Involvement of bone marrow with intravascular large B-cell lymphoma

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Hematol Stem Cell Ther 2010; 3(1): 39-41

Intravascular large B-cell lymphoma (IVLBCL) is a rare subtype of extranodal large B-cell lymphoma characterized by a selective proliferation of lymphoma cells within the lumina of vessels. We report a case of an 86-year-old man who presented with fever, shortness of breath and altered mental status. The diagnosis of IVLBCL was confirmed on a bone trephine biopsy that revealed positivity of CD20 and PAX5 immunohistochemical staining of lymphoma cells confined within the lumina of vessels. The patient had a rapidly deteriorating clinical course with a fatal outcome even before the specific treatment for the underlying disease was commenced.

Intravascular large B-cell lymphoma (IVLBCL) is a rare malignant neoplasm classified as a distinct clinicopathological subtype of extranodal diffuse large B-cell lymphoma according to the WHO classification. IVLBCL usually occur in adults, is usually widely disseminated at presentation and may involve virtually any organ. Clinical signs and symptoms at presentation are non-specific and are usually related to the main organ involved. Neurological and cutaneous manifestations are common in early stages, but the patient may present in the late stages with pancytopenia, hepatosplenomegaly and multiorgan failure. Diagnosis is made when the tissue biopsy shows the selective presence of neoplastic lymphoid cells in the lumina of vessels in various organs and is confirmed when these tumor cells express B-cell-associated antigens. IVLBCL is often diagnosed late or at postmortem because of the non-specific clinical presentation, difficulty in histological diagnosis and aggressive clinical behavior. Even when diagnosed earlier, the response to chemotherapy is often poor. In this report, we describe a case of IVLBCL diagnosed on bone trephine biopsy with a fulminant clinical course and a fatal outcome.

CASE

A 86-year-old male presented with a history of fever, weight loss, shortness of breath and altered mental status. Examination revealed pallor and splenomegaly. At presentation, results of complete blood counts showed bicytopenia with a hemoglobin of 10.7 g/dL (normal reference range, 13.7-16.3 g/dL), hematocrit 32% (normal reference range, 41.9%-48.7%), mean corpuscular volume of 89.7 fL (normal reference range, 76.0-96.0 fL), mean corpuscular hemoglobin of 30 pg (normal reference range, 26.0-32.0 pg/cell), a total white cell count of 5.1×10^9/L (normal reference range, 4.0-10.0×10^9/L), an absolute neutrophil count of 2.2×10^9/L and platelets of 19×10^9/L (normal reference range, 150-400×10^9/L). A peripheral blood film revealed normochromic anemia and thrombocytopenia, with no leukemic blasts or circulating lymphoma cells. Other relevant laboratory tests showed elevated LDH (2864 U/L normal reference range, 253-548 U/L) and uric acid (10.1 mg/dL normal reference range, 4.1-8.0 mg/dL). Abdominal ultrasound showed splenomegaly (18 cm); however, there was no evidence of cervical, thoracic or abdominal lymphadenopathy on CT scan. The patient was hospitalized for management, but his condition deteriorated rapidly with worsening cytopenia and progressive respiratory failure. He was moved to the intensive care unit and required ventilation support on day 3 of admission. He required frequent transfusions with packed red cells and platelet concentrates along with broad-spectrum antibiotics and other supportive care. In view of the cytopenia, splenomegaly and elevated LDH, a bone trephine biopsy was performed, which showed proliferation of large atypical lymphoid cells with a moderate amount of cytoplasm, vesicular nuclei and prominent nucleoli within the vascular and sinusoidal structure of the bone trephine biopsy (Figure 1). Immunohistochemical staining of atypical lymphoid cells showed strong positivity for B-cell marker CD20 and PAX5 (Figures 2, 3). Vascular lining was highlighted by positivity for CD34.
CD5 was also positive in lymphoma cells while other markers like CD3, CD43, CD10, CD30 and cyclin-D1 were negative, confirming the morphological and immunohistochemical diagnosis of the intravascular subtype of large B-cell lymphoma. In the following days, his condition further deteriorated despite continued supportive care leading to a fatal outcome secondary to progressive cardiorespiratory insufficiency and multiorgan failure. The patient died on day 7 of admission.

**DISCUSSION**

IVLBCL, also known as angiotropic large cell lymphoma, is a rare and pathologically distinct sub-type of non-Hodgkin lymphoma characterized by varied clinical spectrum and distinct immunophenotypic profile. Afflicted patients are usually middle-aged or elderly with a median age of 67 years at presentation (range, 41-85 years). The altered mental status of the patient in our report is more likely related to CNS involvement, which is observed in two-thirds of cases with IVLBCL and is attributed to multiple infarcts secondary to vascular occlusion. Most cases of IVLBCL present with bicytopenia, most commonly anemia and thrombocytopenia, along with hepatosplenomegaly; both features were present in this case.

Virtually any organ can be involved in IVLBCL, but bone marrow is usually spared. Bone marrow findings are usually described as unremarkable and involvement with neoplastic lymphoma cells are noted in rare cases. Histopathological findings in IVLBCL show a characteristic proliferation of lymphoma cells within the lumina of vessels exhibiting typical positivity for pan-B immunohistochemical stains, e.g. CD20 and CD79. Although the case described here showed typical positivity of lymphoma cells for CD20, the more recent B-cell immunohistochemical stain PAX5 positivity is reported for the first time in IVLBCL to the best of our knowledge. The IVLBCL case reported here also showed distinct immunophenotypic profile of CD5+ and CD10−, the pattern related to poor prognosis.

IVLBCL usually shows rapid progression and short survival. The poor prognosis in these patients reflects the non-specific signs and symptoms and late stage at presentation, the widely disseminated nature of the disease, the delay in diagnosis, and the delay in initiation of therapy. The patient described here unfortunately had a highly aggressive disease and succumbed to cardiorespiratory insufficiency and multiorgan failure even before the specific therapy could be initiated. Such cases have been reported as ‘catastrophic’ cases of IVLBCL manifesting as adrenal insufficiency, thrombotic microangiopathy, progressive dementia, and interstitial pneumonia or multiorgan failure.
REFERENCES


