10]. We report a case of *B. burgdorferi*-associated primary cutaneous marginal-zone B-cell lymphoma (PCMZL).

Case Report

A 68-year-old man, Egyptian, non-smoker, with a solitary cutaneous nodule on the right ear's helix came to our attention. The lesion had first appeared 2 months earlier as a small skin nodule. The cutaneous lesion was erythematous, non-tender, painless, round and approximately 2 cm in diameter (fig. 1). He had no fever, weight loss or night sweats and he did not remember any insect bite. Physical examination did not reveal any enlargement of regional lymph nodes. The liver and spleen were not palpable. Serological investigations of IgG against *B. burgdorferi* were negative (IFA, Daltec Instrument s.r.l, Milano, Italy). Biopsy of the cutaneous lesion showed nodular infiltrates in the entire dermis (fig. 2).

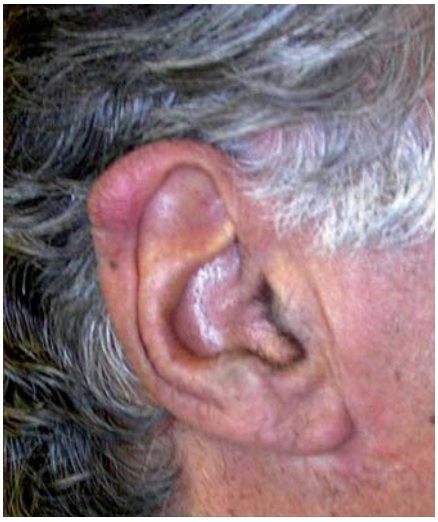

Fig. 1. Erythematous nodule on the patient's right ear.

The nodules consisted of a predominance of small-sized lymphoid cells with irregular nuclei; within the infiltrates there were also cells with the features of centroblasts. At immunoperoxidase studies the mononuclear infiltration was positive for CD20, CD3 and CD5 while CD10 and CD21 were negative (fig. 3). These morphological and immunohistochemical features were consistent with those of low-grade marginal-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2007 S. Karger AG, Basel
1018–8665/07/2153–0229$23.50/0

Accessible online at:
www.karger.com/drm

Paola Monari, MD
Department of Dermatology, University of Brescia
Azienda Spedali Civili, P.le Spedali Civili 1
IT–25123 Brescia (Italy)
Tel. +39 030 399 5300, Fax +39 030 399 5015, E-Mail paola.monari@libero.it

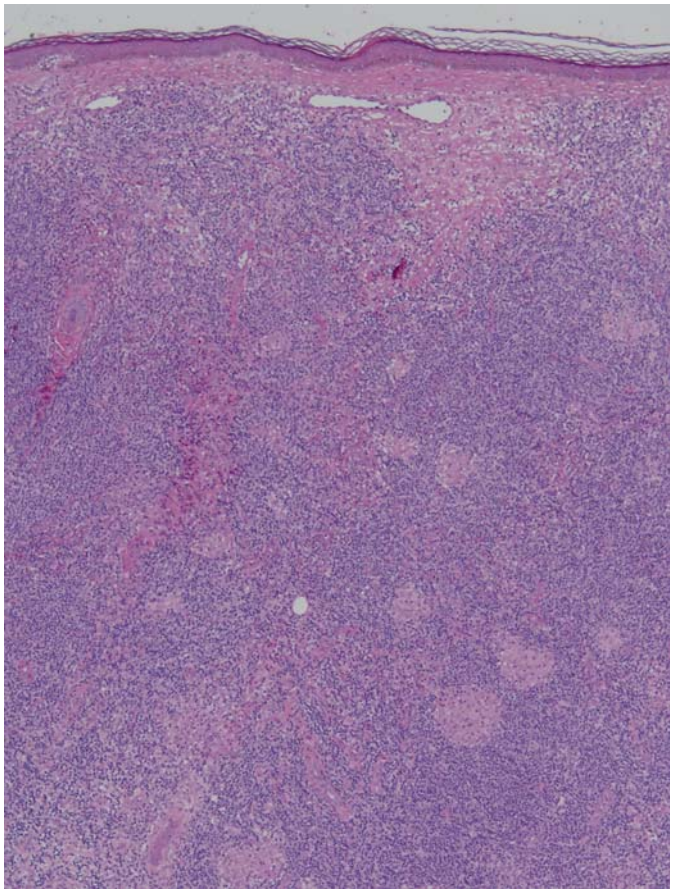

Fig. 2. PCMZL: dense nodular lymphoid infiltrate in the dermis. Haematoxylin and eosin. Original magnification ×10.

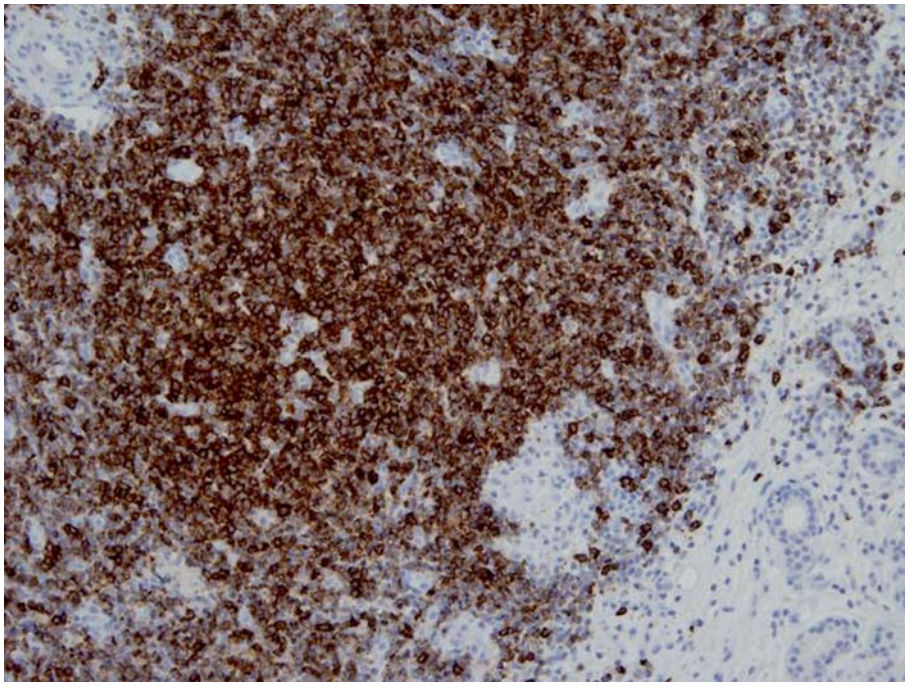

Fig. 3. PCMZL: strong CD20 positivity of the tumoral cells. Original magnification ×10.

zone B-cell lymphoma. PCR upon punch biopsy showed a dominant band supporting a diagnosis of lymphoma, and specific DNA sequences of *B. burgdorferi* were identified in lymphoma tissue. Further investigations (blood cell counts, chest X-ray examination, ultrasound scan of abdomen) were carried out and did not demonstrate any visceral manifestations, and there was no history to suggest previous symptomatic infection with *B. burgdorferi*. The patient was treated with doxycycline 100 mg twice daily for 4 weeks. The skin lesion persisted and so after 8 weeks to the end of administration of oral tetracyclines, the patient underwent a radical excision of the cutaneous lesion and PCR analysis of *B. burgdorferi* DNA on tissue was shown to be negative. No evidence of recurrence or a new lesion has been noted in the 5 months following the operation.

Discussion

PCMZL is an indolent lymphoma composed of small B cells, including marginal-zone (centrocyte-like) cells, lymphoplasmacytoid cells and plasma cells. It includes cases previously designated as primary cutaneous immunocytoma [11] and cases of cutaneous follicular lymphoid hyperplasia with monotypic plasma cells [12]. PCMZL is considered part of the broad group of extranodal marginal-zone B-cell lymphomas commonly involving mucosal sites, called mucosa-associated lymphoid tissue lymphomas. PCMZL is characterized by red to violaceous papules, plaques or nodules localized preferentially on the trunk or extremities, and presentation with multifocal skin lesions is frequent. These lymphomas have a tendency to recur in the skin but dissemination to extracutaneous sites is exceedingly rare [13]. The prognosis of PCMZL is excellent with a 5-year survival close to 100% [14–17]. An association between *B. burgdorferi* with PCBCL has recently been confirmed thanks to a PCR technique [6–10]. Probably chronic antigenic stimulation caused by *B. burgdorferi* infection leads to persistent lymphoid hyperplasia from which a malignant lymphoma subsequently evolves. *B. burgdorferi* has long been recognized as one of the aetiological factors of the so-called cutaneous pseudolymphomas, just like many drugs including anticonvulsants, atenolol, griseofulvin, angiotensin-converting enzyme inhibitors, allopurinol, cyclosporine, antihistamines and also phytotherapeutic agents [18]. It has recently been suggested that several of the cases classified in the past as B-cell pseudolymphoma of the skin represent PCBCL of low-grade malignancy [6]. In our case, the diagnosis of lymphoma was based on histopathological features, immunohistochemical criteria and was confirmed by monoclonality of the B-cell infiltrate. The real incidence of *Borrelia*-associated PCBCL is not clear but it seems that regional variations are possible. *B. burgdorferi* was present in 35% of patients with PCBCL in the Highlands of Scotland [9] and in only 18% of Austrian patients with PCBCL [6]; both are endemic regions for *B. burgdorferi* infection. In northern Italy, where our patient lives, *B. burgdorferi* infection is not endemic and the incidence of seroprevalence of antibodies is only 3.2% [19]. Locating cases of PCBCL that are related to *B. burgdorferi* infection could be really important for therapeutic implications. Like gastric marginal-zone lymphoma that resolves after antibiotic therapy to eradicate *Helicobacter pylori* [20], there are reports of PCBCL responding to antibiotic therapy designed to treat *B. burgdorferi* infection [10, 21]. However, like in our case, not all PCBCL related to *B. burgdorferi* infection respond to antibiotic therapy. In our case antibiotic therapy was effective against *B. burgdorferi* so that PCR analysis of organism DNA on tissue was negative after treatment but there was no clinical regression of the PCBCL. We can conclude that all patients with PCBCL can be examined for *B. burgdorferi* by PCR and if specific DNA of the spirochete is found, antibiotic therapy must be the first-line treatment before more aggressive therapies such as radiotherapy or surgical therapy are initiated. However, additional studies are necessary in order to establish the use of antimicrobial therapy in *B. burgdorferi*-associated PCBCL and to evaluate why only some of these cases respond to this approach.

References

1 Hovmark A, Asbrink E, Olsson I: The spirochetal etiology of lymphadenosis benigna cutis solitara. Acta Derm Venereol 1986;66:479–484.

2 Mitchell PD, Reed KD, Vandermause MF, Melinski JW: Isolation of *Borrelia burgdorferi* from skin biopsy specimens of patients with erythema migrans. Am J Clin Pathol 1993;99:104–107.

3 Ashbrink E, Hovmark H: Successful cultivation of spirochetes from skin lesions of patients with erythema chronicum migrans Afzelius and acrodermatitis chronica atrophicans. Acta Pathol Microbiol Immunol Scand 1985;93:161–163.

4 Weber K, Wilske B: Mini erythema migrans: a sign of early Lyme borreliosis. Dermatology 2006;212:113–116.

5 Aberer E, Kahofer P, Binder B, Kinaciyan T, Schauperl H, Berghold A: Comparison of two- or three-week regimen and a review of treatment of erythema migrans with phenoxymethylpenicillin. Dermatology 2006;212:160–167.

6 Cerroni L, Zochling N, Putz B, Kerl H: Infection by *Borrelia burgdorferi* and cutaneous B-cell lymphoma. J Cutan Pathol 1997;24:457–461.

7 Goodlad JR, Davidson MM, Hollowood K, Batstone P, Ho-Yen DO: *Borrelia burgdorferi*-associated cutaneous marginal zone lymphoma: a clinicopathological study of two cases illustrating the temporal progression of *B. burgdorferi*-associated B-cell proliferation in the skin. Histopathology 2000;37:501–508.

8 Garbe C, Stein H, Dienemann D, Orfanos CE: *Borrelia burgdorferi*-associated cutaneous B-cell lymphoma: clinical and immunohistologic characterization of four cases. J Am Acad Dermatol 1991;24:584–590.

9 Goodlad JR, Davidson MM, Hollowood K, Ling C, MacKenzie C, Christie I, Batstone PJ, Ho-Yen DO: Primary cutaneous B-cell lymphoma and *Borrelia burgdorferi* Infection in patients from the Highlands of Scotland. Am J Pathol 2000;24:1279–1285.

10 Kutting B, Bonsmann G, Metze D, Luger TA, Cerroni L: *Borrelia burgdorferi*-associated primary cutaneous B-cell lymphoma: complete clearing of skin lesions after antibiotic pulse therapy or intralesional injection of interferon alfa-2a. J Am Acad Dermatol 1997;36:311–314.

11 Rijlaarsdam JU, van der Putte SC, Berti E, Kerl H, Rieger E, Toonstra J, Geerts ML, Meijer CJ, Willemze R: Cutaneous immunocytomas: a clinicopathologic study of 26 cases. Histopathology 1993;23:119–125.
12 Schmid U, Eckert F, Griesser H, Steinke C, Cogliatti SB, Kaudewitz P, Lennert K: Cutaneous follicular lymphoid hyperplasia with monotypic plasma cells: a clinicopathologic study of 18 patients. Am J Surg Pathol 1995; 19:12–20.
13 Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, Chimenti S, Diaz-Perez JL, Duncan LM, Grange F, Lee Harris N, Kempf W, Kerl H, Kurrer M, Knobler R, Pimpinelli N, Sander C, Santucci M, Sterry W, Vermeer MH, Wechsler J, Whittaker S, Meijer CJLM: WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105: 3768–3785.
14 Torne R, Su WPD, Smolle J, Kerl H: Clinicopathologic study of cutaneous plasmacytoma. Int J Dermatol 1990;29:562–566.
15 Li C, Inagaki H, Kuo TT, Okabe M, Eimoto T: Primary cutaneous marginal zone B-cell lymphoma: a molecular and clinicopathologic study of 24 Asian cases. Am J Surg Pathol 2003;27:1061–1069.
16 Cerroni L, Signoretti S, Hofler G, Annessi G, Putz B, Lackinger E, Metze D, Giannetti A, Kerl H: Primary cutaneous marginal zone B-cell lymphoma: a recently described entity of low-grade malignant cutaneous B-cell lymphoma. Am J Surg Pathol 1997;21:1307–1315.
17 Bailey EM, Ferry JA, Harris NL, Mihm MC, Jacobson JO, Ducan LM: Marginal zone lymphoma (low-grade B-cell lymphoma of mucosa-associated lymphoid tissue type) of skin and subcutaneous tissue: a study of 15 patients. Am J Surg Pathol 1996;20:1011–1023.
18 Meyer S, Vogt T, Obermann EC, Landthaler M, Karrer S: Cutaneous pseudolymphoma induced by *Cimicifuga racemosa*. Dermatology 2007;214:94–96.
19 Santino I, Dastoli F, Sessa R, Del Piano M. Geographical incidence of infection with *Borrelia burgdorferi* in Europe. Panminerva Med 1997;39:208–214.
20 Wotherspoon AC, Doglioni C, Diss TC, Pan L, Moschini A, de Boni M, Isaacson PG: Regression of primary low-grade gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of *Helicobacter pylori*. Lancet 1993;342:575–577.
21 Roggero E, Zucca E, Mainetti C, Bretoni F, Valsangiacomo C, Pedrinis E, Borisch B, Piffaretti JC, Cavalli F, Isaacson PG: Eradication of *Borrelia burgdorferi* infection in primary marginal zone B-cell lymphoma of the skin. Hum Pathol 2000;31:263–268.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.