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Lymphocytoma Cutis: Cases Linked With Lyme Disease

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Lymphocytoma cutis (LCC) is a cutaneous B-cell pseudolymphoma representing a wide variety of disorders that share clinical and histologic features.[1-4] Although the cause in most cases is unknown, it can be induced by a variety of stimuli, including insect bites, *Borrelia burgdorferi* infection, trauma, vaccination, drug or antigen injections, and tattoos.[1,5-18] When the bite is from a tick carrying Lyme disease, the result is sometimes called borrelial lymphocytoma (BL). We describe 2 children whose lesions were probably best classified in this latter category. LCC in endemic regions such as Connecticut, New Jersey, or central Europe should be evaluated as a possible sign of Lyme disease.

Case Reports

Patient 1—A 7-year-old boy from a forested region near Bialystok, Poland, was seen for cutaneous nodules of the periumbilical skin, pubic skin, and scrotum of 6 months duration. They had slowly enlarged and were asymptomatic. There was no history of a tick bite. On examination, 3 bluish-red soft painless well-demarcated nodules were evident, 0.5 to 1.5 cm in diameter, on periumbilical and pubic skin and anterior surface of scrotum (Figure 1). There was no significant lymphadenopathy. Ophthalmologic and neurologic evaluations were within normal limits.

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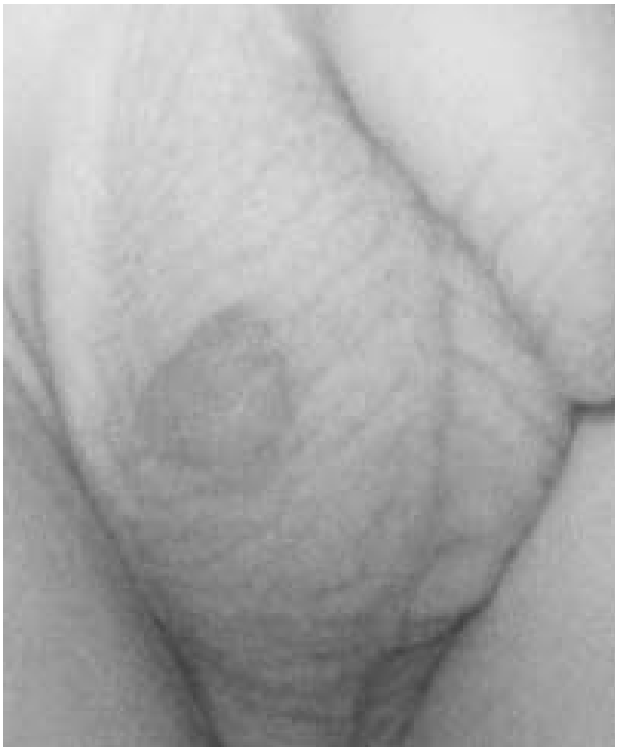

FIGURE 1. Lymphocytoma cutis of pubic region and scrotum.

Laboratory evaluations showed a normal complete blood cell count and differential. Indirect immunofluorescence assay showed IgM antibodies against *B burgdorferi* titered to 1:256 and by enzyme-linked immunosorbent assay (ELISA) antibodies. Histologic examination of the skin biopsy specimens showed acanthotic epidermal hyperplasia overlying an impressive superficial and deep infiltrate of small mature lymphocytes, with less numerous neutrophils and eosinophils. The formation of lymphoid follicles

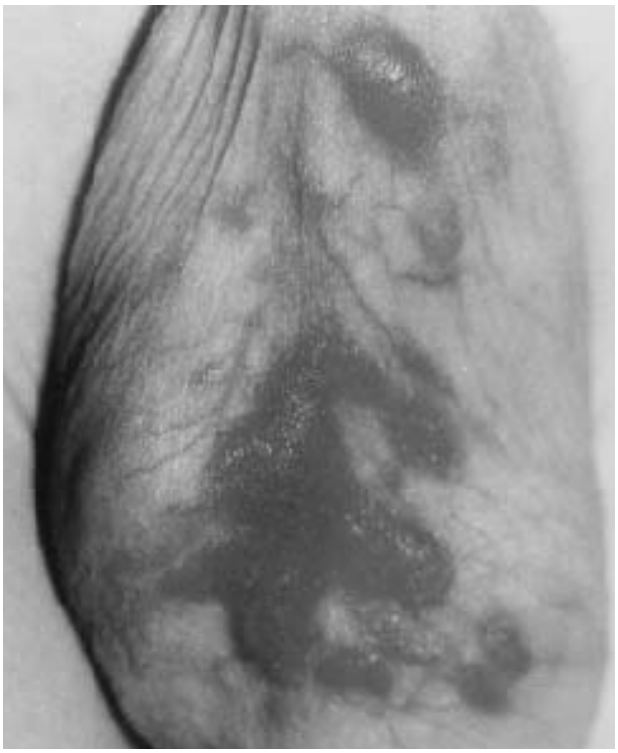

FIGURE 2. Lymphocytoma cutis of scrotum.

without distinct germinal centers was evident. In deeper sections, a perivascular pattern of these cells was seen. Skin appendages were preserved. Neither Warthin-Starry nor Steiner and Steiner staining was used. Erythromycin was given orally 250 mg twice a day for 14 days. The lesions resolved without any trace. Follow-up serologic tests, performed 1 and 3 years later, did not reveal any antibodies against *B burgdorferi*.

Patient 2—A 7-year-old boy from a forested region of western Sweden was seen with red slightly pruritic scrotal nodules 6 months after a tick bite at that site. An attached tick had been removed 5 months prior to onset. A cluster of bright red painless nodules was evident on the anterior surface of the scrotum. (Figure 2) There was no significant lymphadenopathy.

The blood cell count and peripheral smear were normal. ELISA did not show IgM or IgG antibodies against *B burgdorfi*. Histologic examination of the skin biopsy specimens showed a dense superficial and deep infiltrate of small mature lymphocytes, with scattered neutrophils and no eosinophils. The formation of lymphoid follicles was not evident. The infiltrate was more prominent in the upper and mid dermis than in the deep dermis. Few mitotic figures were observed. A proliferation of small blood vessels within the cellular infiltration was seen. In deeper sections, a perivascular pattern of these cells was noted. Skin appendages were preserved. Neither Warthin-Starry nor Steiner and Steiner staining was used. The tissue was not examined under polarized light for retained tick mouth parts. Penicillin V 750 mg twice daily for 2 weeks was given. The lesions resolved without trace.

Discussion

LCC is an uncommon disorder still also known as pseudolymphoma of Spiegler and Fendt.[2] Each described the entity about a century ago.[19,20] The name *lymphocytoma cutis* was coined in 1921 in a description of childhood scrotal nodules by Kaufmann-Wolf.[21] Bäfversted[22] classified Spiegler-Fendt disease as a lymphocytoma, which he called lymphadenosis benigna cutis, observing the formation of lymphoreticular tissue in skin. LCC tends to appear as a reddish blue nodule, plaque, or tumor. It is typically without symptoms, although it may be painful to touch and persist for months.

When associated with Lyme disease, LCC is usually solitary or a cluster of erythematous or violaceous nodules or plaques about 1 to 5 cm in diameter on the ear lobes or other head regions, the trunk (especially areolae), or extremities.[22-28] A predilection for earlobe, nipple and areola mammae, nose, and scrotum probably reflects the preference of spirochetes for regions of low body temperature. This seems a valid concept with regard to the earlobe, but is less clear for the breasts. In one series of 36 patients, 17 had lesions on the earlobe and 15 had them on the breasts.[6] The average age of those 17 patients with earlobe LCC was 12 years, whereas there were mainly adults with breast involvement. Another study of 8 children showed 6 with ear nodules.[5] Benign lymphocytic infiltration (Jessner-Kanof disease), which usually appears as a erythematous facial nodule or plaque, may also be a form of borrelial lymphocytoma,[2,3] as may the dispersed subcutaneous form of LCC.[23,25] Because LCC is much more frequent in those who probably acquired a Lyme disease infection in Europe rather than North America, a distinct species or subspecies of the organism has been postulated. A recent study of 13 patients showed that BL is caused not only by the *B burgdorferi* genospecies *B afzelii* but also by another genomic group that is seen in North America as well.[18]

In most patients with BL, BL is the first and only cutaneous sign of Lyme disease. In the minority of cases when BL is observed with erythema chronicum migrans (ECM), BL tends to appear weeks after the onset of ECM, and lasts longer.[5,18,29-31] However, BL and ECM may occasionally develop simultaneously, sometimes with nodules of BL within a patch of ECM. BL seems to be more common in children than adults.

BL may represent an early localized infection or be a sign of an early stage of disseminated Lyme disease. It may appear at the site of the primary spirochete entry within weeks to months after the tick bite. Rarely, BL may be associated with acrodermatitis chronica atrophicans,[22,26] a late cutaneous finding in Lyme disease.[32] Systemic findings of Lyme disease may also be evident, including carditis, polyradiculitis, and facial palsy with meningitis.[5,27,28] It has been suggested that every child with BL should receive an electrocardiogram.[5]

The histologic features of LCC should prompt elicitation of a history of preceding erythema chronicum migrans or a tick bite, serum antibody titer to *B burgdorferi*, and histologic examination of skin biopsy specimens to demonstrate spirochetes.[33-35] Both Warthin-Starry and Steiner and Steiner methods can be used. Identification of the organism can also be made by polymerase chain reaction or by culture.[5,18,36] However, even culture cannot be relied upon, as it was positive in only 38.5% in a recent work.[18] The presence of specific antibodies seems to confirm the diagnosis of Lyme disease in our first patient, despite no history of a tick bite. In the second one, the history of a tick bite, the development of a nodule after 15 weeks and its successful treatment with penicillin suggests this diagnosis too,[37,38] despite a negative serology.[39] In any case it is important to attempt to diagnose this complex multisystem disease because efficacious treatment is available, and delayed or inadequate therapy can be associated with unfortunate sequelae.[40]

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