Case report

Primary central nervous system germinal center B-like diffuse large B-cell lymphoma: a case report

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Summary

We report a case of a 54-year-old HIV-negative female who presented with a 2-month history of ongoing post meridiem low-level fever and new onset progressive paralysis. On MRI (magnetic resonance imaging), an infiltrative enhancing lesion was noted, which initially resembled that of MS, but she reacted not sensitively with immunosuppressive therapy, we performed a brain biopsy to her, it turned out to be primary CNS (central nervous system) diffuse large B-cell lymphoma (DLBCL). And the morphology, the flow cytometric findings were consistent with germinal center B-like diffuse large B-cell lymphoma. There were only a few case reports concerning primary CNS DLBCL of GCB. The misdiagnosis of this patient should alarm the bell, and we should consider biopsy when the lesion is near the cortex in the brain. Why she reacted not sensitively with immunosuppressive therapy later is analyzed.

KEY WORDS: primary nervous system; germinal center B-like; diffuse large B-cell lymphoma.

Introduction

Primary CNS diffuse large B-cell lymphoma (DLBCL) is a highly malignant disease of the brain, which accounts for more than 96% of primary central nervous system lymphoma (PCNSL) (1). According to gene expression profiles, DLBCL could be categorized into two subtypes: germinal center (GC) B cells and activated B cells DLBCL. PCNSL can be confused with multiple sclerosis (MS) due to clinical, radiological and histological similarities. Patients of PCNSL with the administration of corticosteroid present with clinical improvement and regression which may be interpreted as a steroid-induced remission from an exacerbation of MS (2). When the definite diagnosis was hardly obtained for those patients with lesions in the cortex or other sites which are easy to gain samples like our case, a biopsy is recommended as diagnostic routine (3).

Case report

A 54-year-old woman presented sustained post meridiem low-fever, fluctuating from 37.6°C to 38.0°C, without a definite cough, expectation, arthralgia from February 2013. The chest CT scan revealed no obvious lesion, and the blood routine test was normal. Cephalosporin antibiotics and antiviral agents were administered to the patient, but ineffective.

She was hospitalized on 6th June, 2013 with onset of progressive paralysis (left muscle power grade 4+ according to MRC scale) and decreased muscle strength in the affected limb, abnormality in gait, hyperfunction in tendon reflex of both sides, but showed intact cranial nerves, normal sensation, as well as negative Babinski sign. The laboratory examination demonstrated HBsAb (+)/HBeAb (+)/HbcAb-IgG (+), additionally, no response to HIV antigen and antinuclear antibodies were found, the CSF detection presented no positive evidence of infection or demyelination, and cytology revealed no malignant cell; abdomen and pelvic cavity B-ultrasound revealed splenomegaly and cervical cyst, respectively. Brain MRI revealed multiple lesions in both cerebral hemispheres, encephalitis probably (Figure 1 a); 2 weeks later, follow-up enhanced brain MRI and spectral analysis prompt multiple abnormal signals in pons varolii, basal ganglia, lateral ventricles, centrum ovale, corpus callosum, parietal lobe, occipital lobe of both sides, multiple sclerosis probably (Figure 1 b); but without any loss of neuronal cells. Methylprednisolone was administrated (80 mg, qd) for a week, and obvious improvement was seen in clinical manifestation. The patient was discharged later with slightly unsteady gait only on 30th March.

On 7th April, the patient was recharged in the same hospital for right hemiparesis (muscle power grade 1+ according to MRC scale), along with urinary and fecal incontinence, and treated with methylprednisolone for 2 days before she was transformed into our hospital, where related examinations were tested again. And the blood, urine, manure routine, liver renal function, immune analysis, tumor index, LDH, T-SPOT, serum Kap, Lam were all found to be normal or negative; pelvic cavity and abdomen B-ultrasound revealed no significant changes compared with that of previous one; besides, thyroid gland, as well as lymph nodes in neck/arm pit/ groin, were checked by ultrasound, revealing no malignant lesions, except for benign thyroid nodule. The patient accepted pulse therapy (methylprednisolone; 500mg qd vgtt) for 6 days along with IVIG treatment (20g, qd, vgtt) for another 5 days, but got mere clinical improvement (muscle power grade were 1+ and 2 for the right upper and lower extremity, respectively). During this period we reviewed the enhanced brain MRI on 15th and 22nd (Figure 1 c, d), before and after the treatment, both of which showed newly onset lesions, the scope of the latter one comparatively decreased to a slight extent. Under the consent of the patient herself, a stereotactic biopsy was performed on the right frontal lesion.
The pathology findings revealed large B-cell malignant lymphoma, and the immunohistochemical study revealed these large lymphoma cells were CD20(+) and CD3(-), which was consistent with germinal center B-like DLBCL (Figure 1 e, f, g).

Discussion

PCNSL can be confused with multiple sclerosis (MS) due to clinical, radiological and histological similarities. Patients of PCNSL with administration of corticosteroid present with clinical improvement and regression which may be interpreted as a steroid-induced remission from an exacerbation of MS (4), often times, the white matter on neuroimaging studies shows abnormal signals in both PCNSL and MS, even brain biopsies may fail to detect tumor cells and show only demyelination because of different sites of sampling (5), radiographic improvement of PCNSL is not a consequence of restoring an impaired blood-brain barrier like MS, but is due to cytolytic effects of corticosteroid drugs on malignant lymphocytes (6). In some cases, repeated brain biopsy may, therefore, be necessary to provide. But several clues alert the clinician to consideration of PCNSL, like patients of our case can not continue to make any progress even with threshold dosage of methylprednisolone and IVIG treatment later (7), which is uncommon in MS.

When the definite diagnosis was hardly obtained for those patients with lesions in the cortex or other sites which are easy to gain samples like our case, a biopsy is recommended as diagnostic routine. At the same time, application of new technology in neuroradiological field shows status of a gradual increase as a noninvasive method. Kuhlmann et al. report the use of single voxel proton MRS for differential diagnosis of MS versus PCNSL (8), MR Spectra of multiple sclerosis plaques are characterised by reduced NAA concentrations reflecting neuroaxonal damage as well as increased Cho and Ins concentrations, while image of PCNSL lymphomas shows markedly decreased NAA, increased Cho and Ins. New imaging techniques of this kind like SPECT scanning, MR spectroscopy, and perfusion MR imaging, can help distinguishing neoplastic compared with demyelinating lesions and should be further investigated (9). But not all hospitals could get access to these equipment.

Making an early definitive diagnosis is of great importance because the treatments and long-term outcomes of these disorders are very different. Immunosuppressive therapy is not enough for the treatment of the tumor. Early diagnosis of PCNSL and a combined treatment with surgery, chemotherapy, and radiation may improve its prognosis. PCNSL is frequently diagnosed late because more common CNS diseases are considered first (10). When the indefinite diagnosis was encountered, a biopsy is recommended.

Acknowledgements

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References