Case Report

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

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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 PCBCL 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).

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-
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 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, histamitines 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**


