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Acute Lymphoblastic Leukemia presenting with oculomotor nerve palsy

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Abstract

A 48-year-old man presented with left ptosis and double vision. Laboratory test findings indicated acute lymphoblastic leukemia (ALL). Lymphoblastic infiltration of both cavernous sinuses was observed on pituitary gland magnetic resonance imaging. Leukemias may present by many clinical conditions, but isolated cranial nerve palsy is very rare. To our knowledge, this is the first case of ALL presenting with oculomotor nerve palsy. Clinicians should consider oculomotor nerve palsy as the first ALL indication.

Key words: Acute lymphoblastic leukemia; cranial nerve; oculomotor nerve palsy; magnetic resonance imaging.

Introduction

Acute lymphoblastic leukemia (ALL) is a malignant hematological disease caused by multistep somatic mutations during lymphoid precursor cell differentiation. ALL rarely involves the cranial nerves in isolation. In such cases, seventh cranial nerve palsy is the most frequent, although involvement of third and sixth cranial nerves has also been reported (1, 2). We present the case of a patient who initially presented with left ptosis and double vision. Physical examination indicated third cranial nerve involvement, and laboratory test findings led to the diagnosis of ALL.

Case

A 48-year-old man presented with left ptosis, nausea, vomiting, and double vision. He had experienced double vision 1.5 months previously. Neurological examination of the left eye showed ptosis, difficulty in medial, superior, and inferior eye movements and weak direct and indirect light reflexes. Systemic examination after hospitalization indicated petechial hemorrhage at the shoulders and feet and gingival hemorrhage. Multiple overlapping painless lymph nodes were detected in the right inguinal region, the largest one with a diameter of 2-3 cm.

A complete blood count revealed a platelet count of 6000/µl. Peripheral blood smear examination showed 42% atypical lymphoid cells that were uniform in shape and size, relatively large and narrow and contained an agranular basophilic cytoplasm; some cells contained cytoplasmic vacuoles and sparse cytoplasmic projections. Examination of bone marrow aspirate showed infiltration by lymphoid blasts those were homogeneous in shape and heterogeneous in size, narrow, and contained agranular basophilic cytoplasm with few nucleoli and vacuoles. The proportions of $CD3^+$, $CD10^+$, $CD19^+$, $CD38^+$, $CD20^+$, $CD22^+$, $CD34^+$, and $CD13^+$ cells in the bone marrow aspirate were 22%, 61%, 65%, 78%, 69%, 0%, 0%, and 0%, respectively. Examination of cerebrospinal fluid (CSF) smear showed the following: protein, 71 mg/dl; glucose, 47 mg/dl (simultaneously serum glucose, 90 mg/dl); lymphocytes, 5-10/mm^3 and no malignant cells. Finally, ALL was diagnosed.

Pituitary gland magnetic resonance imaging (MRI) showed bilateral lesions (right: 8 × 7 mm; left: 13 × 7 mm) infiltrating both cavernous sinuses and blurring their boundary with the pituitary. The lesions had directly invaded the left Meckel's cave and significantly surrounded the cavernous segment of the left internal carotid artery. Throughout the dynamic series, these lesions showed less and delayed contrast enhancement than the normal pituitary gland (Fig. 1). Therefore, we concluded that there was lymphoblastic infiltration of both cavernous sinuses.

The hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) chemotherapy regimen was initiated. However, the patient developed

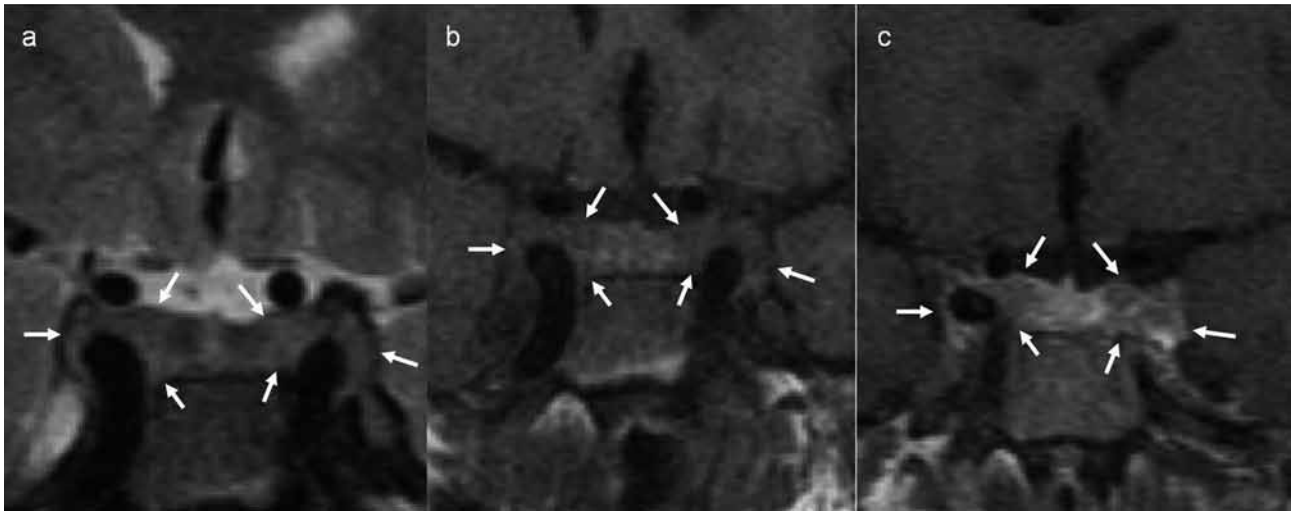

FIG. 1. — Coronal T2-weighted (a), T1-weighted (b), and contrast-enhanced T1-weighted (c) MR images showing bilateral lesions infiltrating both cavernous sinuses and obliterating the view of their boundary with the pituitary gland (arrows). On the left side, the lesion has directly invaded the left Meckel's cave and significantly surrounded the cavernous segment of the left internal carotid artery (a-c). In contrast-enhanced image (c), the lesions show less and heterogeneous contrast enhancement than the normal pituitary gland.

respiratory distress, underwent intubation, and eventually died of pneumonia.

Discussion

Lymphoproliferative disorders rarely present with cranial nerve involvement. Leukemia causes neurological dysfunction directly by invading the central nervous system (CNS) or indirectly by altering hematological factors; the former occurs by dissemination of leukemic cells in the subarachnoid space and leptomeninges, while the latter occurs because of hyperviscosity syndrome due to very high levels of intravascular leukemic cells (3). Infiltration of individual nerves with leukemic cells or ischemia-induced damage of the vasa nervorum causes cranial nerve manifestations.

In leukemia cases, contrast-enhanced cranial MRI is useful for the early detection of CNS involvement and tracking treatment outcome. Leptomeningeal invasion by tumor cells is usually characterized by high protein and low glucose levels. A CSF leukocyte count of > 5 cells/mm^3, presence of leukemic blast cells in CSF supernatant, or leukemia-induced cranial nerve palsies are considered indicators of CNS involvement (4). High protein and low glucose levels, 5-10 lymphocytes/mm^3, but no lymphoblasts were observed in our patient's CSF.

Paresis of the oculomotor, facial, and abducens nerves has been reported as the first sign of leukemia (5-9). Chen *et al.* reported a case of leukemia presenting with isolated sixth cranial nerve involvement (6). Krishnamurthy *et al.* described a case of childhood leukemia presenting with the seventh cranial nerve involvement (7). Celebisoy *et al.* reported a case of acute myeloid leukemia (AML) presenting with the third cranial nerve involvement (9).

To our knowledge, this is the first case of ALL presenting with oculomotor nerve palsy, which was probably caused by leukemic invasion of the left cavernous sinus or ischemia of the third cranial nerve or the associated vasa nervorum due to mechanical compression by leukemic cells. The current patient with oculomotor palsy without a systemic disorder, could be diagnosed with ALL only after hemorrhagic foci, thrombocytopenia, and lymphadenopathy appeared.

It is difficult to prove neurological involvement such as leptomeningeal metastasis or cranial nerve palsies. MRI and CSF examinations can be normal in the early stages. For patients presenting with oculomotor palsy, the following common possible causes should be considered: infiltration of intracavernous and retrocavernous sinuses, inflammatory or glaucomatous changes, ischemic or hemorrhagic cerebrovascular diseases involving the brain stem, increased intracranial pressure syndrome, aneurysms of the superior cerebellar and posterior cerebral arteries, uncal herniation, ophthalmoplegic migraine, and ischemic neuropathy in diabetic patients. In addition, alpha II-interferon should also be considered as a rare cause (10). Further, cranial nerve palsy should be considered the first indication of ALL.

Early detection and timely treatment of neurological complications are crucial to improve patients' quality of life and reduce mortality.

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