Case Report

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Blindness due to leptomeningeal carcinomatosis as an initial manifestation of recurrent acute lymphoblastic leukemia

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Abstract:

Leptomeningeal carcinomatosis (LC) is an uncommon presentation of acute lymphoblastic leukemia (ALL), and it is a devastating and life-threatening complication. The disease affects all levels of the central nervous system, and most patients present with different multifocal neurological symptoms. This case was a 34-year-old male who had acute bilateral blindness secondary to recurrent ALL with meningeal infiltration. Diagnosis of LC is made based on the clinical symptoms and the test results including cranial and spinal magnetic resonance imaging and cerebrospinal fluid (CSF) survey. The differential diagnosis of meningeal enhancement and early treatment are also important for prognosis. This case had a good visual recovery after treatment.

Keywords:

Acute lymphoblastic leukemia, blindness, leptomeningeal carcinomatosis

Introduction

Leptomeningeal carcinomatosis (LC) is a serious and life-threatening complication of systemic malignancies.[1] The disease involves infiltration of malignant cells into the leptomeninges and seeding in the cerebrospinal fluid (CSF). Consequently, most patients present with different multifocal neurological symptoms due to invasion of the cranial nerves (oculomotor, facial, cochlear, and optic nerve), the spine, and the cerebrum.[2]

The incidence of LC varies according to the tumor site. Among solid tumors, the most frequent causes of LC are lung and breast adenocarcinoma. Lymphomatous meningitis is reported in 5%–15% of patients with diffuse high-grade non-Hodgkin's lymphoma.[3] The occurrence of the disorder correlates with clinical risk factors such as raised serum lactate dehydrogenase, low serum albumin, young age (<60 years), or the involvement of the testis, breast, or bone marrow, or more than two extranodal sites.[4,5] LC is usually a terminal sign of malignancy. If left untreated, median survival is 4–6 weeks; if treated, median survival is 2–3 months.[6] Currently, no case report emphasizes on the improvement of visual acuity after treatment, so we present this case.

Case Report

A- 34-year-old male had experienced a fever of unknown origin 5 years previously. Later, acute lymphocytic leukemia, B cell type, was confirmed and he underwent the Taiwan Pediatric Oncology Group – acute lymphoblastic leukemia (ALL)-2002 very high-risk chemotherapy protocol,[7] including maintenance chemotherapy, in another medical center. After completion of the chemotherapy regimen, a complete remission was achieved.

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About 3 months previously, the patient had experienced painless, bilateral and progressive visual loss, intermittent headache, dizziness, and ataxia. An ophthalmic examination revealed a best-corrected visual acuity of 20/1000 and 20/400 in the right and left eyes, respectively. Pupils were amaurotic and nonreactive to light. Optic disc and fundus examination were normal in both eyes. Full extraocular movements were observed. Optical coherence tomography (OCT) [Figure 1] examination showed normal average thickness of retinal nerve fiber layer in both eyes. A brain magnetic resonance imaging (MRI) [Figure 2] scan revealed diffuse leptomeningeal enhancement of the brain and a suspected hemorrhagic lesion about 26 mm × 31 mm × 24 mm in the cerebellum. Optic nerve did not show an enhancement on T1-weighted image. A visual-evoked potential test supported the presence of a visual pathway lesion. A peripheral blood cell count revealed a hemoglobin level of 13.3 g/dL, platelet count of 168 × 103 cells/μ L, white blood cell (WBC) count of 6.4 × 103 cells/μL, and a differential count of 65.8% segmented neutrophils, 24.4% lymphocytes, and 8.5% monocytes.

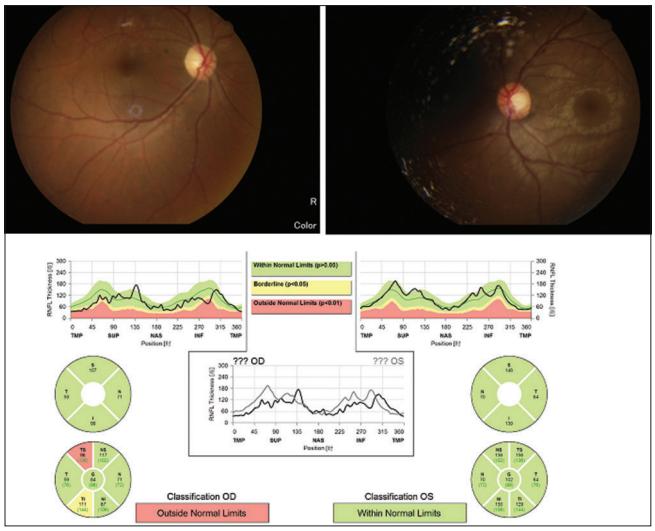

Figure 1: Normal binocular fundi and optical coherence tomography examination showed normal average thickness of retinal nerve fiber layer in both eyes

The patient received a lumbar puncture by a neurologist and the CSF showed a clear appearance, with a WBC count of 215 cells/μL (5% lymphocytes, 2% monocytes, and 93% blast cells), a low glucose level (31 mg/dL), and an elevated protein level (640.7 mg/dL). A subsequent bone marrow biopsy by an oncologist demonstrated focal aggregation of atypical cells with hyperchromasia. Immunohistochemistry showed atypical cells that were CD79a (+), CD3 (−), CD34 (−), terminal deoxynucleotidyl transferase (−), and myeloperoxidase (−). The diagnosis was ALL – B cell type, with isolated involvement of the central nervous system (CNS). The patient underwent intrathecal chemotherapy (hydrocortisone 50 mg/cytarabine 30 mg/methotrexate 12 mg) twice, followed by systemic chemotherapy with dexamethasone and high-dose methotrexate (5000 mg/m^2). He had fever, nausea, and vomiting during a period of chemotherapy. After 2 months of treatment, he had no headache and other neurological symptoms also subsided. His visual acuity improved to 20/25 in right eye and 20/20 in left eye. Both pupils were round and active. However, he had a residual cecocentral scotoma after 6 months of treatment [Figure 3]. OCT showed an atrophy of temporal retinal nerve fiber layer [Figure 4]. After 1 year of treatment, brain MRI showed a resolution of the cerebellar hematoma and nearly total-disappeared leptomeningeal enhancement.

Discussion

LC, also referred to as carcinomatous meningitis, meningeal carcinomatosis, and neoplastic meningitis, was first described in 1870.[8] It is usually associated with advanced systemic cancer and is reported as a presenting sign of systemic cancer in 5%–11% of patients.[9] LC occurs with increasing incidence because of longer survival of cancer patients due to more effective systemic treatments.

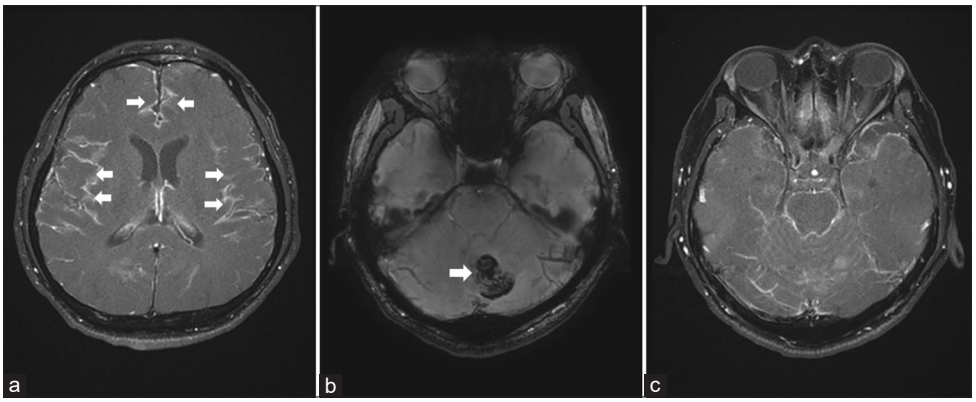

Figure 2: Brain magnetic resonance imaging revealed (a) diffuse leptomeningeal enhancement (arrows) of the brain on T1-weighted image; (b) a cerebellar hemorrhagic lesion (arrow) on T2-weighted angiography (SWAN) image; (c) Optic nerve did not show an enhancement on T1-weighted image

It arises when tumor cells disseminate and grow in the leptomeningeal space and/or the CSF. Therefore, the characteristics of the disease are neurologic dysfunctions affecting multiple levels of the CNS, including the cerebral, cranial nerve, and spinal root regions. Headache is the most common presenting symptom and occurs in 40% of patients.[10] Other common signs and symptoms are weakness, mental status change, and ataxia.[11]

Ocular deficits of patients with LC include loss of vision, ocular motility deficits, pupillary abnormalities, papilledema, and optic atrophy. Unilateral or bilateral blindness occurs in 30%–40% of patients with LC, and blindness is the presenting complaint in approximately 3% of patients.[9] Blindness typically begins in one eye, with the second eye affected shortly thereafter, occasionally within 24 h.[12] The mechanisms of blindness are various including papilledema from increased intracranial pressure,[13] direct infiltration of the optic nerve/sheath complex,[14] and treatment-related toxicity.[15] As demonstrated in this case, our patient had acute bilateral blindness because tumor cells directed seeding to CSF and then infiltrated to the optic sheath. Thus, brain MRI did not show obviously enhancement on optic nerve, but CSF survey proved atypical lymphocytic leukemia. Besides, we should mind that the combination of headache, rapidly progressive visual loss, sluggish pupil reactions, and unremarkable optic discs are a quartet of ocular signs and symptoms for LC.[16]

Early diagnosis is extremely important in cases of LC. If LC is suspected based on the clinical findings, the National Comprehensive Cancer Network recommends a workup that includes MRI with and without gadolinium enhancement.[8] On MRI, leptomeningeal enhancement can be focal or diffuse and can include tumor nodules. However, these radiographical findings are nonspecific. The differential diagnosis of leptomeningeal enhancement includes acute or chronic infectious meningitis, inflammatory, or an autoimmune disease on MRI image.[17] Thus, lumbar puncture should be performed in all suspected cases of LC. CSF abnormalities associated with LC include several malignant aggregated cells, elevated intracranial pressure (50%), pleocytosis (60%), elevated protein levels (80%), and low glucose level (25%).[18] Unfortunately, although CSF cytology is highly specific for LC, it is limited by a low sensitivity because of the typically low number of malignant cells in the CSF.[19] Accordingly, diagnosis of LC is made based on the clinical symptoms, laboratory findings, examination of the CSF, and histopathological examination.

Treatment commonly involves systemic chemotherapy, intrathecal chemotherapy, radiotherapy, or a combination of therapies. However, LC has no standard treatment. Intrathecal chemotherapy allows a better distribution throughout the subarachnoid space with less systemic toxicity. Wu *et al*.[20] reported that 27 patients with LC were treated by intrathecal methotrexate and 70.4% had clinical remission. They also reported side effects which appeared 55.6% patients were all appropriate, 25.9% had lower limb numbness and mild pain, and no serious irreversible adverse reactions happened.

Nevertheless, even with aggressive treatment, survival is typically only extended to 2–3 months, and the survival rate at 1 year is approximately 20%.[21] An analysis of prognostic factors by Palma *et al*., which included initial Karnofsky performance status >60, showed that the initial CSF protein level (<112 mg/dL) and time from diagnosis of the primary tumor to diagnosis of LC (>67 weeks) were significant and independent predictors of increased survival.[22] Fortunately, our patient had only an initial high CSF protein level (640.7 mg/dL); otherwise, he had a good prognostic outcome.

LC is a rare complication of ALL. Visual loss is soon in one eye and then in another eye. Thus, according to our

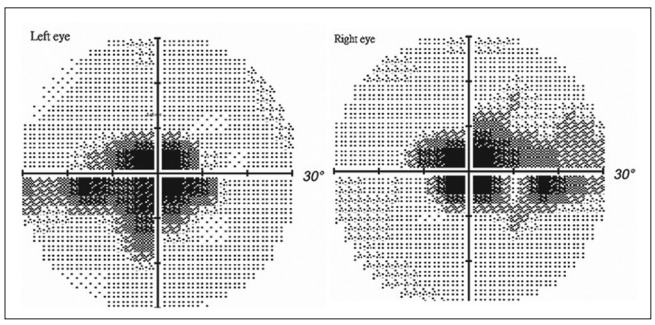

Figure 3: Visual field in automated perimetry test showed a cecocentral scotoma after 6 months of treatment

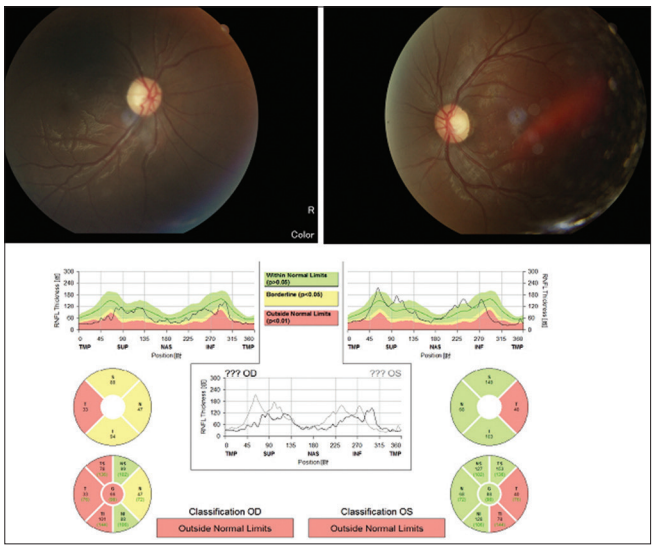

Figure 4: After 6 months of treatment, he had a temporal pallor of optic disc and optical coherence tomography showed an atrophy of temporal retinal nerve fiber layer

patient and experience of treatment, we suggest that early diagnosis and treatment can have an opportunity to recover vision.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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