Borrelia spirochetes found in a patient with Flegel disease

Flegel disease (Hyperkeratosis lenticularis perstans - HLP) is a rare autosomal dermatosis, characterized by small, asymptomatic, reddishbrown, keratotic papules occurring most frequently over the dorsa of the feet and the lower parts of the arms and legs. The majority of cases have been reported in European patients of 35 to 60 years old. All treatment options as external medications, phototherapy, or invasive methods tend to have only a partial effect.

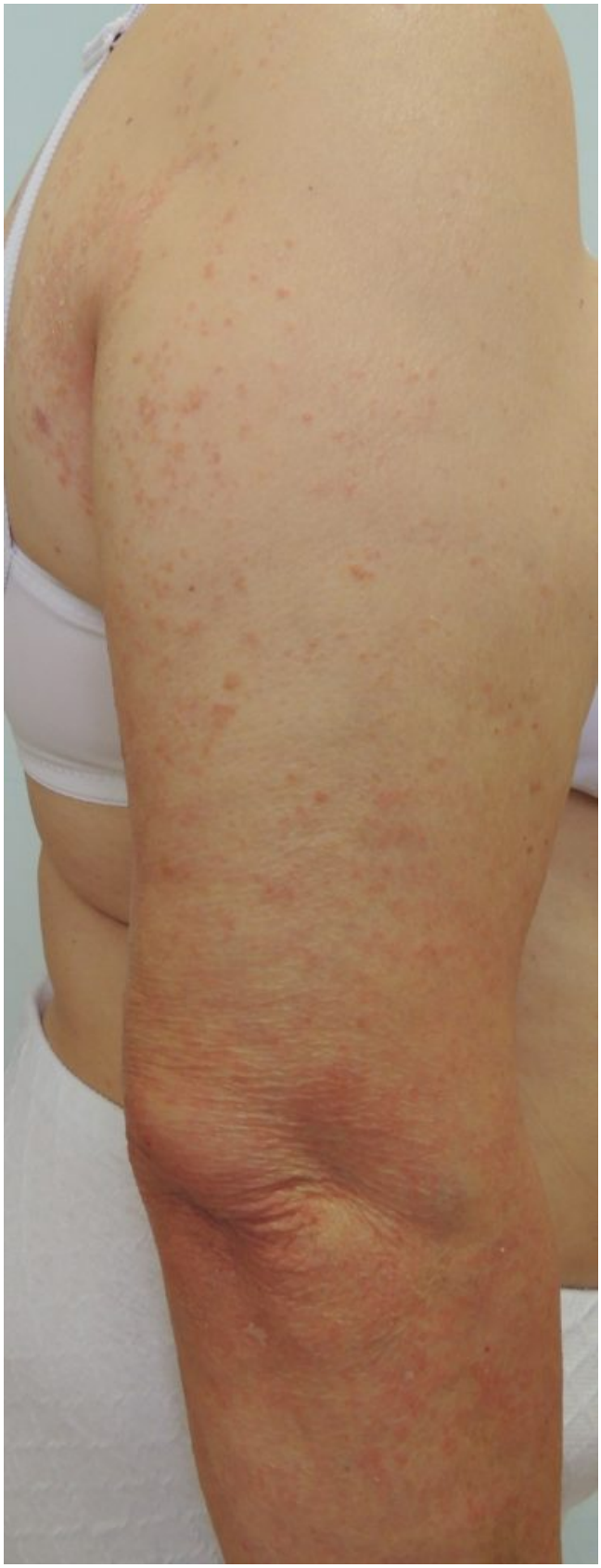

Fig. 1. The presence of small multiple red-brown keratotic papules with the scales on the surface on the patients upper limb

Our study published in Folia Microbiologica in 2016 shows the presence of two species from *B. burgdorferi* sensu lato complex isolated from a patient with HLP - *B. burgdorferi* sensu stricto (s.s.) and *Borrelia garinii*. The spirochete *Borrelia burgdorferi* is a tick-borne obligate parasite causing Lyme disease. The skin plays a central role in the development of Lyme disease as the entry site of *B*. *burgdorferi* before the bacteria may to spread through the bloodstream.

We present a case report: a 61-year-old patient came to the dermatologist with minor papules, pinkish-red in color with whitish scales on the surface (Fig. 1). Papules were located both on the upper and lower limbs and not spreading to the main body. The first symptoms were observed in patient at the age of 58. At that moment, the disease was diagnosed as psoriasis or psoriasiform eczematid, later as nonspecific superficial perivascular dermatitis. Histological examination, however, supported the last version of the diagnosis - Flegel disease.

The patient repeatedly received phototherapy, that was ineffective. The treatment with methotrexate (an antimetabolite drug) for 9 months was initiated. The medication was effective in joints treatment, the skin lesions, however, persisted as before. No one in the family had the history of the same symptoms. The patient was treated for arterial hypertension, diabetes mellitus, and coronary heart disease. Upon visiting the dermatologist, skin biopsy from papules at the upper and lower limbs was taken and histological findings confirmed the diagnosis of HLP. During the three following months, the patient received systemic corticosteroid (betamethasone) administered intramuscularly once a month. After this treatment, the skin problems were completely resolved. Continuous peroral application of total corticosteroid at low doses was prescribed; however, this treatment was denied by the patient. No abnormalities in blood and biochemistry tests were revealed. The patient underwent complex examinations with the purpose to detect any possible agent associated with HLP.

We used multiple detection methods to accumulate evidence to identify the ethiologic agent. These included fresh specimens from skin lesions and blood that were placed in a special culture medium to grow spirochetes in the lab. We then looked for specific proteins that are produced by spirochetes using analytical technique. The antigens are specifically and with high affinity bound by antibodies in the blood to form an antigen-antibody complex (antigen-antibody reaction), making detection specific. Lastly, using molecular techniques, we looked for DNA and searched for sections of code found in *Borrelia*, but not other organisms (DNA sequencing) providing the highest level of evidence for spirochete infection.

We found evidence of *Borrelia* infection in skin biopsy (*B. burgdorferi* s.s.) as so as in patient serum (*B. garinii*) in a different ratio. It is interesting to note that both species showed different tissue

specificity or disseminating ability.

The patient was treated with doxycycline for 30 days (to kill spirochetes). However this therapy did not have any clinical efect on the lesion. Examination of the patient by the clinical infectious diseases specialist and neurologist excluded the early and late stage of Lyme borreliosis. A histological examination supported rather the latter diagnosis of Hyperkeratosis lenticularis perstans (Flegel disease).

Even though an association of Flegels' disease with spirochete infection has never been confirmed before, the similarity in etiology and manifestations of especially skin condition and Flegels' diseases is obvious and thus require the deeper analysis of larger number of human samples for definite confirmation.

In our report, the presence of *B. burgdorferi* s.l. DNA and anti-borrelia antibodies in a patient with histologically confirmed diagnose of Flegel's disease was verified. Further analysis of probable spirochetal etiology of Flegel disease will show whether this was just an isolated case, or *Borrelia* can trigger the immune reaction that will result in HLP manifestations.

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Detection of Borrelia burgdorferi sensu stricto and Borrelia garinii DNAs in patient with Hyperkeratosis lenticularis perstans (Flegel disease).
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