Sir,

Introduction

Intravascular lymphoma (IVL) is a rare aggressive non-Hodgkin’s lymphoma with varied clinical presentation and propensity of multiorgan involvement predominantly affects elderly patients. Nearly 300 cases have been notified worldwide but its prevalence is certainly under-estimated.

We report a fatal case of IVL presenting as a multiorgan failure and review the current literature with the aim to increase awareness and prompt early detection of this highly rare lymphoma.

Case report

A 72-year-old healthy man was hospitalized for progressive asthenia and dementia evolving during the last month. On admission, the patient complained of myalgia and diarrhea. Biological abnormalities includes: neutrophil count $= 1.1 \times 10^9/L$, lymphocyte count $= 0.5 \times 10^9/L$, platelet count $= 89 \times 10^9/L$, aspartate aminotransferase $= 5 N$, ferritine $= 4N$, myoglobine level $= 4N$ and creatinine $= 140 \mu mol/L$ with mixt proteinuria $= 0.29$ g/day. Bacterial assays and serology for HIV, B and C hepatitis virus, EBV, CMV and autoimmune investigations were negative. Sternal medullar exam was considered as normal. Abdominal sonography was normal.

One week later, the patient presented a febrile confusional syndrome with severe dyspnea. Brain computed tomography (CT) and magnetic resonance imaging (MRI) showed no abnormalities. cerebro-spinal fluid (CSF) sample revealed hyperproteinorachia $1.6 g/L$, 12 leukocytes/mm$^3$ (70% of lymphocytic cells) without microbial agent and malignant cytological character. Meningoencephalitis was suspected and empirical antibiotherapy was administrated.

Figure 1. Kidney: B lymphoma cells are highlighted by immunohistochemical staining for CD79a ($\times 100$).

The following day, he was transferred in intensive care unit for coma, hemodynamic, respiratory and renal failure. Biological abnormalities includes: pancytopenia, C protein reactive $= 58 mg/L$, lactate dehydrogenase (LDH) $= 16N$ and $\beta 2$-microglobuline serum level $= 5.2 mg/L$ with disseminated intravascular coagulation. Bleeding diathesis appeared in his back whereas platelet count was $< 30 \times 10^9/L$. Supportive therapy was carried out. Lung CT showed pulmonary infiltration, pleural and pericardic suffusion. Bronchioalveolar lavage showed 680 cells/mm$^3$ with 7% of lymphocytic cells and predominance of macrophage. A second sternal ponction was performed, showing only rare atypical lymphocytes. Suspicion of lymphoma or diffuse systemic vasculitis leads to administration of bolus of methylprednisolone (1 g daily over 2 days followed by 1 mg/kg/day). But clinical status continued to worsen and hemodynamic monitoring disclosed a septic profile despite sterile bacteriologic samples. Patient died rapidly due to multiorgan failure.

Autopsy found obstruction of small vessels by large neoplastic lymphoid cells involving thyroid, kidneys, lungs, liver, pericard and lymph node. The diagnosis of widespread B-cell IVL was established with mature B-cells staining for CD5, CD20, CD22 and CD79a (Figure 1).

Discussion

Also referred as intravascular lymphomatosis or angiotropic lymphoma, IVL is a form of non-Hodgkin’s lymphoma of mostly B cell type, and less commonly T or natural killer cells. IVL is extremely heterogeneous in its clinical presentation and clinical symptoms of the disease are related to the specific organ involved.
Its presentation may range from monosymptomatic forms, such as organospecific local symptoms to rapid progressing multiorgan failure. Although IVL is a clonal proliferation of lymphocytes, it is uncommon to find significant adenopathy, hepatosplenomegaly or circulating cells in smear blood, bone marrow or CSF. Hence, diagnosis of IVL is difficult to be established. Clinical presentation is often confusing, mimicking systemic disease such as vasculitis. Classically, it is considered that IVL has a tropism for CNS (78% of cases) and skin (53% of cases). But these organs are probably more easily symptomatic when proliferating neoplastic cells alter their vascular irrigation. IVL is most often a disseminated disease as it had been demonstrated by autopsies but several cases report have described an apparently unique site of disease (heart, prostate, articulations, pulmonary circulation, etc).

Skin lesions are habitually violaceous papules, ulcerated nodules and erythematous plaques but telangiectasias are the most evocative clinical symptoms of IVL. Our patient presented hemorrhagic diathesis in his back but these lesions were disregarded in the context of disseminated intravascular coagulation.

Neurological abnormalities could also be extremely variable but more often it displays diffuse encephalopathy or subacute progressive multifocal neurological deficiencies. MRI is the best exam despite its relative low sensitivity and specificity. Indeed MRI images may look like vasculitis. In the largest series of IVL patients with neurologic disease, six of seven patients had a lymphocytosis in the CSF. Only one patient had CSF cytopathology positive for malignant cells. Two of the seven patients had malignant cells identified by polymerase chain reaction for immunoglobulin gene rearrangement.

Rarely, patients may develop anasarca as was seen in our case. This could be explained by massive obstruction of vessels. Fever is often associated with this type of lymphoma (45% of cases) and is probably due to production of proinflammatory cytokines directly in blood circulation by neoplastic cells. This may delay diagnosis because of the exhaustive autoimmune and infectious etiology research carried out, until tissue biopsy is performed.

Regarding laboratories findings, anemia (63%), high LDH (82%) and β2-microglobulin serum levels (86%) are the most common abnormalities seen in IVL. Thrombocytopenia and leucopenia are less often seen (24 and 29%, respectively). It is rare (5%) to observe circulating neoplastic cells in peripheral blood smear. Bone marrow infiltration was seen in only 38% of cases.

Concerning management and prognosis, the course of IVL is rapidly fatal and sustained remissions are rarely achieved. They have been obtained more often under chemotherapy such as CHOP especially when combined with anti-CD20 antibody (rituximab). Anti-CD20 could be interesting as sole treatment modality in our patient unable to tolerate cytotoxic therapy. Plasmapheresis as steroids used alone provide inconstant and transient improvement. In our case, high doses of steroids were totally inefficient.

Antemortem diagnosis of this lymphoma is challenging because there is no pathognomonic features or markers of IVL. The unique reliable mean of diagnosis remains tissue biopsies of any involved organ. Skin is the first target but brain, muscle, liver, kidney and lung may be concerned. Multiple biopsies are required due to focal localization. Biopsies of suspicious skin’s lesions as well as clinically uninvolved skin may give diagnosis of IVL and be useful in differential diagnosis. Kidneys and gastro-intestinal tract seem interesting targets for biopsies because first, they are frequently involved and second, are rich vascularized tissues easily biopsied. There is no pathognomonic immunophenotypic markers or clonal rearrangement gene detecting by PCR for this lymphoma. Only demonstration of an intravascular growth of atypical lymphocytic cells really allows diagnosis of IVL.

References


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