

Intravascular large B-cell lymphoma presenting as panniculitis



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INTRODUCTION

Intravascular large B-cell lymphoma (IVLBCL) is a rare disease with an incidence of less than 1 person per 1 million. It is a subtype of diffuse large B-cell lymphoma in which the lymphoma cells reside predominantly within the lumina of blood vessels (particularly capillaries) with circulating neoplastic cells detectable in the peripheral blood in less than 10%.¹ Presenting clinical features are extremely variable. We describe a case of IVLBCL presenting as panniculitis. This case emphasizes the importance of collaboration between dermatology and pathology in considering rare but serious diagnoses when clinical features and histologic findings are discordant.

CASE REPORT

A 77-year-old Iranian woman was admitted for investigation of a 3-month history of painful abdominal and inframammary subcutaneous nodules in the setting of right upper quadrant abdominal pain, known gallstones and elevated amylase, lipase, and C-reactive protein levels. She also had a history of taking warfarin for atrial flutter, previous transient ischemic attack, and carotid endarterectomy. The nodules were extremely tender to palpation and had overlying retiform purpura extending across the abdomen (Fig 1). Clinical differential diagnosis included panniculitis, warfarin necrosis, thrombosis/vasculitis, infection, and lymphoma.

Fat necrosis was seen on ultrasound scan and was later confirmed on incisional biopsy taken from a lower abdominal nodule because of pain in the

Abbreviation used:

IVLBCL: Intravascular large B-cell lymphoma

inframammary area. The specimen showed extensive fat necrosis with scant inflammation (Fig 2). No granulomas, vasculitis, atypical lymphoid infiltrate, or organisms were seen (Gram, periodic acid–Schiff–diastase and Ziehl–Neelsen stains were performed). Flow cytometry of the tissue was negative. The histology results were consistent with those of pancreatic panniculitis. Culture of the subcutaneous tissue grew actinomyces. Further panniculitis screening blood tests (including antinuclear antibody, double-stranded DNA, α -1-antitrypsin, QuantiFERON-TB Gold In-Tube assay [Celestis Australia], complement levels, and angiotensin converting enzyme) were negative or within normal parameters.

Computed tomography scan found a bulky pancreas, necrotic peripancreatic lymph nodes, and a left adrenal nodule. The patient also had B symptoms but no clinical lymphadenopathy. Amylase and lipase levels increased further, and endoscopic ultrasound scan and sampling of the pancreas did not confirm malignancy but suggested an inflammatory mass. The lymph node showed reactive changes, and flow cytometry was negative. The node cultured *Escherichia*, *Neisseria*, *Streptococcus*, and *Haemophilus* species. Significance of this mixed growth was difficult to determine, and despite broad-spectrum intravenous

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Fig 1. Intravascular B cell lymphoma. Subcutaneous nodules in the left inframammary region with overlying retiform purpura and extension across the abdomen.

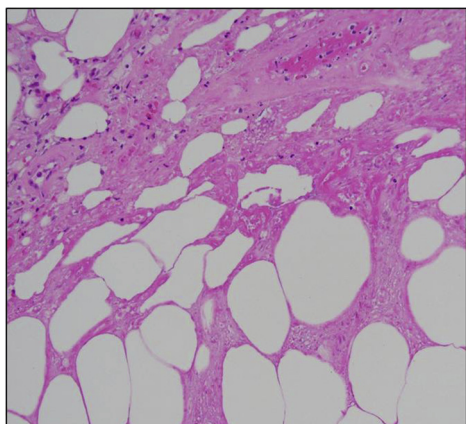


Fig 2. Scant mixed inflammatory cell infiltrate in fat lobules, comprising neutrophils and a few eosinophils, with vascular congestion with extensive fat necrosis and ghost outlines of fat cells. (Original magnification: $\times 200$.)

antibiotics and repeatedly negative blood cultures, fevers and elevated C-reactive protein persisted. Lactate dehydrogenase level increased from 423 U/L to greater than 1000 U/L, and a cholestatic liver picture developed followed by labile blood pressure and syndrome of inappropriate antidiuretic hormone secretion.

A positron emission tomography scan was planned and the original skin biopsy was reviewed. Positron emission tomography scan found extensive aorto-caval, para-aortic, and retroperitoneal lymph node uptake and avid uptake in subcutaneous areas corresponding with the subcutaneous nodules. Review of the sections found focal and subtle intravascular collections of intermediate to large lymphocytes within occasional small-caliber vessels in the reticular dermis and subcutis, away from the areas of panniculitis. The lymphocytes were hyperchromatic with slightly irregular nuclear outlines, and extension beyond vessels was not seen. Immunohistochemistry confirmed a diagnosis

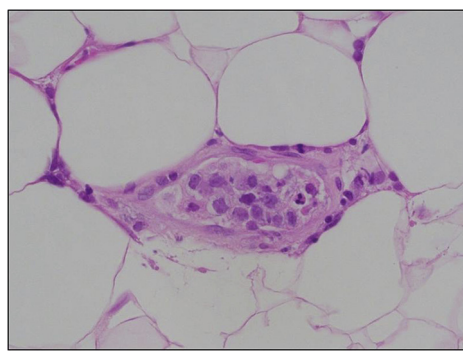


Fig 3. Intravascular B cell lymphoma. A vessel shows occlusion by a proliferation of intermediate-sized cells with scant cytoplasm and hyperchromatic and irregular nuclei. (Original magnification: $\times 400$.)

of intravascular large B-cell lymphoma, with the tumor cells positive for CD20, CD5, BCL2 (focal), BCL6 (focal), MUM1, and MIB-1 ($>90\%$) but negative for CD3, CD10, CD23, EBER ISH, cyclin D1, and c-myc ($<40\%$) (Figs 3 and 4). Galectin-3 provides potential research interest in this disease but is not typically used in routine diagnosis and was not available at our laboratory.

The patient was transferred to the care of the hematology team with stage IVB IVLBCL and commenced on R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy. After 2 cycles, the subcutaneous nodules were almost clinically undetectable.

DISCUSSION

IVLBCL occurs predominantly in the sixth to seventh decades and can involve any organ but mostly the central nervous system, skin, kidney, lung, adrenal system, and liver. There are no known risk factors, and in most instances, it is considered to be a disseminated disease at diagnosis (approximately 90% are stage III or IV).²

Clinical features are variable and nonspecific and reflect vascular involvement in the affected area. Lymphadenopathy is classically absent. Fever is present in 45% of cases²⁻⁴ and may lead to extensive investigation for infection, as in this case. Skin is affected in one-third of cases and reports show that the most common areas of involvement are the abdomen, proximal limbs, and inframammary areas (which are generally fat-rich areas). Skin features are also variable and include nodules, plaques, purpura-like lesions, maculopapular eruptions, ulcers,^{3,4} and a report of IVLBCL panniculitis.⁵

Clinical features in IVLBCL are found to be relatively ethno-specific with central nervous system and skin involvement predominating in Western

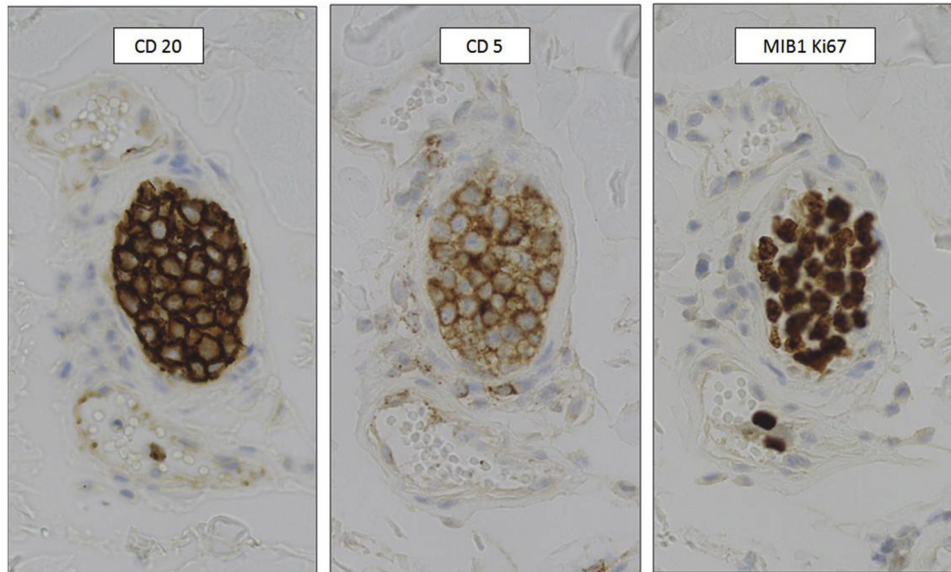


Fig 4. Strong CD20 positivity with weak co-expression of CD5 and a very high proliferation rate, indicating a B-cell intravascular lymphoma. (Original magnification: $\times 400$.)

populations and a variant with fever, bone marrow involvement, hepatosplenomegaly, and hemophagocytic syndrome in Asian populations.

There are no pathognomonic laboratory or radiologic tests, and the diagnosis is made from affected tissue. IVLBCL therefore presents a challenging diagnosis in the antemortem period. Skin biopsy can determine IVLBCL in the absence of any skin findings, and some investigators advocate random skin biopsy in patients with fever of unknown origin.^{2,6} This diagnosis should be considered in any situation in which panniculitis occurs in an unusual site, especially if there is overlying purpura.

IVLBCL is an aggressive disease and has a poor prognosis with cutaneous-only disease having a 3-year survival rate of 56% versus 22% if spread beyond the skin.² The disease can be rapidly fatal if untreated. Anthracycline-based chemotherapy has shown an improved overall 3-year survival rate, and the addition of rituximab to chemotherapeutic regimens has improved this further.^{1-4,7-9}

This case highlights the importance of considering rare but serious diagnoses when there is discordance between the clinical picture and histologic findings. Effective communication and collaboration between dermatology and pathology was instrumental in unravelling this highly unusual presentation of a

rare lymphoma, which is frequently diagnosed postmortem.

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