

Third nerve palsy as an isolated manifestation of herpes simplex virus type 2 meningitis in a patient with chronic lymphocytic leukaemia

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Abstract

Isolated third nerve palsy as the sole manifestation of meningitis is rare. We describe a patient with chronic lymphocytic leukaemia who developed third nerve palsy due to HSV2 meningitis. HSV2 PCR was positive in CSF and patient was partially recovered upon treatment with acyclovir.

Keywords: Herpes simplex virus type 2; oculomotor nerve; chronic lymphocytic leukaemia; meningitis

INTRODUCTION

In adults, genital herpes is typical presentation of herpes simplex type 2 (HSV-2) infection. Central nervous system (CNS) manifestations such as acute or recurrent meningitis, radiculitis with or without myelitis, and rarely encephalitis are uncommon.^{1,2} Chronic lymphocytic leukemia (CLL) is a common lymphoproliferative disease with a variable natural history ranging from an indolent to a very aggressive disease.³ Immunodeficiency in CLL is mainly due to hypogammaglobulinemia.⁴ Although high incidence of HSV infection has been predominantly described in CLL patients as a result of defects in cell-mediated immunity following treatment with fludarabine⁵, HSV2 infection of the CNS in particular have not been previously reported in CLL. Here, we report a unique case of HSV2 meningitis presented with an isolated oculomotor nerve palsy in a CLL patient.

Case Report

A 77-year-old man presented with a 3 day history of diplopia and left partial ptosis that was preceded by two weeks of left facial dull pain. This was not associated with or preceded by fever, rash, headache, or constitutional symptoms. There was no past history of recurrent infections. He underwent fludarabine based chemotherapy for CLL on multiple occasions in the past, most recently 7 years ago. His sole vascular risk factor was dyslipidemia and there was no family history of aneurysms.

On admission, the examination revealed

anisocoria with left pupillary dilatation and a sluggish response to light. There was a partial left eyelid ptosis and mild limitation of left eye adduction. He was afebrile and had no nuchal rigidity or other cranial nerve involvement. There was no evidence of oral or genital lesions. A day after, he developed complete ptosis (Figure 1A). In primary gaze, his left eye was in “down and out” position. Adduction, elevation, and depression of the left eye were restricted with preserved abduction and intorsion (Figure 1A).

Full blood examination revealed marked lymphocytosis (lymphocyte count: 45.9×10^9 /L) without neutropenia. Peripheral blood flow cytometry showed monoclonal B lymphoid cells consistent with CLL. Renal, hepatic, thyroid function tests were normal. Glycated haemoglobin was 5.3% and inflammatory markers were normal. Vasculitic screen was negative. Most recent serum protein electrophoresis, from four months prior, was normal and did not show hypogammaglobulinemia. CT brain and angiography excluded bleeding and aneurysms. Brain MRI with gadolinium contrast did not show brainstem lesion, lepto- or pachymeningeal enhancement, or abnormal enhancement of the oculomotor nerve.

Cerebrospinal fluid examination revealed a markedly elevated protein level (1.08 g/L) with lymphocytic pleocytosis (405 cells/ μ L; lymphocyte 95%). CSF flow cytometry revealed that 97% of lymphocytes were T-Cells with the rest being polyclonal B lymphocytes. CSF polymerase chain reaction (PCR) was positive

for HSV2. Other viral pathogens, cryptococcal antigen, and culture was negative.

Intravenous acyclovir, 10 mg/kg q8hr, was started on day five of his stay and continued for 10 days. On completion, there was a partial improvement of ptosis and extra-ocular movements (Figure 1B).

DISCUSSION

Microvascular ischemia is the most common cause of isolated third nerve palsy and a posterior communicating artery (PCoM) aneurysm is a major concern for clinicians in this setting and should always be excluded. Other causes of third nerve palsy including trauma, compression from neoplasm, stroke, inflammatory, infiltrative, and infective conditions (including meningitis) are rather associated with other neurological abnormalities than isolated.^{6,7} Pupil involvement can occur with most of these causes and not solely due to compressive lesions.⁶

CSF lymphocytic pleocytosis without bacterial growth is consistent with an aseptic meningitis with HSV2 meningitis being a

common cause.² Whilst meningitis can present with cranial nerve III palsy, this is usually in association with meningism and multiple other cranial neuropathies.⁷ An isolated oculomotor nerve palsy has however been rarely reported with infective causes including cryptococcal meningitis⁸ and tuberculous meningitis (9). Postulated mechanisms include intermittently raised intracranial pressure, inflammation and direct invasion of cranial nerve by the pathogen.⁸

In our case, very high CSF protein and profound lymphocytic pleocytosis, with an accompanying positive HSV2 PCR makes the diagnosis of HSV meningitis likely. This is further strengthened by the CSF flow cytometry excluding a clonal population making leptomeningeal infiltration of chronic lymphocytic leukaemia unlikely. The clinical improvements seen with treatment also support the diagnosis of HSV meningitis.

In conclusion, we report a case of HSV2 meningitis presenting with an isolated third nerve palsy in a CLL patient. Viral meningitis should be considered in the differential diagnosis of patients presenting with an isolated third nerve palsy. Absence of classical symptoms of meningitis in

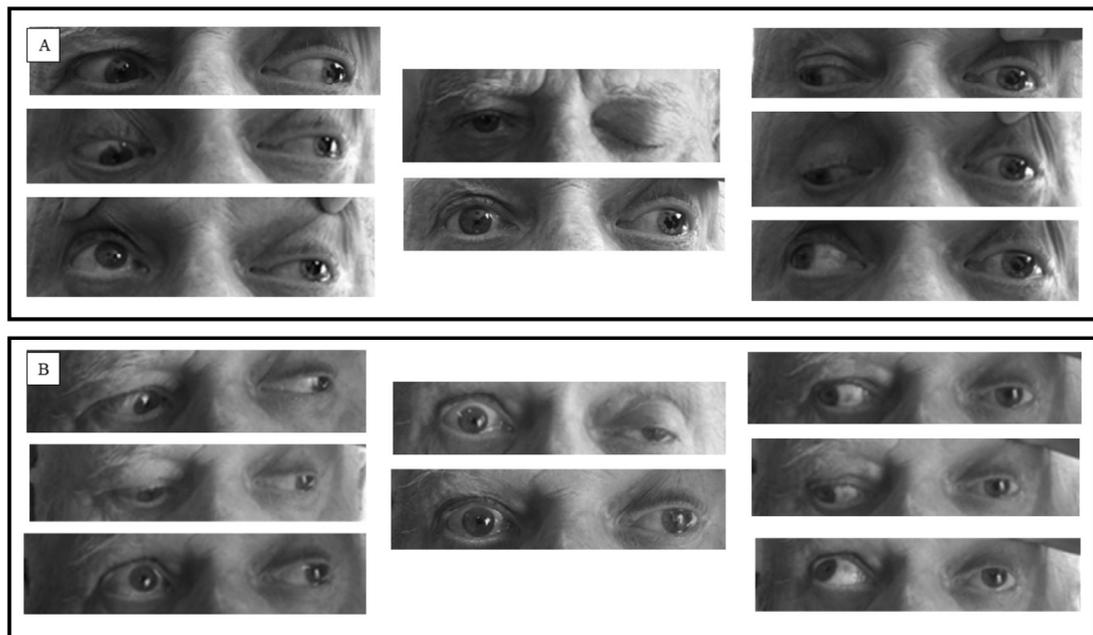


Figure 1. A. Different positions of gaze before acyclovir therapy. Note left upper eyelid ptosis (top panel of centre column) and anisocoria together with “down and out” position of left eye in primary gaze (bottom panel of centre column). There is limitation of left eye adduction (top panel of right column), depression (centre panel of right and left columns), and elevation (bottom panel of right and left columns). B. Different positions of gaze after acyclovir therapy. Note that patient can overcome ptosis to some extent (top panel of centre column) and primary position of left eye is more central (bottom panel of centre column). Left eye adduction (top panel of right column) and elevation (bottom panel of right and left columns) partially improved.

immunocompromised patients does not exclude this diagnosis.

DISCLOSURE

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Conflict of interest: None

REFERENCES

1. Savoldi F, Kaufmann TJ, Flanagan EP, Toledano M, Weinshenker BG. Elsberg syndrome: A rarely recognized cause of cauda equina syndrome and lower thoracic myelitis. *Neurol Neuroimmunol Neuroinflamm* 2017;4(4):e355.
2. Gilden DH, Mahalingam R, Cohrs RJ, Tyler KL. Herpesvirus infections of the nervous system. *Nat clin Pract Neurol* 2007;3(2):82-94.
3. Fischer K, Hallek M. Optimizing frontline therapy of CLL based on clinical and biological factors. *Hematology Am Soc Hematol Educ Program* 2017;2017(1):338-45.
4. Hamblin AD, Hamblin TJ. The immunodeficiency of chronic lymphocytic leukaemia. *Br Med Bull* 2008;87:49-62.
5. Melchardt T, Weiss L, Greil R, Egle A. Viral infections and their management in patients with chronic lymphocytic leukemia. *Leuk Lymphoma* 2013;54(8):1602-13.
6. Fang C, Leavitt JA, Hodge DO, Holmes JM, Mohny BG, Chen JJ. Incidence and etiologies of acquired third nerve palsy using a population-based method. *JAMA Ophthalmol* 2017;135(1):23-8.
7. Bhatti MT, Eisenschenk S, Roper SN, Guy JR. Superior divisional third cranial nerve paresis: clinical and anatomical observations of 2 unique cases. *Arch Neurol* 2006;63(5):771-6.
8. Mahale RR, Mehta A, Shankar A, Buddaraju K, Srinivasa R. A surprising cause of isolated oculomotor nerve palsy with pupillomotor palsy. *Ann Indian Acad Neurol* 2016;19(1):159-60.
9. Moon S, Son J, Chang W. A case of oculomotor nerve palsy and choroidal tuberculous granuloma associated with tuberculous meningoencephalitis. *Korean J Ophthalmol* 2008;22(3):201-4.