

Multiple pseudolymphomas caused by *Hirudo medicinalis* therapy

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Therapy with medicinal leeches (*Hirudo medicinalis*) is now frequently applied in plastic surgery and in the management of chronic venous insufficiency. We observed a patient in whom firm, brown-red, pea-sized papules developed at each site where leeches had been applied on the lower legs. Histology, immunohistology, and molecular analysis of T-cell receptor and immunoglobulin heavy chain gene rearrangement proved these lesions to be follicular pseudolymphomas. (J Am Acad Dermatol 2000;43:867-9.)

The medicinal leech (*Hirudo medicinalis*) has been used for medical purposes for about 3000 years.¹ In the past decade, this remedy has become popular again. Particularly in plastic and reconstructive surgery, *H medicinalis* treatment has been proven to be effective in avoiding necrosis of congested skin flaps.²⁻⁴ Furthermore, *H medicinalis* is used for the treatment of venous insufficiency.⁵ In both indications, the release of hirudin, an antithrombotic agent, together with effective sucking of venous blood and subsequent spontaneous bleeding are considered to be the responsible therapeutic mechanisms.⁵ In addition, hirudin derivatives can also be produced by gene technology and are currently tested in systemic therapy for vascular occlusive disease.⁶

Side effects of *H medicinalis* therapy are considered to be rare. Scarring and local bacterial infection have been reported.^{4,7-9}

CASE REPORT

A 56-year-old woman presented with multiple lesions on both lower legs, which had appeared several weeks after she had received *H medicinalis* treatment because of chronic venous insufficiency with varicosis, edema, tenderness, and hyperpigmentation.

Several pea-sized, firm, brown-red cutaneous nodules could be observed on both lower legs (Fig 1). In some nodules, small areas of central scarring were evident. A biopsy was performed on one of these lesions.



Fig 1. Multiple firm, brown nodules on the lower legs several weeks after therapy with medicinal leeches.

Histologic examination showed a superficial and deep nodular dermal infiltrate (Fig 2) with germinal center formation (Fig 3). These showed a regular morphology and presence of so-called tingible body macrophages and a normal mantle zone. The infiltrate outside germinal centers consisted of lymphocytes admixed with a few eosinophilic granulocytes and plasma cells. In the center of the lesion, the upper and mid dermis was replaced by scar tissue. Immunohistology performed with a standard 3-step immunoperoxidase technique¹⁰ showed a nodular

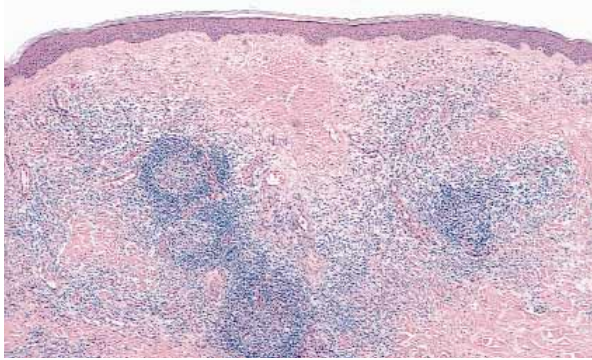


Fig 2. Nodular dermal infiltrate with germinal centers. Scar tissue in the upper and mid dermis. (Hematoxylin-eosin stain; original magnification $\times 50$.)

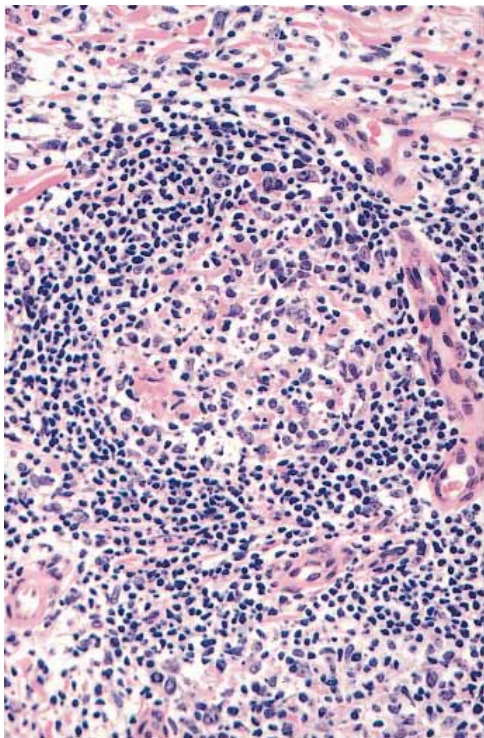


Fig 3. Lymph follicle with well-defined germinal center and mantle zone. (Hematoxylin-eosin stain; original magnification $\times 250$.)

arrangement of the B lymphocytes ($CD20^{+}$) with presence of $CD21^{+}$ follicular dendritic cells (Fig 4) within well-circumscribed germinal centers. T lymphocytes ($CD3^{+}$) were found around the B-cell areas, scattered within germinal centers, and in interstitial distribution. The proliferation rate within germinal centers, as detected by MIB-1 antibody, was more than 90% (Fig 5). Outside germinal centers only a few cells were positive for MIB-1. B-lympho-

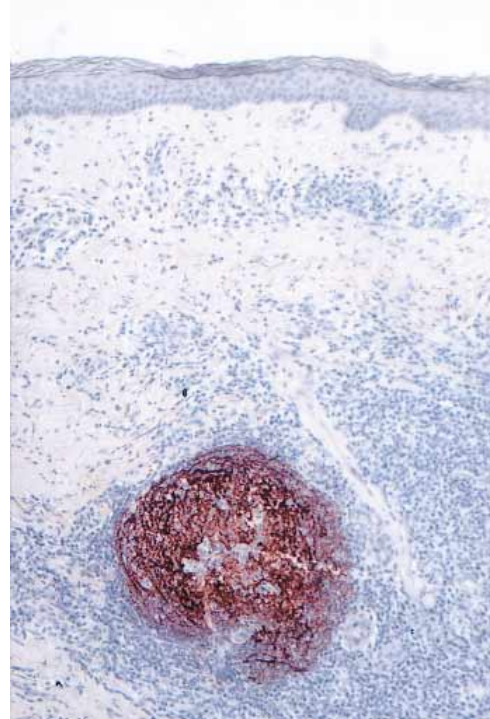


Fig 4. $CD21^{+}$ follicular dendritic cells within a germinal center. (Biotin-streptavidin-peroxidase stain; original magnification $\times 100$.)

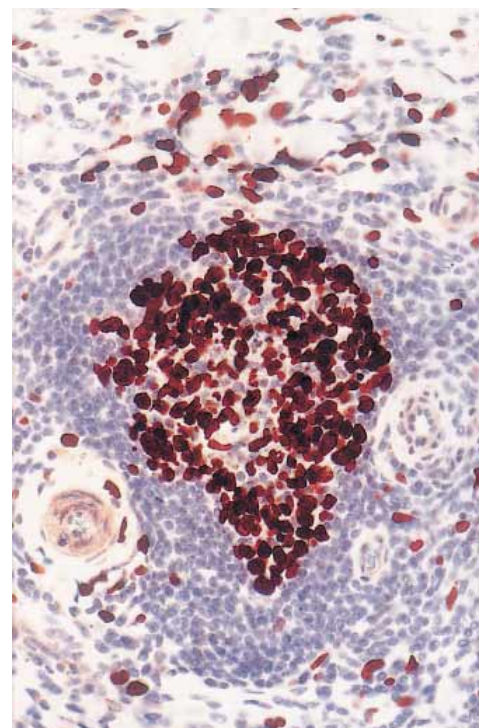


Fig 5. High proliferative activity (MIB-1-positive nuclei) in a germinal center. (Biotin-streptavidin-peroxidase stain;

cyte clusters expressed κ and λ immunoglobulin light chains at equal amounts. Analysis of T-cell receptor and immunoglobulin heavy chain gene rearrangement was carried out with a standard polymerase chain reaction technique on routinely fixed, paraffin-embedded sections of tissue,¹¹ using primers described previously.^{12,13} With both sets of primers a polyclonal smear could be observed, indicating that a monoclonal population of lymphocytes was not present in the infiltrate.

As a therapeutic measure, intralesional treatment with corticosteroids led to gradual clearing of the skin lesions.

DISCUSSION

Cutaneous pseudolymphomas with germinal centers are known to occur because of systemic medications, after arthropod bites, and in conjunction with *Borrelia burgdorferi* infection.^{14,15} To our knowledge, this is the first report of cutaneous follicular pseudolymphomas occurring after medicinal leech therapy. The specific association with *H medicinalis* in this case was supported by the presence of skin lesions only at sites of previous leech therapy. Whether this pseudolymphomatous reaction was due to substances released from the leech or to an infectious agent inoculated during the treatment, however, remains to be determined.

In our patient cutaneous follicular B-cell lymphoma and marginal zone lymphoma could be ruled out because of the presence of regular germinal centers with tingible body macrophages and distinct mantle zone, and of the demonstration of polyclonality of the infiltrate at both immunohistologic and molecular levels.¹⁰ Furthermore, the high proliferation rate of the germinal center cells is a feature typical of reactive follicles.¹⁰

In conclusion, pseudolymphomas seem to be a rare but noteworthy side effect of medicinal leech therapy.

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