CASE REPORT

T-cell primary leptomeningeal lymphoma in cerebellopontine angle

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SUMMARY

Primary meningeal lymphomas are very rare and those derived from T cells are even more infrequent (less than 5% of primary central nervous system lymphomas). Cerebellopontine angle involvement in the primary T-cell lymphoma is exceptional. Clinical presentation depends on the type of lesions, and histological diagnosis is needed. We present a rare case of a 50-year-old woman who presented with clinical cerebellar syndrome with posterior opsoclonus-myoclonus syndrome. Necropsy evaluation revealed primary diffuse leptomeningeal non-Hodgkin's T-cell lymphoma.

BACKGROUND

Malignant lymphomas of the central nervous system (CNS) are uncommon and their location in cerebellopontine (CP) angle are even more rare.^{1 2} T-cell CNS lymphoma is an infrequent disease with unknown incidence and a variety of clinical presentations, depending on the site of lesion and deep brain structure involvement.^{3 4} We report a case of primary leptomeningeal T-cell lymphoma located in CP angle in a middle-aged woman with development of opsoclonus-myoclonus syndrome. Only a few cases of this condition have been described in the scientific literature.

CASE PRESENTATION

A 50-year-old woman presented to this hospital with gait instability. She had been well until 4 months before admission, when progressive gait instability began. One week before admission, vomiting and diplopia developed.

There was no family history of neurological diseases. The patient drank alcohol rarely and did not smoke. She had a history of polymyositis 5 years prior, which had been treated with low doses of corticosteroids (methylprednisolone 4 mg/day) and methotrexate (7.5 mg/week). She achieved complete remission without muscle weakness and recurrence signs, so the methotrexate and steroid treatments were stopped. She remained asymptomatic and without any treatment for the next 12 months before the current presentation.

The patient reported a 4-month history of rapidly progressive gait disorder. On the day of admission, she was alert and cooperative, with normal speech. She had paralysis of the right sixth cranial nerve; results of testing of the other cranial nerves were normal. There was marked truncal ataxia with standing and walking. The strength, tone and sensitivity were preserved and there were no meningeal signs. The remainder of the neurological and

general examinations was normal. Routine blood count was normal, as were the levels of glucose, electrolytes, calcium and total protein; results of tests of renal and liver function were normal. X-ray of the chest was normal. CT and MRI of the brain with contrast agents (T1, T2 and diffusion-weighted images and fluid-attenuated inversion recovery (FLAIR) sequences) reportedly showed no abnormality. Lumbar puncture was performed, analysis of the cerebrospinal fluid revealed a mildly increased protein level with a normal glucose level and a pleocytosis with a preponderance of lymphocytes (protein 79 mg/dL, glucose 51 mg/dL, leucocyte 49 cells/mm³ with 90% lymphocytes). No bacteria, acid-fast bacilli, or fungal organisms were seen on smears or cultures. Cytological examination revealed no malignant cells.

The patient had full strength and intact reflexes symmetrically but she was unable to stand without assistance, secondary to severe truncal ataxia. During hospitalisation, she also developed cognitive impairment, intermittent myoclonic movements in the limbs and trunk, and involuntary, irregular, chaotic saccadic, multidirectional but conjugated eye movements were noted. Two more lumbar punctures were performed due to torpid evolution and neurological impairment but both showed similar results to the first one. The patient was diagnosed with opsoclonus-myoclonus syndrome and a paraneoplastic origin was suspected so further investigations were carried out. EEG performed to exclude non-convulsive status epilepticus was reportedly normal. A repeat MRI of the patient's brain with contrast agent (T1, T2 and diffusion-weighted images and FLAIR sequences) was normal. CT of the chest, abdomen and pelvis, after the administration of oral and intravenous contrast material, showed no abnormality. In addition, the onconeural antibodies and serum antineuronal antibodies (anti-Hu, anti-Ri and anti-Yo) were negative. Other metabolic, toxic and infectious causes were discarded.

TREATMENT

A rapid 24 h-worsening of the patient's neurological condition prompted empiric therapy. As we suspected a paraneoplastic opsoclonus-myoclonus syndrome, intravenous corticosteroids (dexamethasone initially at a dosage of 10 mg once, followed by 4 mg every 6 h) and intravenous immunoglobulins were administered for 5 days without any improvement.

OUTCOME AND FOLLOW-UP

The patient died shortly thereafter on the 15th day of hospitalisation. To clarify the cause of the

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neurological symptoms, necropsy was performed. Final diagnosis was based on postmortem findings. Macroscopic evaluation of the brain revealed no abnormalities. Microscopic examination revealed diffuse leptomeningeal infiltration by lymphoid cells, being more striking near the brainstem and cerebellum. Immunohistochemically, the tumour cells expressed the phenotype of T lymphocytes, with ACL, CD43 and UCHL1 markers positive. Markers for B lymphocytes, histiocytes and Hodgkin's lymphoma were negative. These necropsy findings showed a final diagnosis of primary diffuse leptomeningeal non-Hodgkin's T-cell lymphoma.

DISCUSSION

Primary cerebral lymphoma (PCNSL) is an aggressive non-Hodgkin's disease that originates in the CNS (brain, leptomeninges, spinal cord or eyes) without evidence of any other systemic location. Its incidence is unknown (less than 1% of all intracranial tumours) but has apparently increased during the last two decades in immunocompromised and in immunocompetent patients.^{1 5} Diffuse B cell lymphomas are the most common type (>90%) while those derived from T cells are much more infrequent (<5%).^{3 5} The prevalence of T-cell PCNSL is higher in eastern countries such as Japan (14%) compared with western countries.^{3 6} Ferreri *et al*⁷ described a large series of PCNSL cases in western countries with T-cell lymphomas accounting for only 2% of cases (8 of 370). Shenkier *et al*³ analysed a series of 45 T-cell PCNSLs, only 1 of them confined to meninges, and involvement of deep brain structures (basal ganglia, brainstem or cerebellum) was described in 16 patients (36%). Twenty-five per cent of PCNSLs occur in an infratentorial region.^{1 7} Leptomeningeal lymphoma presenting as a CP angle lesion is a much more rare condition and, to the best of our knowledge, only a few cases have been reported worldwide.^{1 3 5-8} Median age of presentation is around 60 years of age with a preponderance in males.^{3 4 7} Clinical presentation may occur with a variety of focal or non-focal neurological symptoms being the most frequent; such as hearing loss (resembling a vestibular schwannoma). Cerebellar signs such as ataxia or unsteady gait are the second most common symptoms but without B symptoms such as fever or night sweats.^{1 5} The most frequent aetiology of opsoclonus-myoclonus syndrome is the idiopathic cause and paraneoplastic manifestation of the underlying malignancy.⁹ In adults, tumours most commonly involved include small-cell lung cancer, and cancer of the breast and ovary. To the best of our knowledge, association of this syndrome with PCNSL has not been previously reported. Clinical suspicion for PCNSL in case of opsoclonus-myoclonus presentation is complex as there are no pathognomonic clinical or radiological features of T-cell PCNSL. There are no established markers to identify adult patients with paraneoplastic opsoclonus-myoclonus. Therefore, frozen section should always be obtained and immunohistochemical analyses should be performed to aid in the definitive diagnosis.^{5 10} The cytological diagnosis of lymphoma in cerebrospinal fluid requires an abundant cellularity and a clear lymphoid predominance with sufficient atypia to suggest a diagnosis of malignancy.^{3 6} Our patient received corticosteroid and methotrexate for her underlying disease, which contributed to the difficulty of diagnosis. The prognosis of T-cell PCNSL has been controversial, without a consensus in the literature. Median survival time is 1.5–3.3 months in untreated patients.^{5 6} Although chemotherapy

combined with radiotherapy is the best mode of management, treatment of PCNSL continues to raise numerous controversies due to neurotoxicity in patients over 60 years old, and individual treatment regimens analysed have been very different.^{1 3 5-7 10}

In our case, autopsy and immunohistochemical studies revealed the final diagnosis. It is noteworthy that clinical presentation with cerebellar syndrome and posterior development of opsoclonus-myoclonus has not been previously described in the literature, but involvement of CP angle and meningeal extension can explain the clinical symptoms in our patient.

Learning points

- Clinical presentation in our patient (cerebellar syndrome and posterior opsoclonus-myoclonus symptoms) has not been previously described in the literature; this case underscores the importance of having a high level of suspicion when diagnosing these tumours.
- Most PCNSLs demonstrate abnormalities on brain imaging, such as enhancing mass lesions or focal or diffuse leptomeningeal abnormal enhancement, but in our case, CT and MRI taken with contrast agents did not contribute to the definitive diagnosis.
- Concomitant long-term corticosteroid use may reduce abnormal contrast enhancement, which may complicate the interpretation of enhanced MRI. Also, exposure to these drugs may disturb cerebrospinal fluid (CSF) cytology results.
- Definitive diagnosis of leptomeningeal lymphoma is made by a positive CSF cytology together with radiographic features and clinical presentation.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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