Guillain-Barre Syndrome: An Unusual Presentation of Intravascular Lymphoma

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Intravascular lymphoma is a rare subtype of extranodal diffuse large B cell lymphoma characterized by the presence of lymphoma cells only in the lumina of small vessels, particularly capillaries. The lymphoma preferentially involves the vasculature of the skin and central nervous system. Clinical manifestations of the disease are protean and are due to multifocal involvement of medium and small vessels by tumor cells. Most patients present with fever of unknown origin, non-specific cutaneous and neurologic manifestations, and progressive multisystem failure. Neurologic manifestations include headaches, depression, dementia, seizures, cerebrovascular accidents, peripheral neuropathies and visual disturbances [1]

This lymphoma was considered mistakenly in the past to be a neoplasia of endothelial origin (malignant angioendothelomatosis). It is described in only a few hundred case reports. According to prior case studies, 75% of the patients are diagnosed postmortem and delayed diagnosis is common, accounting in part for the poor prognosis. Moreover, it is assumed that many patients are never diagnosed. Most of the diagnoses in live patients were made by skin biopsy, and the few patients who received chemotherapy lived months to years longer than untreated patients [2]. To date, due to the lack of randomized studies, there is no preferred therapeutic protocol recommended for intravascular lymphoma. The present report demonstrates the difficulty in early diagnosis and describes Guillian-Barre syndrome as the presentation of this unusual lymphoma.

Patient Description

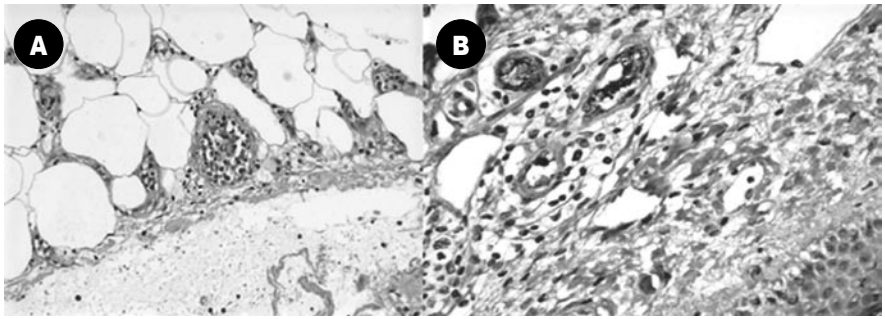
A 78 year old woman was admitted with an acute febrile disease and bilateral leg numbness. Past medical history revealed hypertension of 5 years duration that was treated with beta-blockers and aspirin .During the last 2 years she suffered from multiple large painful, erythema nodosum-like lesions on both thighs. Histopathologic examination of a biopsy taken a year before admission was interpreted as non-specific lobular panniculitis with fat necrosis and slight perivascular chronic inflammation. Since then she was diagnosed as having idiopathic erythema nodosum. She received no treatment. A week prior to hospitalization she had high fever and distal leg numbness. Her family doctor prescribed quinolones, with no response after 3 days of therapy.

On admission, her body temperature was 39.1°C, her neurologic examination revealed agitation, bilateral distal leg weakness and parasthesia (L>R) with no neck stiffness. Large painful reddish plaques were observed on both lateral aspects of the thighs. A second biopsy was taken from one of the lesions. Laboratory examination revealed the following: erythrocyte sedimentation rate 100 mm/hour, lactate dehydrogenase 450 U/L, D-dimer 1890 mg/L, hemoglobin 9.1 g/dl, white blood cells 3900 mm^3 with normal differential, platelets 198,000 mm^3, sodium 121 mmol/L; alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were mildly elevated. Head and body computed tomography scans did not reveal any lymphadenopathy or hepatosplenomegaly.

The leg weakness rapidly progressed proximally, accompanied by urinary retention; electromyography demonstrated a progressive bilateral acute sensory motor polyneuropathy compatible with Guillian-Barre syndrome. Lumbar puncture was not significant except for mildly elevated protein (62 mg/dl). Spinal magnetic resonance imaging did not yield any findings. The patient was treated with intravenous gammaglobulins for 5 days, without any response. She continued to deteriorate, succumbing 10 days later due to methicillin-resistant *Staphylococcus aureus* sepsis and multi-organ failure. Skin biopsies from the red plaques, the results of which were received after the patient had died, demonstrated large atypical lymphoid cells filling the lumens of small dermal and subcutaneous blood vessels. Immunohistochemical stains for CD20 confirmed the diagnosis of intravascular lymphoma [Figure]. Revision of the first biopsy disclosed that the same pathology had been present 2 years earlier.

Comment

To our knowledge this is the first report of intravascular lymphoma presenting with Guillian-Barre syndrome. Guillian-Barre syndrome is an idiopathic acute inflammatory demyelinating polyneuropathy



[A] Skin-punch biopsy demonstrating capillaries in subcutaneous adipose tissue slightly distended by large atypical cells. **[B]** Immunohistochemical stain for CD20 confirms the lymphoid B cell lineage of these cells.

that is believed to be immunologically mediated. Approximately two-thirds of cases are related to a recent respiratory or gastrointestinal tract infection, especially infections due to *Campylobacter jejuni*, cytomegalovirus, and Epstein-Barr virus [3]. Guillian-Barre syndrome has been reported to be associated with some systemic processes such as Hodgkin's lymphoma, human immunodeficiency virus and systemic lupus erythematosus [4].

This is the first report of Guillian-Barre syndrome in a patient with intravascular lymphoma. Regarding our patient we cannot provide data differentiating between immune mediated polyneuropathy and vascular damage to multiple nerves as the basis for this presentation. The patient's diagnosis was elusive due to misinterpretation of the initial skin biopsy. Skin biopsy determines the diagnosis in a large proportion of intravascular lymphoma patients. The first manifestation in our patient was panniculitis-like lesions diagnosed mistakenly as erythema nodosum 2 years prior to her neurologic symptoms. Recent evidence suggests that in contrast to previous reports, hepatosplenic involvement (26%) and bone marrow infiltration (32%) were found to be common features in intravascular lymphoma, while nodal disease was confirmed only rarely (11% of cases) [5]. When our patient presented with Guillian-Barre syndrome her disease was already disseminated and prognosis was poor. Had treatment been initiated earlier, prognosis might have been better. We would like to emphasize the importance of considering this disease in the differential diagnosis in any patient presenting with unclear disease suggesting small vessel disease. A definite clinical suspicion can aid the pathologist in achieving earlier diagnosis, thus improving the patient's prognosis.

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