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Case Report

Lymphocytic Panhypophysitis Mimicking Glaucoma: Case Report

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Abstract
Lymphocytic hypophysitis (LH) is a primary inflammatory disorder of the pituitary gland and infundibulum that commonly manifests in both mass effect and endocrinologic symptoms. Although the exact pathophysiology remains unclear, it has been increasingly linked to an autoimmune process. Complications arise by two separate mechanisms. Inflammation in the sella can lead to headaches and visual field defects. Pituitary inflammation and, chronically, fibrosis interfere with the gland's hormone-secreting capacity, often resulting in various endocrinopathies such as polyuria, polydipsia, amenorrhea, and others. While final histologic classification requires pathologic evaluation, diagnosis can often be made clinically with appropriate imaging. Treatment often consists of conservative management but can also include glucocorticoids or surgical resection. We present a case of biopsy-proven LH involving the entire pituitary, dubbed lymphocytic panhypophysitis (LPH) that was misdiagnosed for years as glaucoma due to the lack of endocrinopathy as well as delay in magnetic resonance imaging. After imaging revealed the sellar mass, the patient responded symptomatically to surgical resection and glucocorticoid treatment. LPH may present without endocrinologic symptoms and therefore mimic alternate diagnoses such as glaucoma. Clinicians should be suspicious of a diagnosis of glaucoma in the setting of a temporal field defect and lack of response to traditional therapy. A personal or family history of autoimmune disease in such patients should prompt

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further imaging and investigation. Therefore, endocrinopathy is supportive but not present in every case of LPH.

Introduction

Lymphocytic hypophysitis (LH) is a primary, autoimmune, and inflammatory lymphocytic process involving the pituitary gland and infundibulum that can result in hypopituitarism [1]. LH occurs more than twice as often in women than in men, usually during the end of pregnancy or the first few weeks after delivery [2]. Anatomical classifications include the most common lymphocytic adeno-hypophysitis, lymphocytic infundibulo-neurohypophysitis, and lymphocytic panhypophysitis (LPH) based on the degree and location of pituitary involvement [1]. Previous reports of LPH document presenting symptoms related to both mass effect and pituitary dysfunction such as diabetes insipidus [3]. We report to our knowledge the first case of LPH presenting only with headache and diplopia, mimicking glaucoma, and avoiding appropriate diagnosis and treatment for several years.

Case Report

A 59-year-old white female presented to the Houston Methodist Hospital neuro-ophthalmology clinic in September 2019 with bilateral progressive blurry vision (left eye worse than right), diplopia, headaches, and difficulty focusing at any distance for 1 year. She carried with her a previous diagnosis of glaucoma diagnosed 18 years ago out-of-state and treated with latanoprost. After 12 years of treatment, she was told by another provider out-of-state that she did not have glaucoma and stopped taking her medication. Her vision was stable until she presented to a glaucoma specialist in 2017 after moving to Houston. She described worsening headaches with an exam showing partial bitemporal hemianopsia and an intermittent esotropia of the right eye.

Past medical history was significant for hypothyroidism and hypertension. Past ocular history was significant for a retinal tear in the left eye (OS) in 2010 which was repaired with laser retinopexy and bilateral laser-assisted in situ keratomileusis surgery in 2005. Her medications included levothyroxine, propranolol, olopatadine, Symbicort/Dulera, estradiol, medroxyprogesterone, and valacyclovir. Family history was significant for glaucoma, hypertension, hypercholesterolemia, diabetes mellitus, myocardial infarction, autoimmune thyroiditis, and migraines.

Magnetic resonance imaging (MRI) with contrast of her brain showed a heterogeneously enhancing intrasellar mass with suprasellar extension causing deviation of the infundibulum and compression of the pre-chiasmatic optic nerve. She was then referred to endocrinology for further evaluation. Her prolactin level was 24.5 (normal: 5–23 ng/mL), cortisol was 22.8 (normal: 6–18 μg/dL), and estradiol was 36 (normal: <55 pg/mL). Insulin-like growth factor, growth hormone, adrenocorticotropic hormone, serum IgG4 levels, testosterone, complete blood count, and hemoglobin A1c were all normal. Her antinuclear antibody testing was positive in a speckled pattern. The remaining autoimmune workup including rheumatoid factor, thyroid-stimulating immunoglobulin, anti-thyroid peroxidase, anti-Sjögren's syndrome-A, anti-Sjögren's syndrome-B, anti-ribonucleoprotein, anti-Smith, anti-scleroderma-70, anti-chromatin, anti-Jo, anti-centromere, and anti-aquaporin 4 antibodies were all negative.

Neuro-ophthalmic examination revealed a visual acuity of 20/20 in both eyes (OU). External examination was normal. She had no dacryoadenitis, retroperitoneal fibrosis, or salivary gland enlargement. Her pupils measured 4 mm in the dark and 2 mm in the light. There was no anisocoria or relative afferent pupillary defect. Her Humphrey visual field mean deviation was −3.98 right eye (OD) and −4.76 left eye (OS) with enlargement of the blind spot OU and a bitemporal hemianopic field defect (shown in Fig. 1a). Optical coherence tomography (OCT) of the retinal nerve fiber layer measured 77 microns OD and 89 microns OS. The macular ganglion cell layer on OCT (acquired using a Heidelberg Engineering HRA+OCT Spectralis machine) was consistent with pre-chiasmatic mass effect (shown in Fig. 1b). Her cup-to-disc ratio was 0.6 in each eye with apparent horizontal cupping. She had a posterior staphyloma from high myopia and evidence of laser therapy OS. Eye motility examination showed a variable esotropia with an abduction deficit in the right eye.

In October 2019, neurosurgery performed a transsphenoidal resection with biopsy, which demonstrated IgG4-negative pituitary lymphocytic adeno-infundibular neurohypophysitis. She was subsequently treated with 3 weeks of hydrocortisone, after which her headaches resolved. In September 2020, she was found to have a worsening field defect but no optic chiasm impingement on repeat MRI. A 12-week course of hydrocortisone stabilized her field defect, and she has since remained without recurrence of headaches, diplopia, or difficulty concentrating.

The patient has had serial evaluations and has shown a stable bitemporal hemianopic field defect with band atrophy in the left eye. Her last MRI scan was performed on July 15, 2022, which showed transsphenoidal postoperative change and the pituitary demonstrated a stable appearance confirmed at our neuro-ophthalmology conference. At follow-up clinics, she has remained completely asymptomatic. On her latest exam with us in December of 2022, her visual acuity was 20/25 (OD) and 20/20 (OS), and intraocular pressure was 16 (OD) and 13 (OS). Humphrey visual field showed a mean deviation of −3.40 (OD) and −4.59 (OS) with a bitemporal hemianopic field defect. OCT global was 92 (OD) and 76 (OS) with sector band atrophy in the left eye. Motility was full. Pupils were normal without an RAPD. The rest of the structural eye examination was normal. Table 1 depicts the patient's pachy-corrected IOP journey since moving to Houston in 2017. The patient was thoroughly pleased with the treatment received and continues to follow up yearly with neuro-ophthalmology though she has been without ophthalmologic or neurologic complaints for the past few years.

Discussion

Much of the details of the pathophysiology of LH remain ill-defined. General understanding involves an autoimmune process that leads to enlargement of the gland in the acute phase and fibrosis of the gland with varying severity depending on the extent/duration of inflammation [1]. Thus, pituitary inflammation and enlargement can lead to various mass effect symptoms such as headaches, diplopia, and temporal visual field defects and impede the gland's hormone-secreting capacity. Chronically, pituitary fibrosis secondary to sustained inflammation commonly leaves patients requiring hormonal supplementation [1, 4]. LH routinely demonstrates symptoms resultant of a dysregulated anterior and posterior pituitary including polyuria, polydipsia, malaise, dizziness, hypo/hyperprolactinemia, loss of pubic and axillary hair, and amenorrhea [3, 4]. An autoimmune association has been further supported by a family history of autoimmune disease, especially those associated with HLA-DQ8 and DR3, predisposing patients to LH [5, 6]. Specifically, the HLA-DQ8 and HLA-DR53 markers have been noted in 87% and 80% of patients with biopsy-proven LH [7]. Differential diagnoses for pituitary lesions can include pituitary adenomas, secondary hypophysitis, pituitary apoplexy, Sheehan's syndrome, pituitary metastases, and physiologic pituitary hypertrophy.

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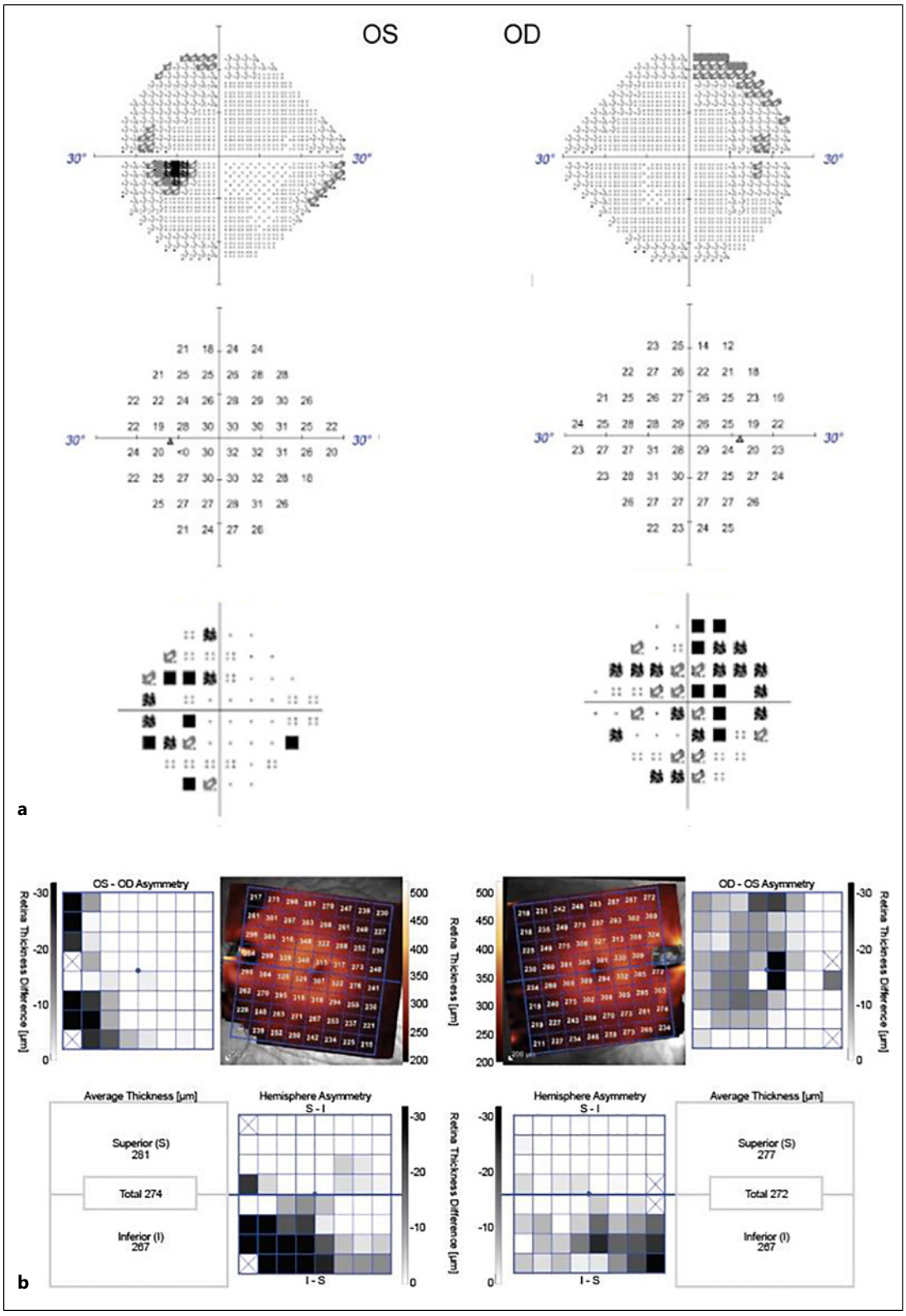

Fig. 1. a Humphrey visual field with total deviation. **b** Macular ganglion cell layer thickness measurement showing a bilateral temporal hemianopic field defect secondary to LH contact of the prechiasmatic optic nerve.

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Table 1. Pachymetry and intraocular pressure data measured over 5 years in our patient

Pachymetry and intraocular pressure				
	intraocular pressure		corrected intraocular pressure	
	OD	OS	OD	OS
12/28/17 Pachymetry	482	484		
1/12/23	17	12	*21*	*16*
12/22/22	33	11	*37*	*15*
12/13/22	14	13	*18*	*17*
11/7/22		17		*21*
11/2/22	14	16	*18*	*20*
10/27/22		37		*41*
10/17/22		15		*19*
9/20/22	14	15	*18*	*19*
11/2/21	16	14	*20*	*18*
4/27/21	16	16	*20*	*20*
11/12/19	17	17	*21*	*21*
7/29/19	14	13	*18*	*17*
7/23/19	9	10	*13*	*14*
12/28/17	18	18	*22*	*22*
11/27/17	14	13	*18*	*17*

Intraocular pressure values are corrected for using the pachymetry results.

In patients diagnosed with LH, visual disturbances are cited to occur in up to 52% of cases, occurring more frequently in adeno-hypophysitis when compared to lymphocytic infundibulo-neurohypophysitis or LPH. Common visual complaints with their reported rates of occurrences in the literature are noted in Table 2.

LPH is a rare form of LH that occurs twice as often in women but does not share a strong association with pregnancy and occurs a decade later in females compared to males [4]. However, isolated cases occur during pregnancy and biopsy-proven cases occur in patients from 20 to 77 years old [3, 12]. As LPH involves the entirety of the pituitary, many disease manifestations are possible. In a case series of 5 patients presented by Wada et al. [3], 80% of patients diagnosed with LPH presented with polyuria, while no patients presented with headache and visual complaints alone. In addition to the mass effect symptoms such as headache and diplopia and subsequent appropriate imaging, these clinical features are often sufficient to uncover the diagnosis. However, the case here described is unique in that, while our patient had a history of treated hypothyroidism diagnosed many years before the onset of her current episode of symptoms, she presented without any common accompanying endocrinologic complaints. Likely because of such an unusual presentation, our patient was misdiagnosed with and treated for glaucoma for several years before undergoing diagnostic imaging.

Clinicians should hold high suspicion for intrasellar lesions for glaucoma diagnoses with nonclassical visual field defects, especially bitemporal hemianopsia. Though the differential of sellar masses is broad and diagnosis of LH/LPH is only possible with biopsy, the association with other autoimmune diseases should decrease the threshold for pituitary imaging [4]. Hypopituitarism symptoms are diagnostically useful but not present in every case of LPH. The

Table 2. Reported visual disturbances associated with LH are cited to occur at varying frequencies

Visual disturbance	Rates of occurrence, %
Chiasmal syndrome [8]	15
Ocular motor paresis with diplopia [9, 10]	7
Decrease in visual acuity [11]	16
Visual field defects [11]	34

CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531445).

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. This report does not include any identifying patient information. All actions related to this study were performed in accordance with the World Medical Association Declaration of Helsinki. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

Phillip Keys, Patrick Hunt, Clement Anozie, Samir Cayenne, Pamela Davila Siliezar, Noor Laylani, and Andrew G. Lee declare that they have no conflict of interest.

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Author Contributions

Phillip Keys, Patrick Hunt, Clement Anozie, and Samir Cayenne drafted and edited the manuscript. Andrew Lee, Pamela Davila-Siliezar, and Noor Laylani performed the medical treatment, conducted the follow-up of the patient, and critically reviewed the manuscript. All authors were involved in the conception and design of the manuscript as well as the acquisition and interpretation of data. All authors approved the final version of the manuscript and attest to meeting ICMJE criteria for authorship.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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