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Short communication

Intravascular large B-cell lymphoma presenting as slowly progressive paraparesis with normal MRI features

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ABSTRACT

Intravascular large B-cell lymphoma (IVLBCL) is a rare, high grade extranodal B-cell lymphoma, characterized by the proliferation of tumoral cells in the lumen of small vessels of several organs without the tendency for tumor formation in other areas usually affected by lymphomas, such as lymph nodes, bone marrow, or peripheral blood. Diagnosis is generally delayed by variable presentation with non-specific constitutional and neurological symptoms, lack of reliable ancillary tests and it is often obtained only at autopsy.
We report a case of IVLBCL presenting with a slowly progressing isolated paraparesis without any evidence of spinal damage at MRI though neurophysiological examinations showed signs of spinal cord injury. Laboratory findings showed markedly elevated levels of lactate dehydrogenase, low albumin values, raised ESR, mild thrombocytopenia and progressive impairment of hepatic function. Bone marrow examinations and total body CT scans were negative. Although clinical history appeared too long, we considered the hypothesis of IVLBCL on the basis of the laboratory constellation and proposed a liver biopsy, but the patient refused the procedure. The diagnosis was confirmed only at autopsy. Our case should make us aware that the disease has to be considered in the differential diagnosis of unexplained paraparesis associated with elevated level of lactate dehydrogenase and only relatively non-specific laboratory findings even without any spinal cord abnormalities at MRI.

1. Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare, high grade extranodal B-cell lymphoma, characterized by the proliferation of tumoral cells in the lumen of small vessels of several organs [1] without the tendency for tumor formation in other areas usually affected by lymphomas, such as lymph nodes, bone marrow, or peripheral blood [2].

Patients generally present with non-specific and sometimes misleading clinical symptoms such as fever of unknown origin, general fatigue, marked deterioration of performance status and neurological alteration with rapid progression of the disease to death [1].

Moreover, laboratory findings are usually not specific and conventional diagnostic procedures, including total body CT and bone marrow biopsies, are associated with a high rate of false negatives [3].

2. Case report

We report a case of IVLBLC with neurological symptoms characterized by an atypical course and unusual MRI findings. Diagnosis was suspected ante-mortem, but was documented only postmortem.

A 76-year-old woman was admitted to our Department of Neurology because of progressive paraparesis associated with hypoesthesia and numbness at the legs and urinary dysfunction for over six months. Two months before admission she had underwent surgery for ovarian cystadenoma, and 40 years earlier splenectomy for hereditary spherocytosis.

On examination she had spastic paraparesis with mild hypertonus, bilateral extensor plantars, perineal and lower limb hypoesthesia.

Blood tests showed markedly elevated levels of lactate dehydrogenase (LDH, 2400 UI/l; normal range 230–460 UI/l), β2-microglobulin (11.8 mg/l; normal range 1.2–2.5 mg/l), and ESR (Erythrocyte Sedimentation Rate) (65 mm). Tumor markers were all negative, except for neuron specific enolase (29.4 and 44.8 ng/ml; upper normal value 16.5 ng/ml). Immunological tests including antineural antibodies associated with neurological paraneoplastic syndromes (anti-Hu, anti-Yo, anti-Ri, anti- Ma, anti-amphipysin, anti-cerebellum) were also negative.

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The CSF examination revealed slight increase in protein level (59 mg/dl, normal range: 20–40) with normal glucose and cell count. Oligoclonal bands were absent with sign of blood–brain barrier damage (increased IgG/Alb ratio). On cytology no malignant cells were found, and microbiological and serological examination of CSF were also negative.

Brain MRI showed patchy, non-specific lesions (hyperintense on T2-weighted and FLAIR images, without post-gadolinium enhancement) in the subcortical and deep white matter of both cerebral hemispheres, in particular involving centra semiovale and corona radiata (Fig. 1), suggestive for small-vessel ischemic disease [4]. MRI with gadolinium of the spine revealed no areas of abnormal intensity signal, although neurophysiological examinations (Motor Evoked Potentials, MEP and Somatosensory Evoked Potentials, SEP) were abnormal. MEP showed increased central motor conduction time for lower limb muscles. SEP showed normal cauda equina responses and absence of segmental centro-medullary response N14 after stimulation of right and left peroneus nerve, and increased latency of cortical response after stimulation of left peroneus nerve.

Brain and spinal cord MRI with contrast were repeated after two months (about 20 days before death) and showed again no remarkable findings. Because of clinical progression, steroid therapy (methylprednisolone intravenously 1 g per day for five days) was started, with no beneficial effects on neurological symptoms.

Laboratory findings showed a progressive increase of LDH levels up to 4295 UI/l, associated with decrease in albumin levels (2.7 g/dl), progressive impairment of hepatic function and thrombocytopenia, with elongation of aPTT. Abdominal and hepatic ultrasonography showed no morphological alterations, and total body CT scan was normal, except for the presence of some subcentimetric reactive lymph nodes, localized in many different districts (jugular, submandibular, submental, mesenteric, iliac, retroperitoneal, inguinal).

Bone marrow aspiration and biopsy revealed hypercellularity with granulocytic hyperplasia (high increase of megakaryocytes, neutrophil granulocytes 81%, eosinophils 2%, monocytes 2%, blastes 3%, erythroid series 9%, lymphocytes 3%), but no evidence of malignancy was found.

Despite negative bone marrow biopsy and CT findings, a lymphoproliferative disease, in particular an intravascular large B-cell lymphoma, was suspected on the basis of markedly increased LDH and β2-microglobulin levels, neurological symptoms, and progressive deterioration of performance status. As alterations of hepatic function were indicative for liver involvement, we proposed a diagnostic hepatic biopsy, but the patient refused to undergo the procedure.

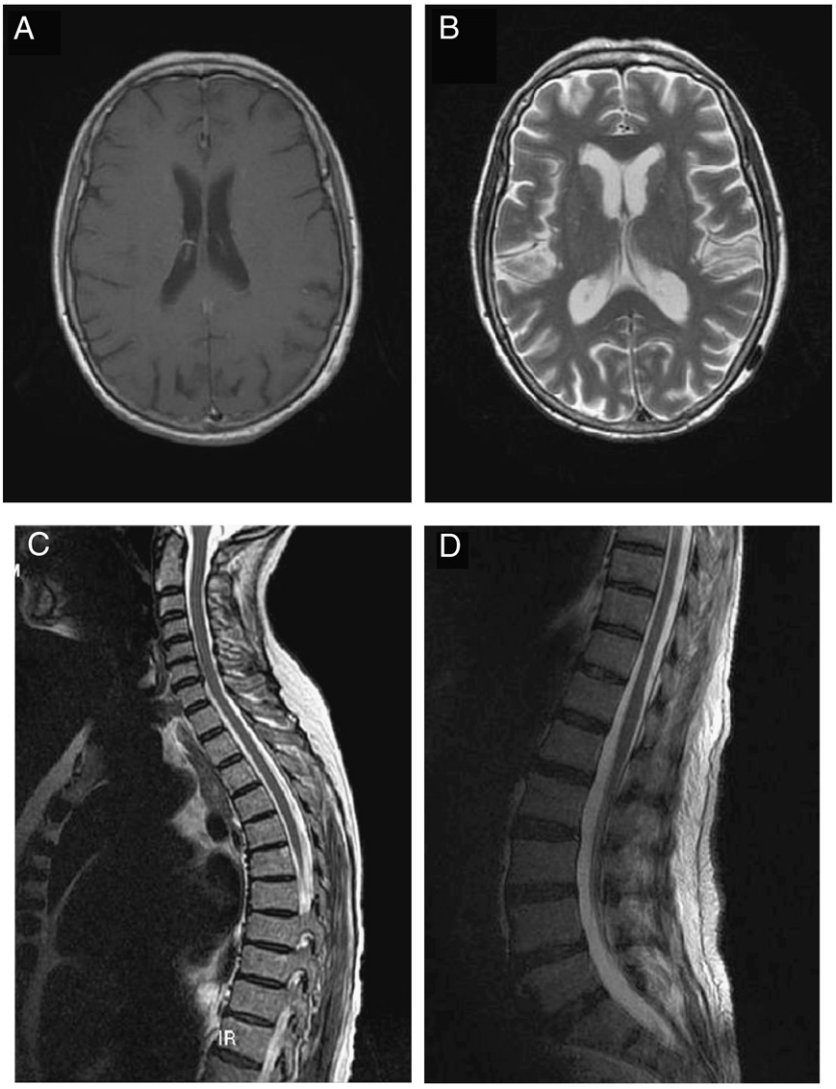

Fig. 1. MRI. A. Brain MRI: T1-weighted images post-gadolinium showing no contrast enhancement. B. Brain MRI: T2-weighted images showing patchy, non-specific lesions hyperintense in the subcortical and deep white matter of both cerebral hemispheres C–D. Spinal cord MRI showing no areas of abnormal intensity signal.