Borelijski limfocitom areole pri devetletnem dečku: prikaz primera

Borrelial lymphocytoma of the areola in a 9-year-old boy: a case report

Avtor / Author

Darja Arko[1,2], Rajko Kavalar[1], Iztok Takač[1,2], Nina Čas Sikošek[1], Vida Gavrić Lovrec[1]

Ustanova / Institute

[1] Univerzitetni klinični center Maribor, Maribor, Slovenija; [2] Univerza v Mariboru, Medicinska fakulteta, Maribor, Slovenija;

[1] University Medical Centre Maribor, Maribor, Slovenia; [2] University of Maribor, Faculty of Medicine, Maribor, Slovenia;

Ključne besede:
limfocitom, limska borelioza, areola, histologija

Key words:
lymphocytoma, Lyme borreliosis, areola, histology

Članek prispel / Received
5. 5. 2023
Članek sprejet / Accepted
27. 11. 2023

Naslov za dopisovanje / Correspondence
Vida Gavrić Lovrec
Division of Gynaecology and Perinatology, Maribor University Medical Centre, Ljubljanska ul. 5
2000 Maribor
vida.ga.lo.1@gmail.com
02 321 2435, 041 708878

Izvleček

Namen: *Namen poročila je predstaviti redko obliko lymske borelioze – borelijski limfocitom, ki je prizadela bradavico pri otroku. Anamnestičnega podatka o ugrizu klopa ni bilo.*
Poročilo o primeru: *Predstavljamo primer devetletnega dečka, ki je bil pregledan zaradi mesec dni trajajoče eritematozne otekline areole brez drugih simptomov. Sprva so mislili, da gre za ginekomastijo, kasneje je bil neuspešno zdravljen zaradi mastitisa. Histološka preiskava je pokazala, da je šlo za psevdolimfom, najverjetneje zaradi pika žuželke. Serološka preiskava je potrdila okužbo z bakterijo Borrelia burgdorferi. Po dveh tednih zdravljenja z oralnim amoksicilinom je lezija izginila.*
Zaključek: *Pri prepoznavanju kožnih lezij v tipičnih območjih je*

Abstract

Purpose: *This study presents a rare skin manifestation of Lyme borreliosis, specifically affecting the areola in a child in the absence of a history of a tick bite or erythema migrans.*
Case report: *A 9-year-old boy presented with symptomless erythematous swelling of the breast areola for one month. Initial treatment for gynecomastia and then mastitis proved ineffective. A biopsy was performed, with histological findings revealing lymphocytoma, likely stemming from an insect bite. Serology for Borrelia burgdorferi was positive. Following a two-week course of oral amoxicillin, the lesion completely resolved.*
Conclusion: *The consideration of Lyme disease should be a component of the differential diagnosis*

https://doi.org/10.18690/actabiomed.260, CC BY 4.0

treba upoštevati tudi možnost lymske bolezni, če bolnik prihaja iz endemičnih krajev.

of skin lesions localised in typical areas, particularly in patients living in endemic regions.

INTRODUCTION

Slovenia is a region with a high prevalence of Lyme borreliosis (LB), where approximately 41% of ticks carry the borrelia bacterium. Annually, from 3,000 to over 7,000 infected individuals are registered, making LB the most prevalent infectious disease transmitted by ticks (Ixodes ricinus) in the country. The risk of infection is the highest from February to November, enhanced by mild winters and wet springs (1-4).

LB impacts various bodily systems and follows a diverse course that is divided into distinct early and late stages. The early stage is further divided into localised and disseminated forms of the disease. In the late stage, which is rare, LB is characterized by skin lesions and damage to circulatory and nervous systems. However, in most patients, only some symptoms are expressed (5).

Cutaneous lymphocytoma, also known as lymphocytoma cutis and cutaneous lymphoid hyperplasia, is a benign reactive lymphocytic proliferation that occurs in response to either known or unknown stimuli (6). It can be an early manifestation of LB, typically emerging a few days to a few weeks after the tick bite. Early skin lesions manifest in over 90% of patients with LB, with erythema migrans being the most prevalent and pathognomonic. In addition, this skin lesion is crucial for diagnosis (5). While other signs and symptoms only suggest the disease, laboratory confirmation is necessary in all cases, except for typical skin lesions in the early stage, such as erythema migrans (5, 7). However, a diagnosis of Lyme disease should be considered for individuals residing in endemic regions, even in the absence of a documented history of a prior tick bite.

CASE REPORT

A 9-year-old boy presented to the paediatric outpatient clinic with a one-month history of erythematous swelling of the right areola. He mentioned a traumatic injury of the same breast four months prior, with no other symptoms or tick bites. Upon physical examination, a painless, soft, 1.5 cm × 1.5 cm erythematous swelling of the right breast areola was observed (Figure 1). Ultrasound revealed a 2.6-cm hypoechoic structure, and Doppler imaging demonstrated increased blood flow. Laboratory tests, including red and white blood cell counts, as well as serum levels of prolactin, follicle stimulating hormone, luteinizing hormone, beta-estradiol, and sex hormone-binding globulin, were within reference ranges. The initial recommendation was observation.

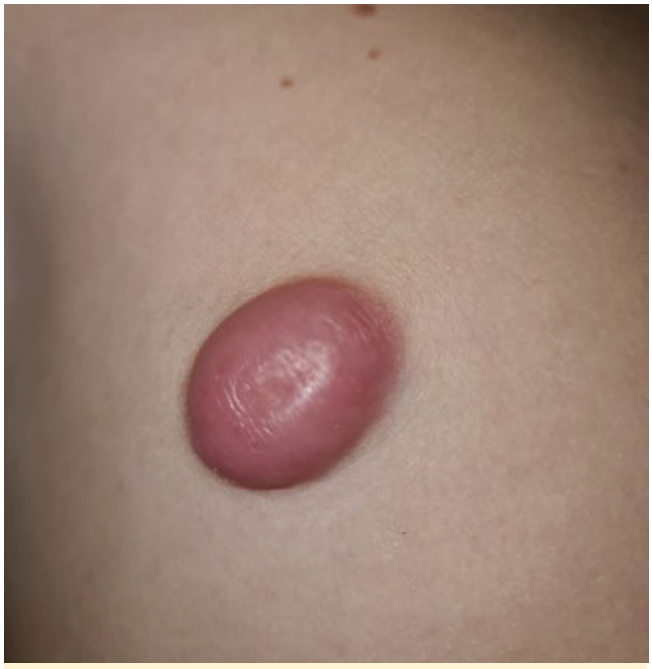

Figure 1. *Clinical manifestation before treatment.*

Two months later, the patient's mother sought a second opinion at the outpatient breast clinic. The clinical status persisted, and ultrasound confirmed the findings from three months prior. Inflammation was suspected, and local antibiotic therapy with clindamycin was recommended. However, there was no improvement after two weeks of therapy. Subsequently, a breast biopsy was conducted, and histological findings revealed cutaneous lymphocytoma, likely caused by an insect bite.
Further examination revealed that the excised skin lesion was reddish. Upon microscopic examination, no epidermal hyperplasia was observed. The dermis was infiltrated with a dense cellulare infiltrate predominantly composed of lymphocytes, histiocytes, and rare plasma cells. The formation of lymphoid follicles with blurred germinal centres was observed. The minimal subcutaneous fat was free of infiltration. Immunohistochemically, a mixture of B and T lymphocytes was observed, and the dendritic cells' mash was present within the follicles (Figure 2).
The serology for Borrelia burgdorferi was positive for IgG (176 AU/ml) but negative for IgM, as determined by indirect chemiluminescent immunoassay (CLIA) Additionally, the immunoblot for IgG was positive. Following the administration of oral amoxicillin at a dosage of 500 mg, three times a day for a duration of 2 weeks, there was a notable regression of the erythematous swelling. The lesion completely resolved within 8 weeks.

DISCUSSION

There are three characteristic cutaneous manifestations of LB: erythema migrans, localised borrelial lymphocytoma, and acrodermatitis chronica atrophicans (8). Symptoms of early localised Lyme disease single erythema migrans (EM) lesion, and early disseminated diseasemultiple EM lesions, headache, cra-

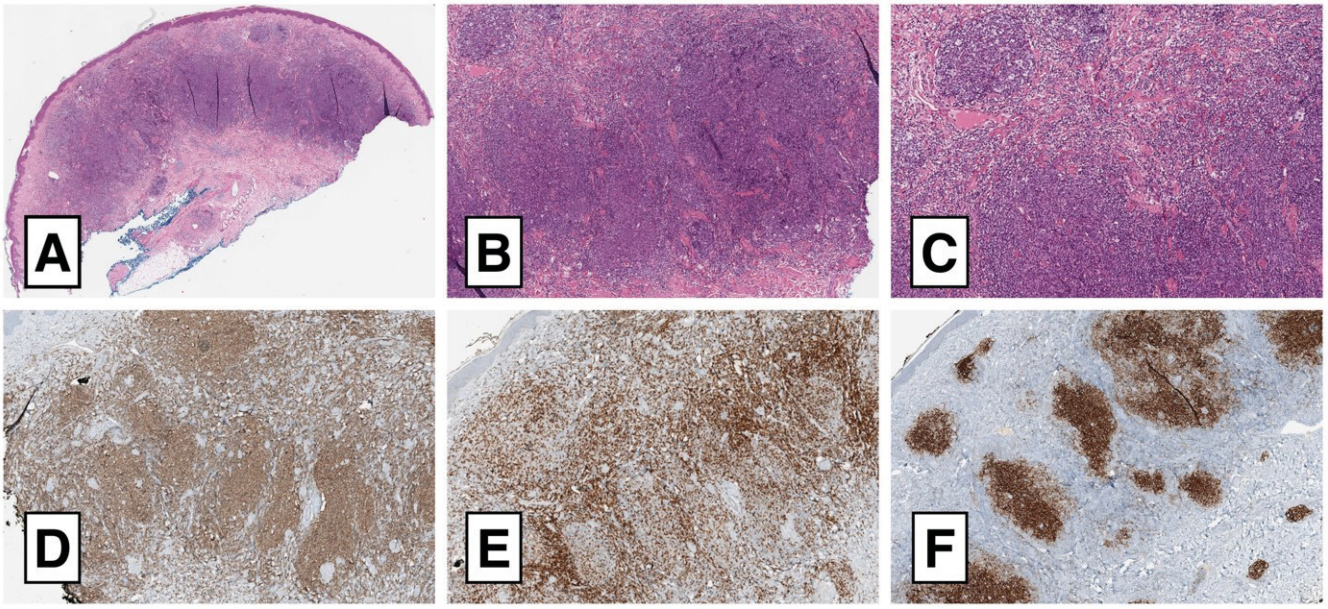

Figure 2. *Microscopic and immunohistochemical features of the dermal infiltrate. (A) Whole-mount image of the skin lesion with intact epidermis and dermal infiltrate not reaching the subcutaneous fat. Haematoxylin–eosin; magnification 1×, 2×. (B, C) Dense mononuclear dermal infiltrate composed of lymphocytes, histiocytes, and rare plasma cells with lymphoid follicle formation. Haematoxylin–eosin; magnification 25×, 50×. (D) B lymphocytes in the irregularly formed germinal centres of the follicles. CD20; magnification 25×. (E) T lymphocytes in the paracortical area, with fewer cells in the germinal centres. CD3; magnification 25×. (F) Dendritic cells in newly formed germinal centres of the lymphoid follicles. CD23; magnification 25×.*

nial neuropathy, or carditis, can present within days to weeks of a tick bite, late disease often manifests months later (9). In most patients, only some symptoms are expressed (5).

Borrelial lymphocytoma is a rare early localised manifestation of LB which appears between 2 days and 6 months after tick bite (10). It appears as a solitary red nodule with a diameter of a few cm, most commonly localized on the earlobe in children and in the areola or nipple in adults. It has been suggested that Borrelia spirochetes may have a tropism for cooler body sites. Other rare locations are nose, scrotum, upper arm, shoulders, the nape of the neck, axilla, and the back of the foot (11). Mostly it is solitary and occurs more frequently in children than in adults (12). In the absence of appropriate treatment, the lesion may persist for months and other manifestations of LB may follow (4).

Our patient had no history of a tick bite or concomitant/previous erythema migrans, nor were there any accompanying symptoms.

Despite Slovenia being a highly endemic region for LB, the disease was initially not considered in our case, primarily due to the absence of a history of a tick bite and lack of other clinical manifestations. Indeed, the lack of a tick bite and absence of other clinical symptoms and signs, are not uncommon, occurring in 70% and 64% of children, respectively (13). Anamnestic data on a previous traumatic injury further complicated the diagnostic process.

Our initial clinical diagnosis was gynecomastia and then mastitis. Both diagnoses turned out to be unlikely based on the laboratory findings and lack of other symptoms. Consequently, we opted to perform a biopsy. Histological examination is recommended in patients with lymphocytoma at a location other than the earlobe (14). According to a study by Arnez and Ruzic-Sabljic, borrelial lymphocytoma was present on the earlobe in 88% of children with the disease (15), whereas it is predominantly localised on the breast in the region of the areola mammae in adults (16). Furthermore, microscopic examination of the excised skin lesion revealed a characteristic dense mononuclear dermal infiltrate composed of mature B and T lymphocytes, admixed with rare mature plasma cells. The presence of irregularly formed reactive lymphoid follicles confirmed the diagnosis of lymphocytoma.

The patient exhibited positive borrelial serology, with IgG testing positive at 176 AU/ml and IgM testing negative. This pattern is observed in half of adults with borrelial lymphocytoma (16). In cases where borrelial lymphocytoma patients have negative serology, it is advisable to perform repeated serological testing, with the anticipation of seroconversion in a short time period (17). Although the cultivation of the borrelia bacterium from a skin biopsy in a specific cultivation medium remains the gold standard, this approach is successful in only one-third of adults (16). Additionally, nuclear acid amplification can be used to detect the borrelia bacterium in skin biopsies from borrelial lesions.

Three and a half months after the onset of symptoms, the patient started an oral antibiotic treatment according to the Slovenian recommendations for the treatment of early LB in children (18). In our case, the patient presented with a typical characteristic clinical presentation of borrelial lymphocytoma, despite no documented history of a prior tick bite. The diagnosis was confirmed by histological findings suggestive of LB. Initially, in spite of residing in an endemic region for LB, the disease was not suspected at the beginning, proving the need, to remind physicians of the importance of recognizing less common signs of infectious diseases in order to provide timely diagnosis and treatment.

It is important to highlight that LB should be considered in a differential diagnosis of skin lesions located in typical areas, particularly in patients residing in endemic regions. LB is prevalent in these areas but likely underreported (15). While erythema migrans typically poses no diagnostic challenges, atypical cases demand a heightened level of suspicion, as prompt treatment in the early stages often leads to a cure.

REFERENCES

1. Reported cases of Lyme borreliosis and tick-borne meningoencephalitis in Slovenia 2009 – 2019 [cited 2021 March 9] Available from: http://kazalci.arso.gov.si/en/content/reported-cases-lyme-borreliosis-and-tick-borne-meningoencephalitis-slovenia-0
2. Lymska borelioza, last updated 18. 3. 2016. Available from https://nijz.si/nalezljive-bolezni/nalezljive-bolezni-od-a-do-z/lymska-borelioza/
3. Vovk M, Ružić-Sabljić E, Arnež M. Children with Lyme Arthritis in Slovenia: Demographic, Clinical and Laboratory Characteristics. JSM Arthritis. 2016; 1: 1012
4. Strle F, Pleterski-Rigler D, Stanek G, Pejovnik-Pustinek A, Ruzic E, Cimperman J. Solitary borrelial lymphocytoma: report of 36 cases. Infection. 1992; 20: 201–6
5. Strle F. Lymska borelioza. In Tomažič J, Strle F, eds. Infekcijske bolezni. Ljubljana: Združenje za infekcijske bolezni, Slovensko zdravniško društvo 2014; 505–12.
6. Mitteldorf C, Kempf W. Cutaneous pseudolymphoma-A review on the spectrum and a proposal for a new classification. J Cutan Pathol 2020; 47:76–97.
7. Ruzic-Sabljic E, Cerar T. Progress in the molecular diagnosis of Lyme disease. Expert Rev Mol Diagn 2017; 17:19 – 30.
8. Müllegger RR, Glatz M. Skin manifestations of lyme borreliosis: diagnosis and management. Am J Clin Dermatol. 2008; 9: 355–68. doi: 10.2165/0128071-200809060-00002
9. Shapiro E.D. Borrelia burgdorferi (Lyme disease) Pediatr. Rev. 2014;35:500–509.
10. Moniuszko A, Czupryna P, Pancewicz S, Kondrusik M, Penza P, Zajkowska J. Borrelial lymphocytoma – a case report of a pregnant woman. Ticks Tick Borne Dis. 2012; 3: 257–8.
11. Maraspin V, Cimperman J, Lotric-Furlan S, Ruzić.Sabljić E, Jurca T, Picken RN, Strle F. Solitary borrelial lymphocytoma in adult patients. Wien Klin Wochenschr. 2002; 114: 515–23.
12. Hofmann H, Fingerle V, Hunfeld KP, Huppertz HI, Krause A, Rauer S, Ruf B. Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society. Ger Med Sci. 2017; 15: Doc14. doi:10.3205/000255
13. Arnez m, Ruzic -Sabljic E. Borrelial lymphocytoma in children. Pediatr Infect Dis J 2015; 34: 1319–22.
14. Stanek G, Strle F. Lyme borreliosis. Lancet 2003; 362: 1639 – 47.
15. Schoen RT. Lyme disease: diagnosis and treatment. Curr Opin Reumat 2020; 32: 247–254.
16. Maraspin V, Nahtigal Klevišar M, Ružić-Sabljić E, Lusa L, Strle F. Borrelial lymphocytoma in adult patients. Clinical Infectious Diseases 2016; 63: 914–21.
17. Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, Kristoferitsch W et al. Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol Infect 2011; 17: 69–79.
18. Arnez M. Antibiotic treatment of children with erythema migrans. Clin Infect Dis. 2007; 44:1133–4.