Cavernous sinus syndrome
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Cavernous sinus syndrome (CSS) is a condition characterized by multiple cranial nerve palsies manifesting with ophthalmoplegia, ptosis, and facial sensory loss due to involvement of adjacent cranial nerves. Tumors, trauma, and vascular, infectious, and noninfectious inflammatory disorders have all been described as causes. Lymphomas have been reported to involve the cavernous sinus, both as primary cavernous sinus lymphomas or as secondary lesions. Here, we describe the case of a 63-year-old-man with untreated chronic lymphocytic leukemia (CLL), diagnosed 4 years earlier, who presented with CSS. Our patient underwent standard chemotherapy, but he succumbed to infection during the neutropenic period.

Neoplastic B-cell infiltration in chronic lymphocytic leukemia (CLL) has been described in skin, lung, pleura, kidney, and gastrointestinal tract tissues. However, involvement of the central nervous system (CNS) is very rare (1), and symptomatic CNS involvement in CLL is known to be rarer (1). Reported cases of CNS involvement in CLL have demonstrated a diverse and nonspecific spectrum of symptoms: headaches, mental status changes, cerebellar signs, cranial nerve abnormalities, and weakness of extremities (1). Here we report an unusual case of a patient with untreated CLL who presented with cavernous sinus syndrome (CSS). To the best of our knowledge, CLL causing CSS has not been reported previously.

CASE REPORT

A 63-year-old man presented with double vision. He first noticed diplopia 2 months prior to evaluation, stating it waxed and waned in intensity. One month later, he had recurrent severe diplopia, most prominent on leftward gaze, accompanied by nausea, headache, and photophobia. His symptoms persisted and progressed to include left-sided eyelid heaviness 1 month after presentation. He had a 4-year history of asymptomatic Rai stage I CLL (lymphocytosis with lymphadenopathy, without organomegaly or cytopenia). He was on regular follow-up during the 4 years with blood counts, along with clinical examination at 3-month intervals.

On examination, his Eastern Cooperative Oncology Group performance score was 2. Neurological exam revealed left ptosis, sluggish pupillary reflex, lateral gaze palsy, diminished medial gaze, and limited intorsion of the left eye. Visual acuities were 6/6 in the right eye and 6/9 in the left eye. Dilated fundus examination was normal. The left corneal reflex was absent, and he also had hypoesthesia in the territory of the first and second divisions of the right trigeminal nerve. In addition, multiple cervical lymph and axillary nodes were palpable, and the spleen was palpated 2 cm below the left costal margin. The rest of the neurological and physical examination was unremarkable.

The white blood cell count was 108,000/μL, and a peripheral blood smear revealed 60% atypical lymphocytes. His hemoglobin level was 11.5 g/dL and platelet count, 163,000/μL. His lactate dehydrogenase level was 736 IU/L (normal range, 313–618 IU/L). Peripheral blood flow cytometric analysis was diagnostic of CLL. Bone marrow aspiration revealed 60% small atypical lymphoid cells, and bone marrow biopsy showed interstitial and nodular infiltration by atypical lymphoid cells, having clumped chromatin among normal hematopoietic elements. Fluorochrome in situ hybridization (deletion 11q, deletion 13q, and deletion 17p) and conventional cytogenetic analysis of the peripheral blood did not reveal any abnormalities. Magnetic resonance imaging (MRI) of the patient’s brain revealed an asymmetric enhancing lesion in the left cavernous sinus, encasing the carotid artery and extending to the trigeminal cave (Meckel’s cave) (Figure). These findings were suggestive of neoplastic infiltration of the left cavernous sinus.

A diagnostic lumbar puncture was performed, and cerebrospinal fluid (CSF) revealed a white blood cell count of 20 leukocytes/mm³ (lymphocytes, 80%; neutrophils, 20%), glucose of 80 mg/dL, and total protein of 54 mg/dL. Cytological examination demonstrated the presence of small monomorphic lymphocytes in the CSF suggestive of CLL cells. The patient received high-dose methylprednisolone and was started on fludarabine (25 mg/m²/day intravenously for the first 3 days), cyclophosphamide (250 mg/m²/day intravenously for the first 3 days), and rituximab (375 mg/m²/day intravenously on day 1) (FCR regimen). He improved symptomatically after steroids; however, his status worsened after chemotherapy and he

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developed sepsis during the neutropenic period. He died on postchemotherapy day 12.

DISCUSSION

Cavernous sinus syndrome is characterized by ophthalmoplegia and sensory deficits over the head due to combined deficits of the three cranial nerves (third, fourth, and sixth) responsible for eye movements and pupil function, and at least one branch of the trigeminal nerve. The wide-ranging types of pathologies that involve the cavernous sinus can be classified as tumoral, congenital, infectious, inflammatory, granulomatous, and vascular.

Among the tumors involving the cavernous sinus, head and neck tumors are the most likely to metastasize to the cavernous sinus. The other common primary sites in patients with cavernous sinus metastases are breast, lung, and prostate. Lymphomas have been reported to involve the cavernous sinus, as primary lymphomas (2–4) or as secondary lesions, and may occur as unilateral or bilateral lesions (5, 6). Lymphomas may involve the cavernous sinus as a result of invasion or metastasis originating in the head and neck region, or metastasis of systemic origin. Burkitt lymphoma (6), diffuse large B-cell lymphoma (7), T-cell lymphoblastic lymphoma (4), and diffuse small B-cell lymphoma (8) have all been reported as primary lymphoma and as metastases in the cavernous sinus, but to our knowledge CLL involvement has never been reported in the literature. Infectious causes such as fungous and tuberculosis were considered because of the immunocompromised status of our patient. However, an infectious cause was less likely in our patient, in view of the presence of CLL cells in the CSF. Moreover, the CSF culture was negative.

CNS involvement of CLL remains a poorly studied phenomenon. The clinical manifestations of CNS involvement in CLL are heterogeneous and include headache, cranial nerve palsies, cerebellar signs, visual problems, and motor and/or sensory deficits. Imaging studies are neither specific nor sensitive in the detection of CNS involvement; the diagnosis is usually confirmed by lumbar puncture. At present, there are no established guidelines for treatment of CLL patients with CNS involvement. Most patients have been treated with intrathecal chemotherapy with or without radiation therapy or systemic chemotherapy (1). Intrathecal rituximab has been found to be effective in aggressive B-cell lymphomas; however, its efficacy in CLL has not been assessed (9). For CLL patients with leptomeningeal disease, fludarabine-based therapy has been found to be effective and may be a favorable therapeutic option (10). In our patient, a combination of fludarabine, cyclophosphamide, and rituximab (FCR regimen) was very toxic, and he succumbed to sepsis during the neutropenic period.


Figure. MRI of the brain with contrast, (a) axial view and (b) coronal view, showing asymmetric enhancing thickening in the left cavernous sinus (arrow).