Case Report

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Lyme borreliosis in Portugal caused by *Borrelia lusitaniae*? Clinical report on the first patient with a positive skin isolate

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Lyme-Borreliose in Portugal verursacht durch *Borrelia lusitaniae*?

Zusammenfassung. *Hintergrund: Borrelia lusitaniae* wurde erstmals im Jahr 1993 in Portugal von einer *Ixodes ricinus*-Zecke isoliert. In der Folge wurde diese Borrelien-Art in Ixodes-Zecken von der Küste Süd-Portugals und Nordafrikas nachgewiesen. Tierische Reservoire dieser Borrelienart sind noch unbekannt. *B. lusitaniae* wurde bisher ein einziges Mal aus der Haut eines Patienten mit einer langdauernden progredienten Hauterkrankung isoliert.

Patient und Methoden: Eine 46-jährige Portugiesin kam mit einer Hautläsion am rechten Oberschenkel, die sich langsam innerhalb von 10 Jahren entwickelt hatte. Die Patientin litt an Paraesthesien der Gliedmaßen, Krämpfen, chronischen Kopfschmerzen und Herzrhythmusstörungen. Weder war ein Zeckenstich erinnerlich, noch hatte die Patientin jemals an einer dem Erythema chronicum migrans vergleichbaren Hautläsion gelitten. Hautbiopsien wurden für histologische Untersuchungen sowie für einen direkten Erregernachweis mittels Kultur und Nukleinsäureamplifikation entnommen, Serum zum Nachweis von Antikörpern gegen Borrelien.

Ergebnisse: Diagnostiziert wurde ein beidseitiges Karpaltunnelsyndrom und Synovitis. Dermato-histologisch fanden sich keine Auffälligkeiten, die Serologie war negativ. Aus einer Hautbiopsie wurden Spirochäten kultiviert und als *B. lusitaniae* identifiziert. Die Patientin wurde über 2 Wochen mit intravenösem Ceftriaxon behandelt. Hierauf war sie subjektiv gebessert, ein Stillstand der Expansion der Hautläsionen war zu beobachten.

Schlussfolgerung: Die durch Anzüchtung von *B. lusitaniae* bestätigte Hautinfektion einer Patientin aus Portugal legt nahe, dass *B. lusitaniae* ein weiterer Krankheitserreger aus dem *B. burgdorferi* sensu lato-Komplex in Europa sein könnte.

Summary. *Background: Borrelia lusitaniae* was isolated from an *Ixodes ricinus* tick in Portugal in 1993 for the first time. Further, this borrelia genospecies has been found in ixodid ticks collected around the coasts of southern Portugal and North Africa. Its reservoir has not been defined yet. *B. lusitaniae* was isolated once until now from a patient with a long standing and expanding skin disorder.

Patient and methods: A 46-year-old Portuguese woman presented with a skin lesion on the left thigh which had evolved slowly over ten years. The patient reported limb paraesthesias, cramps, chronic headaches, and cardiac rhythm disturbances. History of tick bites was negative nor had the patient ever noticed a skin lesion comparable with erythema chronicum migrans. Skin biopsies were taken for histological evaluation, culture and DNA detection. Antibodies to borrelia were searched by indirect immunofluorescence assay and Western-blot.

Results: A bilateral carpal tunnel syndrome and local synovitis was diagnosed. Dermato-histology was normal, serology was negative. Spirochaetal organisms were cultured from a skin biopsy and identified as *B. lusitaniae*. The patient improved after a 2-week course of intravenous ceftriaxone; the skin lesions did not expand further.

Conclusions: This culture confirmed skin infection by *B. lusitaniae* in a patient from Portugal suggests an addi-

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tional human pathogen out of the *B. burgdorferi* sensu lato complex in Europe, particularly in Portugal.

Key words: *Borrelia lusitaniae,* clinical manifestations, human isolate, Lyme borreliosis.

Borrelia lusitaniae is one of eleven genospecies out of the *B. burgdorferi* sensu lato complex [1]. An isolate from a questing *Ixodes ricinus* tick was obtained in 1993 [2] and later identified as a new borrelia genospecies [3]. The tick was collected in a region south of the River Tagus in mainland Portugal [2]. Later investigations in the same region showed that *B. lusitaniae* was the only genospecies detected in *I. ricinus* ticks there [4]. Questing adult ticks presented an infection rate of 75% [4]; this is a significantly higher rate than that reported from other European regions [4]. To date, the reservoir of *B. lusitaniae* has still not been defined but it has been hypothesised that *B. lusitaniae* has found a favoured ecological niche geographically restricted to the Mediterranean Basin [4, 5]. These facts suggest that *B. lusitaniae* can be transmitted to humans there. If this borrelia species can cause infection in humans has become a question to deal with. We have been aware of clinical cases of Lyme borreliosis in Portugal for many years [6–9], and studies on seroprevalence have indicated human infection with borrelia [10].

Case report

Patient

In December 2001, a 46-year-old woman presented with two asymptomatic skin lesions on the posterior lateral area of the left thigh. She reported that the lesions had arisen about 10 years before. More recently she had observed an increase in the perimeter of the left thigh. She further reported persistent headaches, paraesthesia in the hands, cramps in the trunk, especially at night, and palpitations of the heart. One year ago she was troubled with a subdural haematoma which occurred without any apparent traumatic cause. The patient was of normal weight (55 kg) and did not smoke. She lived in the broader environs of Lisbon, in a house with a garden, and she kept dogs. From time to time, she visited her family's country property which is located about 200 kilometres northeast of Lisbon. Although she was aware of ticks outside in her garden and in the countryside she could not recall a tick bite nor had she ever noticed a skin lesion according to erythema chronicum migrans. The skin inspection revealed an area of slight depigmentation on the left thigh where two ill-defined erythematous macules stood out (Fig. 1). Although there was some local, discrete, arborising telangiectasia, there was no atrophy, sclerosis, depression or other skin surface alteration. The circumference of this thigh was about 1.7 cm longer than the other one. The skin surface could not be wrinkled, and pitting appeared when it was pinched (Fig. 2). Circumscribed scleroderma (morphea) and acrodermatitis chronica atrophicans (ACA) were considered in the differential diagnosis. The neurological examination revealed a slight decrease of sensitivity and muscular strength in the extremities.

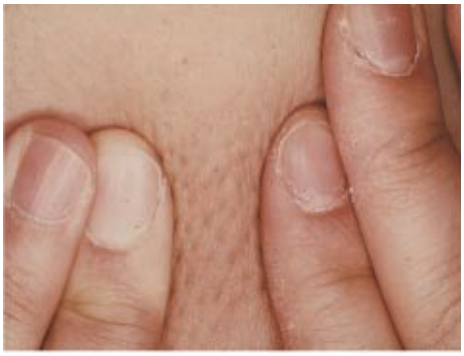

Fig. 2. Pitting appeared when skin surface was pinched

Materials and methods

Skin biopsies were taken from the edge of the lesions for histopathological examination, for culture of borrelia, and for borrelia DNA detection by PCR. Serum antibodies against borrelia were searched by indirect immunofluorescence assay (IFA), and by immunoblot using *B. lusitaniae*, *B. garinii* and *B. afzelii* as antigens [11]. Additionally, blood was submitted for routine testing of medical laboratory parameters. Motor and sensory nerve conduction studies were performed on the median nerves, ulnar nerves, peroneal nerves and cutaneous plantar nerves. Magnetic resonance imaging (MRI) of the head, the spine and the wrists was performed. A Holter's dynamic electrocardiography was also carried out.

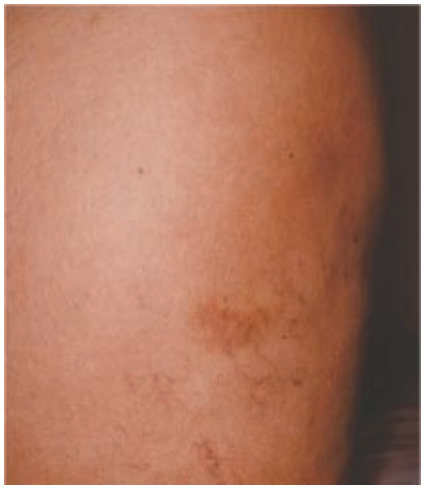

Fig. 1. Two ill-defined erythematous macules on the thigh

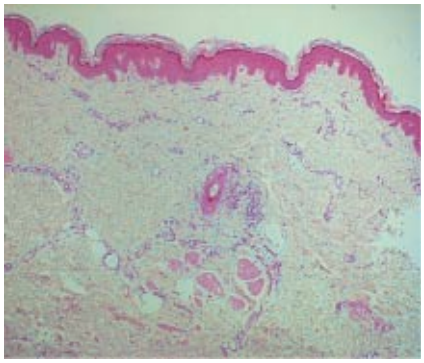

Fig. 3. Normal aspect of the histology of lesional skin

Results

The histopathology of lesional skin revealed normal epidermis, mild dermal telangiectasia and sporadic perivascular lymphocytes (Fig. 3). No spirochaetes were detected in the sections. Culture of the skin samples was positive for borrelia and genotyping identified the genospecies *B. lusitaniae* [11]. No serum antibodies were detected by IFA, and IgM and IgG immunoblots were negative [11]. The nerve conduction study revealed a slight focal demyelination of the median nerves on the wrists, but no evidence of polineuropathy.

MRI of both wrists revealed bilateral synovitis of the radiocarpal joint. Blood tests and electrocardiography yielded normal results. The patient was treated with intravenous ceftriaxone, 2 g daily for two weeks. Thereafter the clinical conditions of the patient improved, and the skin lesions did not expand further. Soon after the administration of ceftriaxone the patient had a febrile rash with myalgia and worsening of the headaches which disappeared the next day.

Discussion

A 46 year old woman presented with a long standing and expanding skin disorder on the left thigh. The presumptive diagnosis comprised morphea, and acrodermatitis chronica atrophicans [12–14] of Lyme borreliosis. However histological and serological results excluded both diagnoses. The skin lesions did not correspond to morphea or to any cutaneous manifestations associated with Lyme borreliosis [15]. However synovitis of the wrists, carpal tunnel syndrome, and the intermittent and nocturnal paraesthesias may point to late Lyme borreliosis [15–19]. The etiologic link was suggested by the cultivation and isolation of *B. lusitaniae* from a biopsy of lesional skin. The etiological link was further supported by the fact that the patient responded well to treatment with ceftriaxone. A transient febrile reaction soon after the first administration of ceftriaxone was suggestive of a Jarish-Herxheimer reaction, a phenomenon which is not uncommonly observed when starting antibiotic treatment of spirochaetal infections [20]. Even the episode of a non-traumatic subdural haematoma could be speculated spirochaetal related. It is known that spirochaetes are neurotropic, and infection may result in chronic inflammation of vascular walls of the central nervous system [21–24]. Finally, the non-specific aspect and the chronic evolution of the lesions in our patient is well in agreement with uncharacteristic dermatoses which were observed in Portuguese patients and of whom skin biopsies contained borrelial DNA which was detected by PCR [25, 26]. In their majority, these cases evolved over more than a year; patients suffered from rheumatic and neurological complaints, and serology was usually negative [25, 26]. In some skin biopsies of these patients genotyping of *B. lusitaniae* has been achieved [26]. However, pathogenicity of *B. lusitaniae* for humans without clinical case definitions cannot be substantiated. Nevertheless, the clinical case we describe here, with a culture-proven skin infection by *B. lusitaniae* [11], in context with the observation of other patients with a similar clinical course and detection of *B. lusitaniae* DNA in skin biopsies [26], allows to speculate that *B. lusitaniae* presents another human pathogen out of the *B. burgdorferi* sensu lato complex.

Moreover, *B. lusitaniae* was detected in high proportions in ixodid ticks from Portugal and north western Africa [4, 5, 27]. The question, however, if an additional causative agent of hard tick-borne borreliosis in Europe has been detected, cannot be answered before controlled clinical studies are completed in order to furnish the evidence of an etiologic role of *B. lusitaniae* in a hitherto clinically not defined condition.

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