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Complete Eye Ophthalmoplegia: the unusual initial presentation of Leptomeningeal Carcinomatosis

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ABSTRACT

Ophthalmoplegia is a paralysis or weakness of extraocular muscles that have a variety of different etiologies including and not limited to Leptomeningeal Carcinomatosis (LC). LC is caused mainly by metastatic cancers and can cause a wide variety of symptoms. We present a case of LC with no preexisting condition who presented with a unilateral ophthalmoplegia as initial presentation who was found to have LC secondary to large B-cell lymphoma.

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1. Introduction

Ophthalmoplegia is the paralysis or weakness of extraocular muscles that results in the eye's inability to move, with the most common symptoms being diplopia [1]. The differentials are extensive including and not limited to multiple sclerosis, trauma, myasthenia gravis and rarely caused by leptomeningeal carcinomatosis(LC) [2]. Moreover, 5% of metastatic cancers involve meninges and causing LC. While LC carries a poor prognosis, early recognition can aid treatment and potentially prolong life. Ocular manifestations are the infrequent presentation of LC [3]. We present a case of LC with no preexisting condition and presented with diplopia, leading to a diagnosis of lymphoma.

2. Case report

We present a 60-year-old male with no significant medical history who presented to the emergency room with a rapidly growing lump in the right axilla for three weeks. Associated symptoms included jaw pain and swelling, bifrontal headache, weight-loss, and double vision for a one-week duration. Of note, he recently underwent dental surgery two weeks before presentation for a periodontal abscess associated with cervical lymphadenopathy and was now concerned about the possibility of disease progression.

On examination, the male patient was alert, oriented and was slightly cachectic appearing. On neurological examination, the patient's extraocular movements in the left eye were completely intact however the right eye had ptosis and complete monocular ophthalmoplegia. Patient's strength, sensation, and reflexes in upper and lower extremity was unremarkable. Neck examination was unremarkable with no palpable masses, S1/S2 was present with no additional heart sounds. Lungs were clear to auscultation, and an 8 cm hard, fixed and painless mass in the right axillary region was palpated. Remained of the examination was unremarkable.

Patient's complete blood count was unremarkable with no leukocytosis, and the comprehensive metabolic panel was only significant for hyperglycemia and mild transaminitis. In the emergency room, a CT of the chest was ordered that showed the large axillary mass as well as multiple liver hypodensities, suspicious of metastatic disease.

At this point, the axillary mass was highly suspicious for malignancy however, we could not explain the neurologic finding as a connective entity thus the patient was admitted for further workup of both the mass and eye findings. Biopsies were scheduled of both the axillary and liver mass. Both sampled returned as high-grade lymphoma and a bone marrow biopsy was scheduled for further differentiation. The bone marrow biopsy showed similar results with flow cytometry confirming the diagnosis of large b-cell lymphoma. In regards to the ophthalmoplegia, further imaging was ordered to rule out other etiologies that included CT Brain and MRI Brain. Both CT and MRI were unremarkable so an additional MRI of the eye orbit was ordered that was unexceptional as well. We performed lumbar puncture for further evaluation that demonstrated elevated protein with numerous atypical lymphocytes. Cytology of the cerebrospinal fluid confirmed CNS involvement with lymphoma as seen in Figure 1, that lead to the diagnosis of LC secondary to Large B-Cell Lymphoma.

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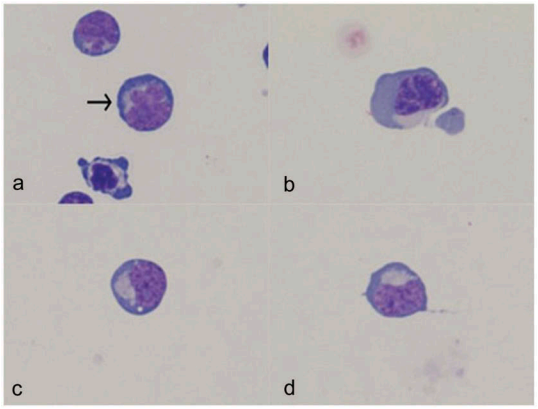

Figure 1. CSF fluid with numerous large B lymphoid cell not normally seen in normal CSF. (a) Tumor cell has multilobed nuclei which predominate. (b) Tumor cell has centrally located nucleolus and an appreciable amount of basophilic cytoplasm. (c and d). Immunoblasts with plasmacytoid differentiation.

Because of the significant disease burden, the patient was started on R-CHOP therapy that includes: Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone. The patient was also started on intrathecal methotrexate treatments for the LC and discharged after the initial treatments. The patient was followed outpatient where he has a significant reduction of the size of his axillary lymph node and continued outpatient chemotherapy with intrathecal treatments with methotrexate. On re-examination during his admissions for intrathecal treatments, re-examination showed slight improvement of extra-ocular movements as the patient was able to abduct his eye approximately 4mm after the multiple treatments however complete resolution was not achieved. After four months, the patient's lymphoma became to treatment however after extensive discussion, the patient opted to defer any further treatment and decided to transfer to hospice care.

3. Discussion

Solid tumors of breast, lung, melanomas, and hematologic malignancies associated with LC, more specifically in 5–30% of non-Hodgkin lymphoma may experience direct CNS involvement [3]. Cancerous spread to the leptomeninges occur by several mechanisms, including a direct extension from brain parenchyma, dura, or bone; hematologic spread, mainly through venous plexi or perineural extension [4]. Most commonly, LC involvement occurs in the basal cisterns of the brain, posterior fossa, and cauda equina [5]. Signs and symptoms vary mainly depend on the site of involvement including cranial and spinal nerves [3]. Its diagnosis is challenging as no single imaging modality have high sensitivity to exclude LC.

If suspected, MRI performed in all patients before lumbar puncture, and it can reveal leptomeningeal enhancement [6]. Cerebral spinal fluid (CSF) containing malignant cells is the gold standard for diagnosis, however, can be falsely negative in 5% of patients if less than 10 ml of CSF fluid obtained for analysis or CSF sample processing has been delayed [7,8]. Positive predictive value of CSF cytology is >90% with a specificity of >95% after three high-volume lumbar punctures [9].

Treatment mainly directed towards palliation that consists of radiotherapy, intrathecal (IT) chemotherapy, and systemic chemotherapy. Radiotherapy can resolve obstructive hydrocephalus by decreasing tumor size [10]. It does not affect mortality but improves symptoms [11]. IT chemotherapy have minimal systemic side effects as it bypasses the blood-brain barrier (BBB) and it also affects overall survival [12]. Systemic chemotherapy depends on the sensitivity of the primary tumor to the chemotherapy and the capability of the drug to cross the BBB. Several retrospective studies have shown improved survival in patients who received systemic chemotherapy [13–15].

The overall survival depends on whether the patient received treatment or not. With treatment, survival is 2 to 4 months [16]. In contrast, death is evident in 4 to 6 weeks in untreated patients [17]. Poor prognostic factors are impaired CSF flow, CSF protein levels >50 mg/dL, and chemotherapy resistant of primary cancer [18]. Overall survival also depends on the type of primary tumor. LC associated with hematologic malignancies had survival of 4.7 months; however, solid tumors had survival of 2.3 months [19].

Prognosis is poor secondary to diagnosis at an advanced stage making early recognition crucial and considering LC as a differential diagnosis for ophthalmoplegia [20].

Disclosure statement

No potential conflict of interest was reported by the authors.

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