Abstract  A 41-year-old man presented with left optic neuritis (ON) without evidence of other autoimmune disease or hormonal imbalance. MRI showed enlargement of the left optic nerve but no sellar lesion. The patient recovered after steroid therapy but later developed right ON and required treatment again. Follow-up MRI revealed an ill-defined, enlarging sellar lesion with enhancement extending into the right cavernous sinus, and the patient developed symptoms of fatigue and loss of libido. Hormonal studies revealed hypogonadism and hypocortisolism. All laboratory investigation for autoimmune and infectious diseases remained negative. A transsphenoidal biopsy of the lesion revealed lymphocytic hypophysitis. The concomitant development of lymphocytic hypophysitis and optic neuritis suggests a common and likely autoimmune etiology. Visual loss in patients with LYH can sometimes be due to ON rather than compression of the optic apparatus, with significant implications for treatment strategies.

Keywords  Lymphocytic hypophysitis · Optic neuritis · Pituitary

Introduction

Lymphocytic hypophysitis (LYH) is one of a spectrum of diseases involving inflammation of the pituitary gland and infundibulum. Patients typically present with signs and symptoms of hormonal deficiencies or visual loss due to compression of the optic nerves or chiasm. An autoimmune etiology has been proposed because of the typical histopathological findings and the frequent association of LYH with diseases such as Hashimoto’s thyroiditis and Type I diabetes mellitus. Optic neuritis (ON) is thought to have an autoimmune etiology as well, and it has rarely been reported in patients with LYH. We report the first case in the English language medical literature of a patient who presented with ON who later developed biopsy-confirmed LYH. We believe that this case report supports the hypothesis that LYH is an autoimmune disease. More importantly, the decision of whether or not to perform surgery in a patient with LYH often hinges on whether mass effect is causing visual loss. This case report demonstrates the need for careful neuro-ophthalmological evaluation and imaging in patients with visual loss and LYH, as ON rather than mass effect may be the cause of visual deterioration.

Case report

A 41-year-old man presented in 2007 with left eye pain and visual loss and was found to have left sided papilledema on fundoscopic examination. Visual acuity (VA) in the right eye was 20/25; with the left eye the patient could count fingers at four feet and only had a functioning superior nasal visual field. MRI revealed subtle enlargement of the left optic nerve (Fig. 1a), and a tiny, non-gadolinium
enhancing area on the left side of the sella thought to represent a microadenoma (Fig. 1b). A lumbar puncture revealed mild pleocytosis with 20 WBCs (mostly lymphocytes) and mildly elevated protein. Infectious disease serologies, serum and CSF angiotensin-converting enzyme levels, and CSF cytology were negative. CSF flow cytometry revealed activated T-cells and atypical B-cells but no evidence of lymphoma. Chest x-ray did not demonstrate evidence of sarcoidosis. The patient was diagnosed with ON and treated with high dose steroids. VA in the left eye improved to 20/40 and the patient was discharged home on a course of oral steroids.

Six months later, the patient developed right-sided visual loss and pain, and an MRI showed no new findings. He was treated again with corticosteroids for ON over several weeks but only partially recovered. Further laboratory investigation for autoimmune disease, including ANA, ANCA, and NMO-IgG antibodies, was negative. Visual field testing showed some cloverleaf activity in the left eye and little response in the right eye. VA was 20/60 in the right eye and 20/25 in the left eye. Over the ensuing months, the patient began to experience intermittent episodes of headache, dizziness, diaphoresis, fatigue, malaise, and worsened vision. Repeat brain MRI showed a homogeneously enhancing, poorly defined sellar mass with extension into the right cavernous sinus and suprasellar cistern and abutment of the optic chiasm (Fig. 1c). Incidental narrowing of the right internal carotid artery was discovered and later confirmed by MRA, but the patient never developed symptoms and was placed on aspirin prophylaxis. Partial endocrinologic testing revealed multiple hormonal deficiencies, including hypocortisolism, which was thought

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**Fig. 1**  
A Coronal, T2 weighted MRI of the sella at the time of initial presentation, showing subtle enlargement of the left optic nerve (arrow).  
B Coronal T1 weighted, gadolinium enhanced MRI of the sella at the time of presentation shows a tiny, non-gadolinium enhancing, lesion in the left side of the pituitary gland, thought to represent a pituitary adenoma.  
C Coronal T1 weighted, gadolinium enhanced MRI of the sella after development of constitutional symptoms and worsened vision shows diffuse enlargement of the sellar contents, abutting the optic chiasm (arrow). Incidental, asymptomatic narrowing of the right internal carotid artery may be noted.  
D Coronal T1 weighted, gadolinium enhanced MRI of the sella three months after surgery and treatment with corticosteroids shows that the sellar contents have decreased significantly in size, and the pituitary stalk and chiasm are well visualized.
to be iatrogenic, and hypogonadism, but normal thyroid function tests. Records of these hormonal studies are unavailable. Prednisone was prescribed and helped to relieve some of the patient’s systemic symptoms, and the patient was referred to our service.

Physical examination demonstrated a relative afferent pupillary defect in the right eye and bilateral optic atrophy, worse on the left. VA was 20/40 in the left eye, and only the ability to count fingers in the right eye, with a central scotoma and preservation of the peripheral visual fields. Extraocular movements and facial sensation were normal. Differential diagnosis at this time included inflammatory and neoplastic processes, including sarcoidosis, lymphoma, lymphocytic hypophysitis, meningioma, and pituitary adenoma. The patient underwent an endonasal transsphenoidal biopsy of the sellar lesion 21 months after his initial presentation. The bony sellar floor was thick and was opened with the pneumatic drill. The dura was unusually thick (at least 3 mm) and a piece was removed and sent as a separate specimen to pathology. No discrete sellar mass was seen; a normal-appearing, yellow anterior pituitary gland was biopsied. The normal, reddish appearing posterior pituitary gland was identified but not biopsied. Frozen specimen examination was nonspecific but showed a large lymphoplasmacytic population in both the pituitary tissue and dura. The patient had an uncomplicated course following his biopsy and was discharged home uneventfully.

Histopathologic analysis showed extensive lymphocytic and plasmocytic infiltration of the pituitary gland and disruption of the normal acinar architecture (Fig. 2) and lymphoplasmocytic infiltration of the sellar dura (not shown). Immunohistochemistry confirmed that the cells did not represent lymphoma, as both B and T cell markers were present. No evidence of granuloma was seen, ruling out histiocytosis or sarcoidosis. Immediate postoperative values revealed low serum cortisol (0.6 mcg/dL) and testosterone (total: < 1 ng/dL, free: < 0.1 pg/mL) with low ACTH (< 5 pg/mL), LH (< 0.1 mIU/mL), and FSH (0.6 mIU/mL). Serum prolactin level was normal (5.6 ng/mL). A transient hypothyroidism (TSH: 0.338 mcIU/mL, free T4: 0.8 ng/dL, free T3: 48.6 ng/dL) developed that was treated with levothyroxine and resolved. Follow-up endocrinologic studies revealed low serum testosterone (84 ng/mL, reference range 350-1030) but normal TSH and free T4 levels. IGF-1 and random growth hormone levels were in the low normal range (128 ng/mL and 0.32 ng/mL, respectively). The patient was treated with another course of steroids for LYH as well as with testosterone for hormone replacement

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**Fig. 2** Pituitary biopsy photomicrographs (×400) show (a) diffuse infiltration of the pituitary with a non-neoplastic lymphocytes and a few plasma cells (arrows), prominently near the capillaries and surrounding the pituitary acini on H&E (b) Immunohistochemical staining with antibodies to leukocyte common antigen (CD45) confirms the lymphocytic nature of the infiltrates (arrow) (c) Immunohistochemical staining with antibodies to Chromogranin, which label normal pituitary acinar cells (arrows) reveals the striking distortion of the normal pituitary micro-architecture.
therapy. His constitutional symptoms improved significantly; three months after surgery, visual acuity is 20/50 in the right eye and 20/25 in the left eye, with full visual fields to finger motion. MR imaging three months after surgery showed regression of the sellar and parasellar mass (Fig. 1d).

Discussion

Lymphocytic hypophysitis (LYH) is an inflammatory lesion of the pituitary gland that may result in a sellar mass with signs or symptoms of mass effect (e.g., headache or visual field abnormalities) or in destruction and fibrosis of the pituitary with resultant endocrinopathy. LYH has an unpredictable natural history and sometimes regresses spontaneously. A symmetrically enlarged and homogeneously enhancing pituitary gland or infundibulum is commonly seen on MRI, with potential involvement and enhancement of adjacent structures such as the cavernous sinus, optic chiasm, or clivus.

LYH may be subdivided into cases involving the anterior gland (lymphocytic adenohypophysitis or LAH), the posterior gland and/or infundibulum (lymphocytic infundibuloneurohypophysitis or LINH), or the entire gland (lymphocytic infundibulopanhypophysitis or LIPH). The classic presentation of LYH is that of LAH occurring in a postpartum woman, although the number of cases of LINH is on the rise, more often affecting men and children. The clinical presentation is typically that of a specific hormonal deficiency and depends on the pituitary segment mostly affected. LAH causes early destruction of corticotrophs, commonly resulting in hypocortisolism and associated symptoms, while LINH usually presents with central diabetes insipidus (CDI) and LIPH presents with symptoms of both disorders. As many as 70% of LYH patients have circulating pituitary autoantibodies, and 25-50% have coexisting autoimmune disorders [1–3]. Very few cases of LYH have been reported previously in association with ON, and each of those patients presented with CDI initially, was diagnosed with a subtype of LYH, and later developed ON [4–6]. There is one case report of a middle-aged man with LIPH presenting with multiple progressive symptoms who initially had unilateral blurry vision four months prior that spontaneously resolved in a few weeks, and while the publication appears to attribute the patient’s visual symptoms to optic chiasm involvement as seen on MRI, these images were not obtained until months after his vision returned [7]. In the case of our patient, the imaging and clinical findings at the time of initial presentation confirm that the initial diagnosis was ON rather than visual loss from compression of the optic apparatus. This case report further supports the linkage between LYH and autoimmune disease, in this case ON. We speculate that the rare cases of ON associated with LYH may be explained by the close anatomic relationship between the optic nerves and sella, with spread of local inflammation to adjacent structures.

The mainstay of treatment for LYH is medical, including hormone replacement and immunosuppression with corticosteroids [1, 2, 7–9], although steroid-unresponsive disease has been described and may be treated with other drugs or radiation therapy [1, 7, 8, 10]. Surgical resection (typically via a transsphenoidal approach) may be required in cases of substantial mass effect on the optic apparatus. Hypopituitarism is almost certainly related to dysfunction of inflamed pituitary gland rather than to compression of functional parenchyma by the affected tissue, and surgery should not be performed with the goal of improving endocrinological function [7].

The major significance of this report is that visual loss in a patient with LYH should not always be attributed to mass effect on the optic apparatus, which would generally be treated by aggressive surgical decompression. The exact nature of the visual loss (for example, central scotoma) and careful examination of the imaging studies may allow confident diagnosis of ON in the setting of LYH and spare patients from having unnecessary decompressive surgery. Our patient, however, did require surgery for diagnostic purposes.

Conclusions

To the best of our knowledge, this is the first reported case of a patient presenting with ON who later developed LYH, and it further supports the theory of an autoimmune etiology of LYH. The case demonstrates the importance of careful neuro-ophthalmologic and radiographic evaluation...
of patients with LYH and visual loss, as ON must be considered in the differential diagnosis, and treatment choice differs depending on whether ON or mass effect is responsible for visual loss.

References