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CASE REPORT

Borrelial lymphocytoma in a child

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ABSTRACT

Borrelial lymphocytoma (BL) is a rare manifestation of Lyme disease characterized by pathological lymphoproliferation on the skin (a type of cutaneous pseudolymphoma) in reaction to a Borrelia infection. It usually manifests itself as red plaques or swollen nodules, most commonly located on the ear lobes, genitals, or around the nipples. We describe a case of a 5-year-old girl with a painful erythematous nodule of the right auricle. The initial symptomatic treatment (with antihistamines and topical anti-inflammatory agents) resulted in temporary partial relief. There was a history of tick bites 3 and 5 months prior to the first manifestation of the disease. A positive serology test result for *Borrelia burgdorferi* (both chemiluminescent immunoassay and Western-Blot) led to the diagnosis of BL. The administration of an oral antibiotic therapy resulted in the quick disappearance of the lesion.

KEY WORDS:

Poland, *Borrelia burgdorferi*, child, pseudolymphoma.

INTRODUCTION

Lyme disease (LD) is the most common cause of tick-borne illness in the USA, Canada, and Europe. This multisystemic illness is caused by various species of the *Borrelia burgdorferi* sensu lato complex, which are transmitted by ixodid ticks. The reported incidence of Lyme borreliosis in Poland between 2017 and 2021 was 32–56 per 100,000 population per year [1]. It decreased during the COVID-19 pandemic (2020–2021) by over 40%. Children under the age of 18 years represent around 11% of the infected, which gives 1400–2400 cases per year [2]. Skin is the most frequently associated tissue in *Lyme borreliosis*, manifesting most commonly as erythema migrans (EM). Borrelial lymphocytoma (BL), also known as lymphadenosis benigna cutis, is a rare manifestation of Lyme disease, which we discuss in this article. A short literature review was also prepared as an addendum to this report.

CASE REPORT

Below we describe the case of a 5-year-old girl with oedema and redness of the right auricle. She was born at term with no perinatal problems. There was no family history of note. The girl completed a routine Polish immunization schedule. She received additional influenza and COVID-19 jabs. She suffers from atopic dermatitis, which is currently in regression. She lived in a house with a garden in a rural area in the West Pomeranian voivodeship in Poland, where there were 2 cats that had outdoor access. She attended a kindergarten and was generally happy, active, and in good health. Of note is the fact that she occasionally wore Paddle Back Clip-On Earrings.

At the beginning of January 2022, the girl started complaining about an earache. Her parents noticed that the right auricle was swollen, flushed, and slightly firmer than the left one (Figure 1). She received ibuprofen 3 times a day for 2 days without any noticeable effect.

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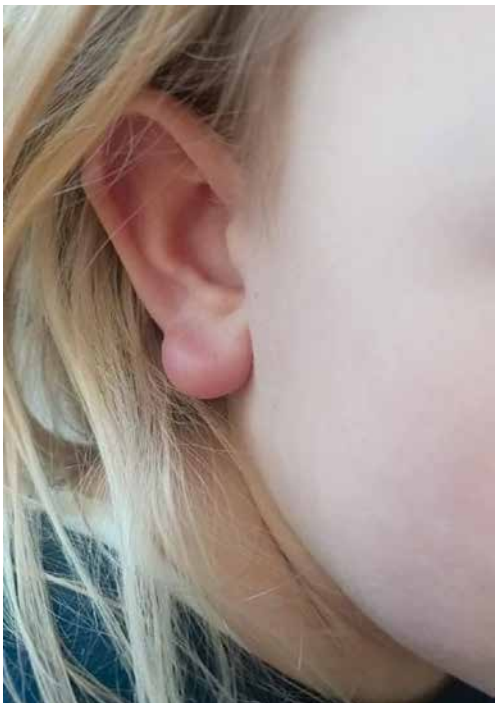

FIGURE 1. First day, when it was noticed that the right auricle was swollen, flushed, and slightly firmer

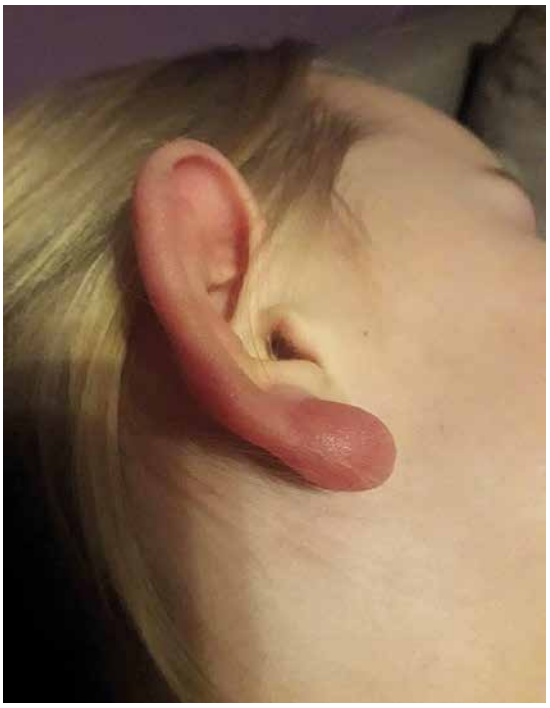

FIGURE 2. Borrelial lymphocytoma 4 weeks after first symptoms

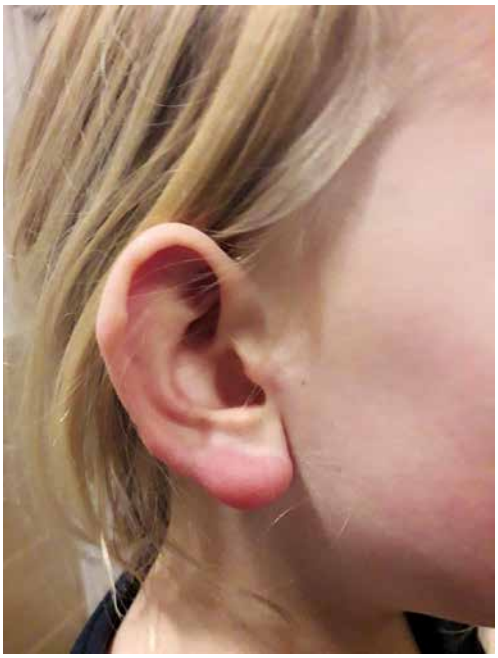

FIGURE 3. Improvement after 2 days of therapy

She was then reviewed by her primary care physician, who suspected a contact dermatitis and recommended a 5-day course of oral antihistamine and topical ointment comprising betamethasone (steroid), clotrimazole (antifungal), and gentamicin (antibiotic). The erythema and swelling decreased noticeably, and the pain resolved completely during the duration of treatment. However, these symptoms re-occurred after the completion of therapy. It was therefore decided to attempt further diagnosis, starting with a more detailed look at the patient's medical history. It was then that the girl's mother recalled that the child had been bitten by a tick twice, firstly 5 months and then 3 months prior to the first observable skin lesions. The initial bite was in the groin followed by a second bite in the neck, with the ticks being removed completely both times within the first day of the bite. The parents denied any symptoms of EM or any flu-like symptoms.

Borrelial lymphocytoma was eventually suspected, and serology tests for LD were requested. The chemiluminescent immunoassay test for antibodies against *B. burgdorferi* was positive in IgG class – 103.7 AU/ml (positive > 15 AU/ml) and negative in IgM class –12.03 AU/ml (negative < 18 AU/ml). A full blood count with differential was normal (white blood cell 10.06 K/mcL, haemoglobin 13.4 gm/dl, platelet 324 K/mL, neutrophil count 5.34 K/mL, lymphocyte count 3.16 K/mL, eosinophil count 0.74 K/mL – slightly above normal). The *B. burgdorferi* IgG Western blot test was positive (IgM-borderline). During the diagnostic process, the skin lesion grew beyond the earlobe to include the auricle, then became oedematous and turned bluish-red (Figure 2). Of note is that the skin lesion appeared a week after the first COVID-vaccine dose, and that reactivation and the most significant change in colour appeared 10 days after the second COVID-vaccine dose. The girl was then commenced on amoxicillin 50 mg/kg per day for a 28-day course. The administration of an oral antibiotic therapy resulted in the quick disappearance of the lesion, and after just 2 days of therapy both the erythema and oedema of the affected area had noticeably improved (Figure 3, 4).

DISCUSSION

There are 3 characteristic cutaneous manifestations of LD: EM in acute LD, BL in subacute LD, and acrodermatitis chronica atrophicans in late LD. Other skin manifestations with a hypothesised relationship to LD are scleroderma circum-scripta, lichen sclerosus et atrophicus, and cutaneous B-cell lymphoma [3]. Erythema migrans, the most frequent manifestation of LD, may represent about 80% of the cases of LD. It is an expanding, round-to-oval, sharply demarcated, salmon-coloured, macular or ring-like skin lesion of at least 5 cm in diameter. Erythema migrans lesions can be solitary or appear in multiple locations. Acrodermatitis chronica atrophicans is a rare manifestation of LD, which develops on distal extremities on average 10 years after infection and does not disappear spontaneously. It starts as a bluish-red discoloration and doughy swelling and evolves into an atrophic stage with thinning and wrinkling of the skin [4].

Borrelial lymphocytoma is a B-cell pseudolymphoma with an incubation period of a few weeks to 10 months. It usually appears as a soft, non-tender, well-circumscribed, bluish-red nodule or plaque of 1–5 cm at the ear lobe, breast, axillary fold, or scrotum. Borrelial lymphocytoma is reported almost exclusively in Europe [5], and in the absence of other clinical findings it can be difficult to diagnose. Cutaneous pseudolymphoma refers to a heterogeneous group of benign lymphoproliferative dermatoses caused by a wide range of agents, such as infectious agents (*Spirochetal bacteria*, Herpesvirus species, Molluscipoxvirus, HIV, parasites), foreign bodies (tattoo dyes, injected vaccination, or allergen extracts for hyposensitization, piercing), insect bites, drugs, and photosensitivity [6].

Above all, while BL may mimic other lymphoproliferative lesions, a differential diagnosis includes the following: lymphomas, lupus erythematosus, arthropod bite, sarcoidosis, foreign body granuloma, cutaneous metastasis, keloid, perichondritis, granuloma faciale, granulomatous contact dermatitis, and Paget disease (breast) [4, 7].

The Polish Association of Epidemiologists and Infectiologists recommends that an antibiotic therapy should commence without additional molecular tests following a serology confirmation of *B. burgdorferi*, which is obligatory in the absence of any pathognomonic symptoms EM. A 2-tier positive serology result for LD is defined as a positive IgG and/or IgM in the immunoenzymatic method confirmed by immunoblot test. If there is any diagnostic doubt, a skin biopsy of the lesion should be carried out. In those cases, both histopathological examination and polymerase chain reaction (PCR) analyses should be performed to detect DNA of the spirochete [8]. Histopathological findings include a polyclonal infiltration with predominance of B-lymphocytes, which may show germinal centres, mixed inflammatory cells including histiocytes, eosinophils, and plasma cells [3]. Borrelial lymphocytoma lesions have marker CD19, high levels of chemokine CXCL13, and lower levels of CXCL9 and CXCL10. CXCL13 is responsible for the formation of lymphoid aggregates and is also found in cerebrospinal fluid in patients with neuroborreliosis [9].

FIGURE 4. Earlobe after treatment

The Polish Association of Epidemiologists and Infectiologists recommends treatment of BL with amoxicillin, doxycycline, or cefuroxime administered orally for 2–4 weeks in doses adjusted according to body weight. Antibiotic therapy is considered to be effective, and around 90% of patients recover completely. Nevertheless, some patients may persist with symptoms – mainly fatigue, musculoskeletal pain, and cognitive symptoms [10].

Borrelial lymphocytoma can cure itself eventually without treatment; however, this can take over a year and often other systemic symptoms may develop [8]. Untreated LD can lead to neuroborreliosis manifesting as encephalomyelitis, meningoencephalitis, or peripheral neuropathy, or to Lyme arthritis. If left untreated, patients with EM develop arthritis in close to 60% of cases and neuroborreliosis in 10–15% of cases. It is important to remember that LD does not cause permanent immunity, and reinfection is possible [7].

To the best of the authors' knowledge, there are no current studies describing the clinical and epidemiological features of Lyme borreliosis amongst Polish children. Ołdak *et al.* reported that BL appears in 5% of children with LD and 2% of adults [10]. The authors of this article conclude that it would be best to analyse and compare data from other European countries to arrive at a more accurate estimate of the actual frequency of BL. A systematic search of relevant articles was performed on 1 March 2022 by using PubMed. It was limited to the English and Polish languages and human species. The following keywords were used as search terms: "borrelial lymphocyto-

ma", "Lyme disease child", "pseudolymphoma", and "*Borrelia burgdorferi* child".

In Sweden Berglund *et al.* conducted an active, population-based, prospective survey to determine the incidence of the LD and its clinical manifestations. They analysed a group of 232 children among whom 7% had BL, while among 1239 adults just 2% [11].

According to Stanek and Strle, BL was diagnosed among 1.5% of 275 children with LD based on data from the Department of Infectious Diseases at the University Medical Centre in Ljubljana (Slovenia) [3].

Arnež *et al*. performed a prospective clinical study investigating cases of BL among children below the age of 15 years, who were diagnosed at the Department of Infectious Diseases, University Medical Centre Ljubljana. Over a period of 7 years, BL was diagnosed in 33 children. Borrelial lymphocytoma was localized on an earlobe in 88% of the cases and on a breast in 12%. 24% of the children complained of local pain, although BL is considered painless. The disease began with a skin lesion in 91% of the patients, but with systemic symptoms in 6% of the cases. Regional lymphadenopathy was found in 24% and conjunctivitis in 3% of the patients. Positive borrelial serum antibody titres were identified only in 40% of the patients. The median incubation period was 10.5 days, ranging from 1–38 days [12].

Glatz *et al.* performed a retrospective study analysing 204 children with skin manifestations of LD seen at the Departments of Dermatology in Graz and Wiener Neustadt (Austria) over a 16-year period. Forty-four children (22%) suffered from BL, and an additional 12 patients (6%) had concomitant BL and EM lesions. Antibodies to *B. burgdorferi* s.l. were present in 76% of children with BL, of which IgG antibodies were predominant. A tick bite was recalled only by 34% patients with BL. The high reported incidence of *Lyme borreliosis* in Austria – around 300 per 100,000 population per year should be taken into consideration when looking at these findings [5].

In Bulgaria, Christova and Komitova analysed data collected over a 4-year period for a total of 1257 adults and children with diagnosis of LD. Children younger than 15 years old accounted for 20.6%. Only 0.3% of all patients presented BL [13].

Forde *et al*. aimed to assess the incidence and clinical presentation of serologically confirmed paediatric LD in the Republic of Ireland over a 5-year period. They analysed 47 cases, and no cases of BL or carditis were identified in that cohort. 40% of the children had single or multiple EM and could have been diagnosed based on clinical findings alone. 14% had Influenza-like symptoms compared with 43% LD with focal symptoms such as facial nerve palsy, central nervous system involvement, or arthritis [14].

Each of the above studies was designed differently, and a meta-analysis is not possible. It seems that in countries with a higher incidence of LD, BL is diagnosed proportionally more frequently. Differences in the prevalence of BL may be related to the different proportions of the individual species of Borrelia responsible for the infection in each country. On the other hand, it is possible that less frequent diagnosis of BL is related to the unawareness of this type of LD manifestation and the fact that doctors may not undertake the diagnosis of LD at all.

CONCLUSIONS

Borrelial lymphocytoma is a mild disease with a good prognosis when treated with the recommended antibiotics. Due to the increasing incidence of LD, it would now appear to be crucial that the medical community is aware of the least common symptoms of this disease to prevent long-term complications and late disseminated LD.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images.

DISCLOSURE

The authors declare no conflicts of interest.

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