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(CASE REPORT)

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Cranial Nerve VI Palsy as the first sign of carcinomatous meningitis from peripheral T-Cell Lymphoma

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Abstract

Carcinomatous meningitis (CM) is a rare but serious complication of both solid organ and haematological malignancies. We present a 63-year-old male patient with newly diagnosed peripheral T-cell lymphoma and a new onset presentation of an isolated right 6th nerve palsy. Computed tomography and magnetic resonance imaging did not show any intracranial abnormalities, infarction, abnormal enhancement or haemorrhage. A lumbar puncture was performed due to persistent symptoms, and CSF flow cytometry showed cerebrospinal involvement. He was treated with systemic and intrathecal chemotherapy but succumbed to his illness. This case illustrates a rare but specific finding of CM as cranial nerve VI palsy in a patient who did not have any significant imaging findings. Diagnosis of CM is multimodal and requires a high index of suspicion, early recognition is needed to improve the patient's quality of life, prolong survival and prevent further neurological deterioration.

Keywords: Leptomeningeal; Carcinomatous; Meningitis; Lymphoma

1. Introduction

Carcinomatous meningitis (CM) is a rare but serious complication of systemic malignancies. It is characterized by disseminating neoplastic cells into the leptomeninges and cerebrospinal fluid (CSF) [1]. The prevalence of this condition is approximately 5 - 10% of patients with solid tumours, most originating from the breast, lung and melanoma [2]. Hematological malignancies such as lymphoma or leukaemias can also present with leptomeningeal involvement [3].

The pathophysiology of CM involves hematogenous, direct or perineural dissemination of malignant cells to the leptomeninges; proliferation of these cells leads to disruption of normal CSF dynamics which can manifest as hydrocephalus, increased intracranial pressure, and a multitude of neurological deficits [4].

The diagnosis of carcinomatous meningitis is challenging due to its varying clinical presentation, coupled with limitations in CSF analysis, and the sensitivity of imaging modalities. Early detection is crucial to provide intervention that is both adequate and targeted [5].

We report our experience with a difficult-to-diagnose case of CM to underscore the importance of early suspicion and further workup despite initial investigations not yielding any conclusive results.

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2. Case Presentation

A 63-year-old male presented with symptoms of loss of weight of 22kg over 5 months, loss of appetite and episodic fever. He denied any headache, blurring of vision, limb weakness or facial weakness. The patient was referred to our medical centre based on a peripheral blood film showing approximately 45% abnormal lymphoid cells.

Physical examination was unremarkable apart from small sub-centimetre left inguinal lymph nodes. Blood investigations were as below: haemoglobin 10.5g/L, white blood cell 3.6 x 10^9/L, platelet 193 x 10^9/L, reticulocyte 1.3%, hematocrit 30.9%. Peripheral blood films were reported to show features suggestive of iron deficiency anaemia with white cell changes suggestive of underlying infection/inflammation.

Bone marrow sampling revealed 10% abnormal lymphoid cells with immunophenotyping indicating 0.1% abnormal B cell population. Trephine biopsy showed an abnormal lymphoid population. Immunophenotyping was performed and showed the presence of 2.25% suspicious T cell population expressing the phenotype CD45 (bright), CD3+, CD5+, CD4+, CD8+, TCRgd- and CD56-. A diagnosis of peripheral T-cell lymphoproliferative disease (T-LPD) was made and the patient was planned for chemotherapy.

Before initiation of chemotherapy, the patient presented with sudden onset double vision for 1 week associated with giddiness, he denied any limb weakness or raised intracranial pressure symptoms. Physical examination was positive for a right eye 6th cranial nerve palsy only with no other neurological deficit. The neurology team was consulted. Non-contrasted and contrasted computed tomography (CT) imaging of the brain revealed no focal enhancing brain parenchymal lesion. Magnetic resonance imaging (MRI) of the brain demonstrated no enhancing brain lesion or abnormal meningeal enhancement.

CT TAP revealed hepatosplenomegaly with small reactive nodes in the upper abdomen with no other significant findings. The patient underwent a lumbar puncture with the results as follows: opening pressure was 18cm H_2O, protein 0.93g/L, glucose 2.1 mmol/L, cell count 60 cells/mm^2, lymphocyte 100%. Cultures for fungal, bacterial and mycobacterium were negative. Cytology was negative for any atypical/malignant cells. CSF for flow cytometry immunophenotyping (IPT) was not sent as it was unavailable at our centre.

Due to the patient's persistent neurological deficit, CSF sampling was repeated for CSF flow cytometry IPT in another centre. CSF flow cytometry IPT showed 19% aberrant T cells consistent with CSF involvement by T-cell lymphoma.

The patient underwent chemotherapy with high-dose methotrexate, cyclophosphamide, doxorubicin, vincristine, prednisolone and intrathecal (IT) methotrexate. The patient was able to complete two cycles of chemotherapy. He unfortunately developed neutropenic sepsis, deteriorated and succumbed to his illness.

3. Discussion

In this report, we describe a patient who was diagnosed with carcinomatous meningitis (CM) via CSF flow cytometry when initial investigations, cytology and further imaging did not yield any positive results. The highest rate of CM tends to occur from solid organ tumours with rates ranging from 5% to 8% [6]. In certain haematological malignancies such as acute lymphoblastic leukemia leptomeningeal involvement is a well-recognized complication with an incidence rate of approximately 5 - 10% at initial diagnosis and up to 30% in relapsed cases [7].

CM can have a multitude of clinical presentations. Symptoms can be related to raised intracranial pressure causing headaches, nausea and vomiting; cranial nerve involvement with diplopia, facial weakness or numbness, hearing loss or tinnitus; infiltration along the nerve roots leading to radiculopathy or myelopathy [8].

Diagnosis of CM requires the use of different modalities. CSF sampling is the gold standard for diagnosis. CSF findings typically include a high CSF pressure (greater than 25cm H_2O) in about 50% of CM patients, this was however absent for our patient [9]. Pleocytosis is detected in 33 - 79% of CM [10]. Elevated protein levels in CSF occur in about 80% of cases as was present in our patient with nearly a two-fold increase from the normal range [11]. Glucose levels in CM are decreased in approximately 25 - 40% of cases and is called hypoglycorrhachia [9]. Normal CSF glucose levels range between 2.7 - 4.4 mmol/L. CSF cytology is the definitive test for diagnosis of CM; however, Glass et al [12] reported approximately 40% of patients with CM are cytologically negative. Higher volumes of CSF (>10ml) can improve the yield. As mentioned this patient's cytology was negative and hence flow cytometry was employed as it is a highly sensitive method for the detection of haematological malignancies even with small CSF volumes.

Neuroimaging with gadolinium-enhanced MRI is suggested for the diagnosis of CM. T1 weighted images with contrast show leptomeningeal enhancement often scattered in a 'sugar coated' manner [13]. FLAIR imaging can show abnormally elevated signal within sulci and rarely within the parenchymal surface [14].

MRI in one study was shown to be capable of successfully detecting a high percentage of cases of CM from solid tumours ~100%, but only around 44% in patients with B-cell acute lymphoblastic leukaemia and 48% from non-Hodgkin lymphoma [7]. Despite the highly sensitive nature of MRIs, our patient did not have any of the typical radiological features associated with CM.

Treatment of CM depends on the site of the primary tumour. Management of patients with CM has been formulated by the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO). In cases such as ours, systemic chemotherapy with intrathecal chemotherapy is the mainstay of treatment. Intrathecal chemotherapy allows for the treatment of CM as most therapeutic drugs are unable to cross the highly selective blood-brain barrier.

The prognosis for CM is poor, as it represents an advanced stage of the disease. The median time of survival is 2 to 4 months, even with treatment [15]. Factors affecting prognosis include early diagnosis, normal CSF protein levels and low disease burden. For patients with a low ECOG score systemic therapy combined with IT administration may be beneficial. For those with poorer functional status, the palliative approach may be a superior option. Literature has shown lymphoma and leukaemia-associated CM have a better prognosis compared to solid tumours [16].

4. Conclusion

This case highlights the diagnostic challenges that are associated with CM in the context of haematologic malignancies. The rapid deterioration of the patient despite rapid diagnosis and treatment of CM underscores the poor prognosis associated with this disease. Ultimately, this case reinforces the combined importance of clinical acumen with adequate investigations to reach the appropriate diagnosis and provide suitable treatment for CM.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare the complete absence of any conflict of interests while carrying out this research work.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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