

## INTRAVASCULAR LARGE B-CELL LYMPHOMA PRESENTING AS CUTANEOUS PANNICULITIS

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**Summary:** In this report the case of intravascular large B-cell lymphoma (angiotropic lymphoma, intravascular angioendotheliomatosis, malignant endotheliomatosis) with panniculitis features is present. The diagnosis was based on finding of typical CD20 positive tumorous cells within capillaries, veins, and small arteries in the biopsy of subcutaneous adipose tissue. An accurate and early diagnosis together with combined chemotherapy resulted in good response and remission of the disease.

**Key words:** Intravascular large B-cell lymphoma; Panniculitis; Chemotherapy

### Introduction

Intravascular large B-cell lymphoma, also known as intravascular angioendotheliomatosis or malignant endotheliomatosis, is characterized by widespread intravascular proliferation of malignant lymphoid cells in capillaries, venules, arterioles, and small arteries (7,5). The vasculature of the skin and central nervous system is most commonly affected, and the patients frequently present with cutaneous findings or neurologic symptoms.

Here we describe a case of a patient with fever, elevated blood sedimentation rate, and migrating subcutaneous infiltrates of low extremities and breasts. Intravascular large B-cell lymphoma was subsequently diagnosed on the base of skin biopsy and the patient gave a good response to chemotherapy.

### Material and methods

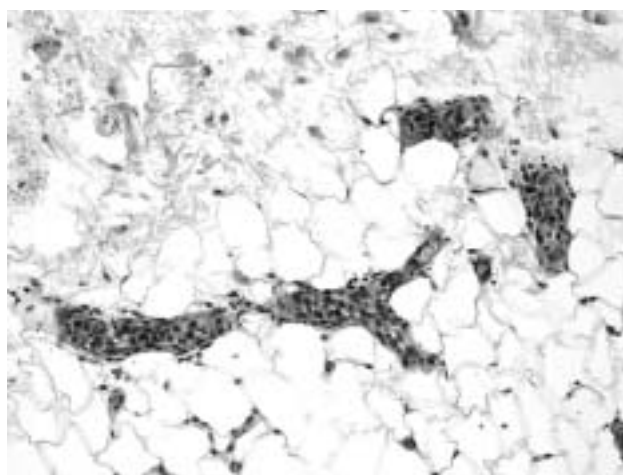
Clinical histories were obtained by review of the case notes and discussion with clinicians. Paraffin sections, 4 µm thick, were cut and stained with hematoxylin and eosin (H&E). Immunohistochemistry was carried out using monoclonal antibodies CD20 (DAKO, 1:100), CD45R0 (DAKO, 1:100), FVIII (DAKO, 1:100), CD31 (DAKO, 1:200), CD68 (DAKO, 1:100), and CD30 (DAKO, 1:25). Labeling was performed by LSAB+ visualization system (DAKO).

### Results

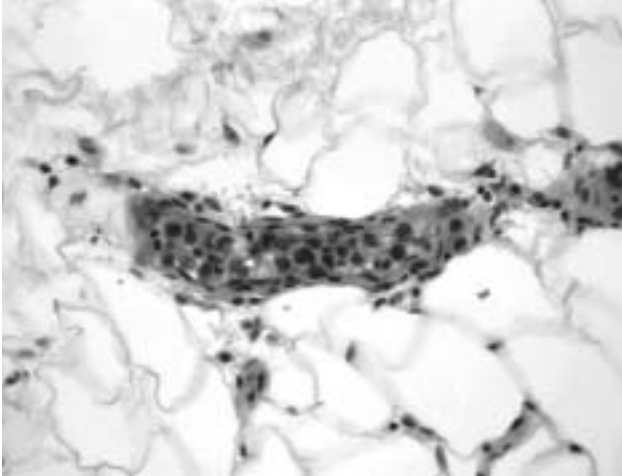
A 59-year-old woman presented with long-lasting fever, elevated blood sedimentation rate, and migrating subcutaneous

infiltrates of low extremities and breasts. Systemic disease was supposed, laboratory examination was performed together with mammography and biopsy of low extremity and breast infiltrates. During hospitalization patient developed low extremities paraplegia. Subsequent CT brain scan together with vertebral canal MRI revealed multiple small lesions.

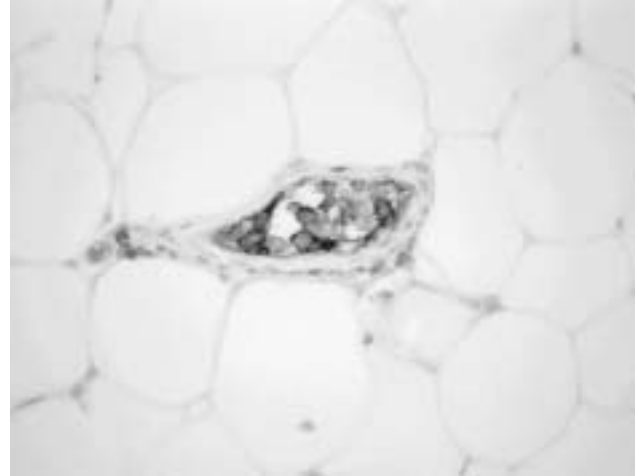
Subcutaneous infiltrate biopsy from low extremity and the breast showed identical histologic picture. Adipose tissue was of normal microscopic appearance. There was striking finding on small veins, arterioles, and capillaries lined by flat endothelial cells and containing large tumorous cells with irregular nuclei (Fig. 1). There were sporadic leukocytes and



**Fig. 1:** Vessels containing lymphoid tumorous cells (H&E, x100).



**Fig. 2:** Dilated vessel containing tumorous cells and scattered leukocytes (H&E, x400).



**Fig. 3:** Tumorous cells positive with CD20 (CD20 immunoperoxidase, x400).

fibrin fibers present among tumorous cells (Fig. 2). Tumorous penetration through the capillary wall was not noticed.

The intravascular lymphoid cells showed strong membranous positivity with CD20 (Fig. 3). CD45R0, FVIII, CD31, CD68, and CD30 were negative.

The patient was treated in first line with combination therapy CODOX-M (three cycles) with minimal clinical response and that is why treatment was converted to continual application of Vincristin + Bleomycin (Vincristin 0,5 mg D1+5, Bleomycin 15 mg D2-4) + methylprednisolon 125 mg D1-5. After six cycles of this chemotherapy and intrathecal application of Methotrexat 15 mg + Alexan 40 mg + Dexona 4 mg the disease was in remission. After-treatment brain MRI was negative, bone marrow biopsy showed normal histology without tumorous infiltration. The patient remains well 30 months after initial histologic diagnosis with normal motility.

## Discussion

The disease was described for the first time by Phleger and Tappeiner as “angioendotheliomatosis systemisata” (6) with extensive intravascular proliferation of atypical mononuclear cells. Subsequently, more than 15 synonyms have been used to describe the disorder. Endothelial origin of the disease was considered; other authors suggested that the atypical cells were disseminated carcinoma cells of unknown primary origin. With the use of immunohistochemical methods, it became apparent that virtually all cases were monoclonal proliferations of B (occasionally T) lymphoid cells (2) and the disorder is now believed to represent an intravascular proliferation of neoplastic lymphoid cells with features of noncleaved large cell lymphoma (9,1). Intravascular large B-cell lymphoma is unique in its variable clinical presentation (8,10). Tumorous cells are not identifiable in peripheral blood smears; superficial lymph nodes

and bone marrow involvement is minimal. The disease can present as primary adrenal insufficiency (3), tumor cells may occlude small vessels and capillaries resulting in organ ischemia and infarction. If the vessels of such blood rich endocrine organs were involved and compressed the adjacent parenchymal cells, cell atrophy and organ dysfunction could result (11).

Intravascular large B-cell lymphoma can originate in the splenic sinuses (4). In this, 10 years ago published case, the disease presented as massive splenomegaly (2150 g) with extensive tumorous infiltration of red pulp sinuses.

The optimal management and prognosis of intravascular large B-cell lymphoma is not clear (12). The diagnosis is often missed until the later stages, and in many reports of the diagnosis is made at autopsy. The recognition of lymphoid origin in our case led to the use of anti-lymphoma chemotherapy. Some patients are responding poorly but others, including our patient, remain in remission. Immunophenotype correlates with prognosis as in other types of lymphoma.

This case illustrate several points - this type of lymphoma may be present without any evidence of lymph nodes enlargement or focal disease and may be mistaken for connective tissue disease (panniculitis). Skin and subcutaneous tissue biopsy with recognition of subtle histological features is very important. If the diagnosis is missed, the patient will progress to death. If proper diagnosis is made, there is opportunity for long lasting remission and potential cure.

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