CASE REPORT

Isolated III cranial nerve palsy: a Hodgkin's lymphoma?

Joana Meireles, Maria Carolina Garrett, Pedro Abreu

Department of Neurology,
Hospital São João, Oporto,
Portugal

Correspondence to
Professor Maria Carolina
Garrett,
garrett.mc51@gmail.com

Accepted 29 March 2014

SUMMARY

A 69-year-old woman developed ptosis and diplopia due to an isolated pupil-involving left oculomotor nerve palsy. General examination was unremarkable. Initial workup showed a mild increase in cerebrospinal fluid proteins. Imaging studies were remarkable for a left oculomotor nerve enhancement in brain MRI and hyperfixation along the nerve's pathway in full body single-photon emission CT. Assuming the possible diagnosis of neurosarcoidosis, the patient was started on high-dose methylprednisolone. Three months later she developed pancytopenia. A bone marrow biopsy was performed and histopathology revealed infiltration by Hodgkin's lymphoma. Adriamycin, bleomycin, vinblastine, dacarbazine protocol chemotherapy was started and full haematological remission obtained after four cycles, despite mild oculomotor nerve palsy persisted. Isolated oculomotor palsy as the first presenting manifestation of a lymphoma is rare and alternative differential diagnosis must be considered in the absence of other lymphoma manifestations. In this case as with many rare initial manifestations of common diseases watchful waiting was crucial to the correct diagnosis and treatment strategy.

BACKGROUND

Cranial nerves and their surrounding leptomeninges and cavernous sinus are often involved in lymphomas.^{1–3} Nevertheless isolated oculomotor palsy as the first presenting manifestation of a lymphoma is rare, particularly when no other lymphoma manifestations are initially identified.¹ We report the case of a patient with an isolated oculomotor palsy as the first and uncommon manifestation of Hodgkin's lymphoma.

CASE PRESENTATION

A 69-year-old woman with a medical history of several vascular risk factors, developed insidious diplopia in the primary position and right gaze associated with right eyelid droop. She presented to the emergency department 3 months after the onset of these symptoms. Neurological examination showed isolated pupil-involving oculomotor cranial nerve palsy (figure 1) and was normal otherwise. General examination was unremarkable; there were neither skin lesions nor palpable lymphadenopathy.

INVESTIGATIONS

- Haematological and biochemical investigations were normal.
- Antineuronal and tumoural marker levels were normal (including $\beta 2$ microglobulin).

- ACE levels in the plasma and cerebrospinal fluid (CSF) were normal.
- CSF study showed a mild increase in proteins of 0.87 g/dL, one cell (immunophenotyping showed an unspecific predominance of T cells, mainly TCD2 lymphocytes), serological and virological investigations were negative, CSF cytology showed no atypical mononuclear cells supporting lymphoma.
- CT angiogram of the Circle of Willis showed no evidence of a posterior communicating artery aneurysm.
- Cerebral MRI performed during initial diagnostic investigation showed a left III cranial nerve enhancement with no brain parenchymal, meningeal abnormalities or cavernous sinus involvement (figure 2).
- Thoracic CT showed the presence of some lymphatic ganglia in the mediastinum and pulmonary hilum, bilaterally; all of them less than 7 mm in diameter and were considered normal otherwise.
- Whole-body single-photon emission CT (SPECT) displayed a localised hyperfixation of the tracer in the lateral region of the left orbit in the III nerve tract. No other foci were identified.

DIFFERENTIAL DIAGNOSIS

Posterior communicating artery aneurysm: Rupture from posterior communicating artery berry aneurysms is one of the most significant causes of morbidity and mortality in III cranial nerve palsies. Pupillary involvement suggested by sluggish or absent response to light is evocative of parasympathetic fibres involvement with its origin in the Edinger-Westphal subnucleus of the third cranial nerve complex. The involvement of these fibres usually occurs due to compressive lesions, given that they are located superficially within the nerve.

Nevertheless, this hypothesis was set aside by the normal CT angiogram of the Circle of Willis, which excluded the existence of any posterior communicating artery aneurysm.

Third cranial nerve ischaemic neuropathy would also be a likely diagnosis in this patient, due to the existence of several vascular risk factors, and the absence of other neurological signs or symptoms. However, this was less likely, since pupillary involvement was evident since the beginning, which is not to be expected as the vascular supply of the peripherally located parasympathetic fibres is usually sufficient.

CrossMark

To cite: Meireles J, Garrett MC, Abreu P. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-203999

Figure 1 (A–D) A pupil sparing (incomplete) left III cranial nerve palsy.

Neurosarcoidosis: Given the pupillary involvement, our investigation focused on a possible inflammatory or infiltrative aetiology, despite the fact that these are more commonly associated

with multiple cranial nerve palsies or other multiple neurological deficits. This possibility was supported by MRI of the brain and whole-body SPECT finding of a left oculomotor

Figure 2 Left III cranial nerve enhancement along its (A) orbital, (B) cisternal and (C) cavernous sinus course.

nerve enhancement and localised tracer's hyperfixation in the lateral region of the left orbit following the III nerve pathway, respectively, and in the absence of aneurismatic structures, we proceeded to investigate an eventual systemic disorder. Nevertheless, all the laboratory and imaging studies were normal or inconclusive. A working diagnosis of possible neurosarcoidosis was initially proposed, despite the absence of evidence on ancillary studies other than MRI of the brain and whole-body SPECT findings and in the absence of skull base involvement, parenchymal mass lesions or granulomas that frequently occur in neurosarcoidosis. Nervous system involvement in sarcoidosis usually occurs in the setting of the systemic disorder and is usually associated with active disease. However, it may occur in isolation in approximately 10% of the patients. The clinical features of neurosarcoidosis depend on the site involved. While it affects most commonly the central nervous system, a subset of patients present with peripheral nervous system involvement. It may occur as a myopathy and/or a peripheral neuropathy depending on the distribution of the granulomas. Nevertheless, patients are usually younger females, aged between 25 and 50 years.

TREATMENT

Assuming the possible diagnosis of a neurosarcoidosis, she was started on methylprednisolone (1 mg/kg/day), and a partial recovery was noticed. Three months after the initial manifestations, she developed pancytopenia and a bone marrow biopsy showed Hodgkin's lymphoma (figure 3). Staging and prognostic evaluation revealed a stage IV-B disease and International prognostic score of 3. She was treated with four cycles of doxorubicin, bleomycin, vinblastine, dacarbazine as part of the protocol. No cranial radiotherapy was needed.

OUTCOME AND FOLLOW-UP

Currently, the patient has completed chemotherapy treatment and a complete haematological remission was obtained. The patient maintains a mild partial III nerve palsy.

Figure 3 Bone marrow histology depicting a high-cellularity area, cells with dense nucleoli and Sterberg-Reed cells (blue arrow). Brown arrows indicate CD30 cells, compatible with Hodgkin's lymphoma.

The left oculomotor nerve enhancement initially observed on MRI of the brain was no longer visible on a follow-up examination performed after approximately 1 year.

DISCUSSION

Some authors^{1–3} have reported cranial neuropathies associated with central nervous system lymphomas, but these neurological manifestations are usually accompanied by other clinical features, namely B-symptoms, other nervous system anomalies or lymphadenopathy. Usually patients with lymphoma have other supportive findings such as leucocyte count increase and mediastinic masses, which were absent in this case, further hindering the diagnosis. Reported cases with milder manifestations are usually associated with other underlying or confounding conditions such as HIV.⁴ This case is peculiar due to the isolated finding of an oculomotor nerve palsy with no other physical examination or laboratory result that could guide us towards a valid diagnostic conclusion. Time and patient surveillance was crucial in this case to the establishment of a correct diagnosis and treatment strategy.

Learning points

- ▶ Central nervous system lymphomas have a wide spectrum of manifestations.
- ▶ Isolated oculomotor palsy may happen in isolation, before the systemic onset of a lymphoma.
- ▶ There are more than 10 cases of oculomotor palsy associated with lymphoma in the literature, but this may be the first report on a case of Hodgkin's lymphoma.
- ▶ In the absence of a definite diagnosis, keep an open mind, watchful waiting may eventually provide the missing clues to a correct diagnosis.

Contributors JM has designed and drafted the manuscript. PA and MCG have revised it critically for intellectual content. All the authors have given the final approval of the version to be published.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Bhatti MT, Schmalfuss IM, Eskin TA. Isolated cranial nerve III palsy as the presenting manifestation of HIV-related large B cell lymphoma: clinical, radiological and post-mortem observations: report of a case and review of the literature. *Surv Ophthalmol* 2005;50:598–606.
- 2 Choi SM, Kim JT, Lee SH, *et al*. Isolated oculomotor nerve palsy due to non-Hodgkin's lymphoma demonstrated by serial MRI. *Chonnam Med J* 2008;44:109–12.
- 3 Sato H, Hashimoto T, Yoneda S, *et al*. Lymphoma as a cause of isolated oculomotor nerve palsy. *J Clin Neurosci* 2011;18:1256.
- 4 Lee WW. Lymphoma presenting as cranial nerve neuropathies in HIV-infected patients. *AIDS Reader* 2008;18:606–10.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow