CASE REPORTS

Lymphocytic Hypophysitis Presenting as Bilateral Abducens Nerve Palsy: A Case Report

Anna M. Waldie^a, Oliver Lau^a, Matti Gild^b, Nicholas S. Little^c, Janice Brewer^d, Mark J. Thieben^e, Roderick Clifton-Bligh^b, and James E. H. Smith^a

^aDepartments of Ophthalmology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; ^bDepartments of Endocrinology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; ^cDepartments of Neurosurgery, Royal North Shore Hospital, St Leonards, New South Wales, Australia; ^dDepartments of Anatomical Pathology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; ^eDepartments of Neurology, Royal North Shore Hospital, St Leonards, New South Wales, Australia

ABSTRACT

Lymphocytic hypophysitis (LYH) is a neuroendocrine disorder characterised by autoimmune inflammation of the pituitary gland with varying degrees of pituitary dysfunction, visual field defects and ocular motility disturbance. The authors report an interesting case of a 50-year-old woman presenting with intermittent bilateral abduction deficits. Neuroimaging and histopathological findings are presented. To the authors' knowledge, this is the first report of recurrent horizontal binocular diplopia and complete bilateral internal carotid artery occlusion in association with LYH.

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Introduction

Lymphocytic hypophysitis (LYH) is a neuroendocrine disorder characterised by autoimmune inflammation of the pituitary gland with varying degrees of pituitary dysfunction, presenting with symptoms of sellar compression, hypopituitarism, diabetes insipidus, and hyperprolactinaemia.¹ Upward expansion of the pituitary mass can lead to visual field (VF) defects and reduced visual acuity (VA) from optic chiasm compression. Very rarely, patients develop diplopia from lateral extension into one or both cavernous sinuses and compression of the oculomotor, trochlear, or abducens nerves.¹ In the report herein, we present a case of bilateral subtle abducens nerve palsies heralding a diagnosis of LYH.

Case report

A 50-year-old woman presented to our ophthalmology clinic with a 3-week history of constant horizontal binocular diplopia on a background of 12 months of intermittent diplopia associated with headache. She had a history of migraine but was otherwise medically well. The patient had a similar presentation to an emergency department 2 years

prior. Then, a non-contrast computed tomography (CT) brain was reported as normal, and she was discharged home with no clear diagnosis or definitive treatment, and her symptoms resolved.

She did not complain of photophobia, pain with extraocular movements, eye redness, photopsia, visual floaters, or blurred vision. Systemically, she denied general malaise, fatigue, weight loss or polyuria. The patient was premenopausal, yet amenorrhoeic.

On examination, her uncorrected VA was 20/15 bilaterally. The pupils were equal and briskly reactive, with no afferent pupillary defect. VFs were full to confrontation and on automated perimetry. The remainder of the ocular examination was unremarkable, including normal fundi.

Ocular motility evaluation revealed subtle bilateral abduction deficits with bilateral end point abduction nystagmus, greater than three beats, more prominent on the right, and hypometric saccades. Thirty prism dioptres of right esotropia in primary position was evident, greater for distance than near. The remainder of the cranial nerve examination revealed no abnormality.

The patient was admitted for further medical workup. Laboratory evaluation revealed a normal

full blood count, electrolytes, and C-reactive protein. An autoimmune screen, including erythrocyte sedimentation rate, antineutrophil cytoplasmic antibody, antinuclear antibody, and angiotensin converting enzyme, was also normal and electrophoresis showed no abnormal monoclonal bands. Serum immunoglobulin subclass G4 (IgG4) levels were normal.

The patient's pituitary profile demonstrated hypogonadotropic hypogonadism and hyperprolactinaemia, likely secondary to a stalk effect. There was no clinical evidence of diabetes insipidus, and the remainder of the pituitary screen was unremarkable.

A subspecialist neuroradiologist assessed her CT brain from 2 years prior and identified a lesion that had been missed in the original reporting. This prompted further neuro-imaging to assess for progression of her intracranial lesion.

Magnetic resonance imaging with angiography (MRI/MRA) of the brain and orbits disclosed diffuse thickening and enhancement within the

parasellar soft tissues with extension into the cavernous sinus bilaterally causing encasement and complete occlusion of the cavernous portions of the internal carotid arteries (ICA); the posterior communicating arteries supplied the middle and anterior cerebral arteries (Figure 1). Base of skull CT demonstrated involvement of the dorsum sellae and superior aspect of the clivus.

The radiological findings were suggestive of an unusual infiltrative or inflammatory condition. An abdominopelvic CT scan was performed to assess for systemic involvement, though there was no evidence of distal disease, or focus for biopsy on this scan. In the absence of systemic involvement, a tissue diagnosis was sought.

The pituitary lesion was biopsied via a stereotactic transphenoidal approach. Histopathology disclosed fibrosis and a patchy mixed lymphoplasmocytic infiltrate without granulomatous features; there was positive immunostaining for IgG4 but this, together with the other morphological changes, was considered

Figure 1. **A.** T1-weighted coronal image demonstrating abnormal soft tissue of the bilateral cavernous sinuses (arrow). **B.** T2-weighted coronal image demonstrating normal enhancement of the pituitary infundibulum. **C.** MR angiogram depicting no flow within the internal carotid arteries due to occlusion in the cavernous sinuses. Flow is seen in the supraclinoid arteries. **D.** MR angiogram aortic arch to circle of Willis showing occlusion of the cavernous carotid arteries.

Figure 2. H&E stained section of anterior pituitary gland with patchy mixed lymphoplasmocytic infiltrate (A: x40, B: x400). The infiltrate disrupts the normal acinar pituitary architecture and damages hormone-secreting cells. The infiltrate is mainly mononuclear and comprises lymphocytes and scattered plasma cells.

insufficient to fulfil a diagnosis of IgG4 hypophysitis based on histology alone (Figure 2). A diagnosis of LYH was proposed and the patient was commenced on pulsed intravenous (IV) methylprednisolone 1-g daily for 3 days then was discharged from hospital with oral prednisone. Upon oral steroid dose tapering, the patient's diplopia relapsed requiring two further hospital admissions for pulsed IV methylprednisolone. The patient remains on a course of tapering oral prednisolone. She has had no further episodes of diplopia. Repeat neuroimaging was unchanged with persistence of her bilateral ICA occlusion.

Discussion

We report a case of a 50-year-old patient with bilateral abducens nerve palsies and pituitary dysfunction in the setting of LYH involving the parasellar soft

tissues and extending laterally into the cavernous sinuses bilaterally. Unlike other previously described cases, the ocular motor disorder was bilateral and intermittent and our patient had complete occlusion of the cavernous portions of the ICAs, with her brain perfused solely from the posterior circulation. She had a favourable response to treatment with high dose glucocorticoids, with resolution of her diplopia and restoration of normal pituitary function, though her ICAs remained occluded.

A presumptive diagnosis of LYH was proposed based on the patient's clinical, laboratory and imaging findings. Given that histopathology is the gold standard for LYH diagnosis, the patient underwent transphenoidal pituitary biopsy under the otolaryngology and neurosurgical teams. Histologically, there was marked lymphoplasmacytic infiltrate with areas of fibrosis and acinar pituitary architecture disruption establishing the diagnosis.

LYH is a neuroendocrine disorder characterised by autoimmune inflammation of the pituitary gland with varying degrees of pituitary dysfunction. Clinical presentation varies and includes symptoms of; headache and mass-effect with visual disturbance and impaired ocular motility, adenohypophyseal hypofunction, hypopituitarism, hyperprolactinaemia, and central diabetes insipidus.^{2,3} As with other autoimmune conditions, LYH is observed more frequently in women. In a significant proportion of women, LYH manifests during pregnancy or the postpartum period, postulated to be due to altered pituitary perfusion and increased accessibility by the immune system.^{2,4} LYH is also associated with other autoimmune diseases including Hashimoto thyroiditis, autoimmune polyglandular syndrome type 2, Graves' disease, systemic lupus erythematosus, and rheumatoid arthritis, with concurrent autoimmune disease present in up to 50% of LYH cases.^{2,3}

Based on histopathology, LYH is the most common cause of primary hypophysitis surpassing granulomatous, xanthomatous, necrotising, and IgG4-related hypophysitides.^{2,5} Secondary hypophysitis occurs due to inflammation originating from neighbouring lesions including craniopharyngiomas and pituitary adenomas, or as part of a systemic disease such as sarcoidosis, granulomatosis with polyangiitis, Langerhans cell histiocytosis, syphilis, and tuberculosis.²

Visual disturbance such as reduced VA and VF defects occur due to optic chiasm compression from upward expansion of the pituitary mass. Although visual disturbances are present in 40% of LYH, diplopia is a rare symptom, reported in less than 10% of cases.³ Patients develop diplopia from lateral expansion into the cavernous sinuses with compression of the oculomotor, trochlear, or abducens nerves and subsequent ocular misalignment.³ We report a unique presentation of LYH with bilateral abduction deficits due to bilateral abducens nerve involvement within the cavernous sinus from the lymphocytic infiltrate.

The natural history of LYH is considered to progress from inflammation, to fibrosis, and ultimately atrophy associated with permanent hypopituitarism.⁶ In some cases, the course of LYH is insidious, though our patient experienced a relapsing and remitting course with an initial presentation 2 years prior.

While non-contrast CT brain is considered the diagnostic modality of choice among radiologists for patients with an acute presentation of non-traumatic neurological symptoms to the ED, the utilisation of IV contrast, in the absence of contraindications, may result in improved sensitivity and better patient care. Our patient's diagnostic delay may have been averted with the administration of IV contrast.

The patient's symptoms were exquisitely responsive to glucocorticoids and her pituitary function normalised at 3 months. Endocrine and exocrine function in glandular organisation, as found in the lacrimal glands, salivary glands, pancreas and pituitary often improve after treatment. However, in concordance with our patient's occluded ICAs, advanced fibrosis and atrophy are less likely to completely recover.¹

This case highlights the notion that prompts diagnosis and treatment results in favourable outcomes, and prevents the inflammation progressing to fibrosis and subsequent pituitary

atrophy with irreversible hypopituitarism. In our patient, diagnosis was delayed, potentially by at least 2 years, culminating in irreversible occlusion to her ICAs. Adequate and aggressive glucocorticoid therapy improved organ function, and radiological and serological findings in our patient. LYH should be considered in the differential diagnosis of a patient presenting with an ocular motor palsy.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

ORCID

Anna M. Waldie <http://orcid.org/0000-0003-0419-6875>

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