A Case of Undiagnosed Craniopharyngioma in an Army Mechanic

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ABSTRACT Primary care providers are often the initial evaluators of soldiers presenting with acute eye complaints. It is crucial for these providers to master performing the basic eye examination with a systematic approach. Obtaining a thorough history is an important first step to the eye examination, but providers need to be careful not to narrow the diagnosis solely based on the history. Regardless of the presentation of the ocular complaints, a complete ocular examination must be performed. This article presents a case of brain tumor in an active duty soldier who was initially undiagnosed because of its unusual presentation.

INTRODUCTION

Craniopharyngiomas, also known as Rathke pouch tumors or hypophyseal duct tumors, are rare, solid or mixed solid and cystic tumors arising from Rathke's pouch remnants.[1] There are an estimated 350 new cases of craniopharyngioma diagnosed each year in the United States alone.[2] Craniopharyngioma has an overall incidence of 0.5 to 2.0 new cases per million per year, and approximately 30 to 50% of all cases are childhood craniopharyngiomas.[3] There is a bimodal age distribution with the first peak between 5 and 14 years and a second peak between 50 and 75 years of age.[4] Typical clinical symptoms include headache, visual disturbances, weight gain, polyuria/polydipsia, and growth retardation secondary to effects on the pituitary gland. We report a case of craniopharyngioma that was undiagnosed initially because of an unusual presentation.

CASE

A 36-year-old active duty male mechanic at a military base in central Texas with history of attention deficit hyperactivity disorder and chronic low back pain presented to his battalion surgeon for decreased visual acuity of his left eye. Before his clinical presentation, he was cleaning tools while at the motor pool when he accidentally splashed his left eye with a few drops of chemical-based cleaner. The patient immediately flushed his eye profusely with tap water. Over the next few days, his vision worsened and he presented to an urgent care clinic for evaluation. During that encounter, the patient's eyes were stained with fluorescein dye and no corneal injury was found. He was diagnosed with dry-eye syndrome and sent home with directions to apply artificial tears. Despite using the eye drops as directed, he reported progressive deterioration in his vision, especially on his left side. Therefore, he presented to the battalion surgeon for re-evaluation of his eye complaints. He denied any foreign body sensation, discharge, pain, new development of floaters, flashes, diplopia, or photophobia. He endorsed having daily moderate frontal headache; he had experienced these headaches before but never this frequently. The patient denied any nausea or vomiting but stated he had been more lethargic which he attributed to decreased sleep from the headaches. He was taking Adderall XR 25 mg daily, Celebrex 200 mg daily and was not allergic to any medication. Family history was unremarkable.

Distant visual acuity assessed using a Snellen chart were OD 20/50 OS 20/160 with no improvement on pinhole test. He stated before the injury he was able to see close to 20/25 when wearing glasses. Intraocular pressures were OD 16 OS14 with Tono-Pen. Extraocular eye movements were full and smooth. His pupils were equal round and reactive to light and accommodation. On confrontation visual field examination, the patient had left temporal heminanopsia. Ophthalmoscope examination revealed lids/lashes clear, bulbar conjunctiva white/quiet, palpebral conjunctiva clear, cornea clear and smooth, anterior chamber deep and quiet, iris flat and intact. Limited posterior segment evaluation with undilated pupil showed no enlarged cup to disc ratio and normal vessels. The rest of the examination was unremarkable. Because of the finding of left temporal hemianopsia and decreased visual acuity, the patient was referred immediately to ophthalmology where a formal visual field examination was completed the next day (Fig. 1). This confirmed the presence of left temporal hemianopsia and demonstrated the beginning of a right temporal hemianopsia. An magnetic resonance imaging (MRI) of the brain/pituitary without contrast was ordered and a suprasellar mass measuring 2.4 × 2 × 1.8 cm was found (Fig. 2). This mass abutted the superior margin of the pituitary gland and appeared to be separate from the normal appearing pituitary gland. Differential diagnosis included pituitary adenoma, craniopharyngioma, meningioma, and Rathke's cleft cyst. He was referred immediately to Neurosurgery. Two days after the MRI results were obtained an endoscopic endonasal transsphenoidal supradiaphragmatic resection of the mass was completed, with final pathology showing adamantinomatous craniopharyngioma.

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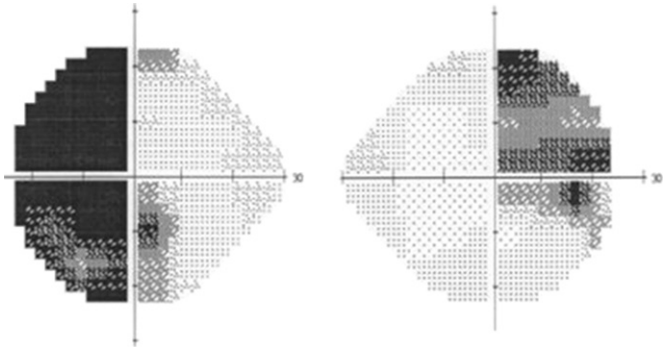

FIGURE 1. Visual field (central 24-2 threshold test) of the patient at initial presentation to ophthalmology, showing bitemporal hemianopia.

The diagnosis was made 8 days after the initial visit with his battalion surgeon.

DISCUSSION

This patient presented originally with unilateral decrease in vision after sustaining a chemical spill to the eye while working at the motor pool. The initial evaluation at the urgent care clinic included a penlight examination, fundoscopic examination, and a fluorescein examination. The history of unilateral decreased vision after a chemical irritant injury to the eye while working with motor vehicles certainly suggests either a foreign metallic body or corneal epithelial defect secondary to chemical burn. A Wood's lamp was used, and no staining

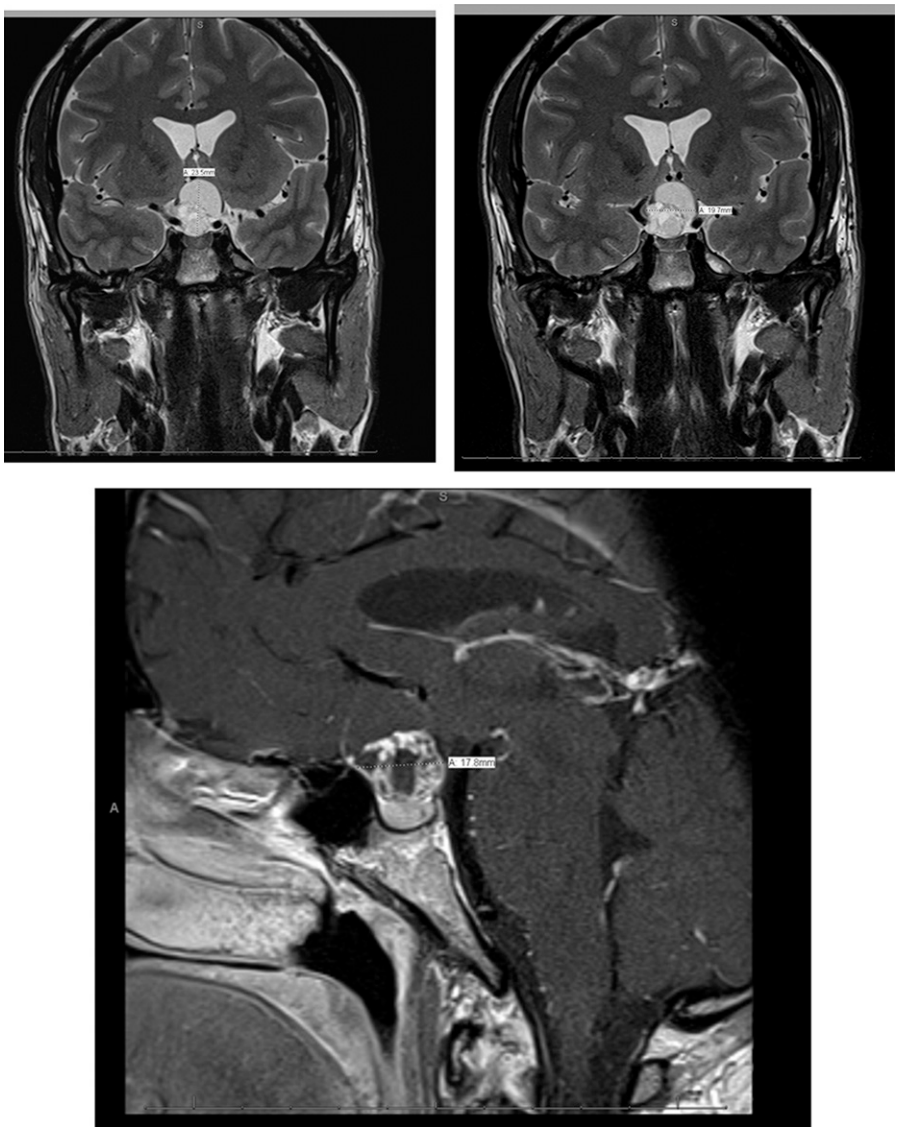

FIGURE 2. MRI of the brain/pituitary gland showing a supracellar mass measuring 2.7 × 2 × 1.9 cm. Mass abuts the superior margin of the pituitary gland and appears to be separate from the normal appearing pituitary gland.

TABLE I. Basic Eye Examination

History	History of present illness, ocular history, medical history, medication, allergies.
Visual Acuity	Should be measured one eye at a time. Right eye first, then pinhole test to determine refractive vs pathologic.
External Examination	Eyelids, lashes, cornea, sclera and conjunctiva, anterior chamber, iris.
Pupils	Should be examined in a medium dark room. Determine size/shape. Check for light reaction. Assess for afferent pupillary defect.
Visual Fields	Finger confrontation in 4 quadrants. One eye at a time.
Extraocular Movements	Horizontal and vertical.
Intraocular Pressure (IOP)	Use tonometer. IOP varies, with the mean at 15 mm Hg. 10 to 21 mm Hg falls within 2 SD of mean.
Fundoscopy	Look for the optic nerve head and note the color, margins, cup to disc ratio, spontaneous venous pulsations. The macula is located a disc and a half temporal and slightly inferior from the nerve head. Assess for exudates and hemorrhages. Follow all 4 sets of blood vessels and assess for caliber changes.

defect was seen with fluorescein dye. Seidel test was negative. With negative fluorescein examination, the patient was sent home with artificial tears and a diagnosis of dry-eye syndrome. Unfortunately, no visual acuity was obtained at the initial visit. Had a visual acuity been performed initially, the patient's diagnosis may not have been further delayed.

In the primary care setting, providers are often uncomfortable as the initial evaluator for eye complaints. Although an ophthalmoscope may be present, the frequent lack of dilating agents makes the examination of an undilated pupil more challenging. Primary care providers should have a systematic approach to the eye examination regardless of the presenting complaint. Vision should be documented for every patient seen with an ocular complaint. This should be done before lights are shined in the eye and pinhole test should be done to determine if the decrease in visual acuity is refractive or pathologic. A pinhole occluder focuses light and can remove the effects of refractive errors as light passes only through the center of the lens. An external examination then should be done with a penlight to evaluate the lid/lashes/lacrimal duct, conjunctiva and sclera, the anterior chamber, and iris. Next the pupils should be examined in a medium dark room. Shape, light reaction, and afferent pupillary defect should be checked. Visual fields can then be assessed using the finger confrontation method. Next, the extraocular movements are tested to determine if the patient has any horizontal or vertical defect with eye movement. If a handheld tonometer is available, intraocular pressures should be determined. Finally a fundoscopic examination should be done with the room lights dimmed as much as possible. Check first for red reflex and attempt to visualize the disc, the macula, the blood vessels, and the retina. If possible, dilate the pupil using 2.5% phenylephrine and 1% tropicamide to enhance visualization of these structures. Table I lists the key elements to a thorough eye examination. By using this algorithm, abnormalities were detected in the visual acuity and the confrontational visual field, leading to an urgent referral to ophthalmology.

Treatment included gross total resection of the suprasellar mass. Microscopically, the tumor demonstrated classic features of adamantinomatous craniopharyngioma including anastomosing epithelial trabeculae with peripherally palisaded areas, microcysts filled with pale pink-staining proteinaceous fluid, looser "stellate reticulum" areas, prominent nodules of "wet keratin" containing anucleate squamous cells, and foci of dystrophic calcification in the absence of characteristic "machine oil" like cyst fluid (Figs. 3–5). Craniopharyngiomas are rare, nonglial, intracranial tumors derived from malformation of embryonic tissue. Current hypotheses on its embryonic origin include ectodermal remnants of Rathke's pouch and residual embryonal epithelium of the anterior pituitary gland.[5] They can arise anywhere along the craniopharyngeal canal, with the majority having a suprasellar location.[1] There are two subtypes, adamantinomatous and papillary, arising in children and adults, respectively. Recent clonal mutations including *CTNNB1* (β-catenin) in adamantinomatous craniopharyngiomas and *BRAF* (V600E) in papillary craniopharyngiomas have been described.[6]

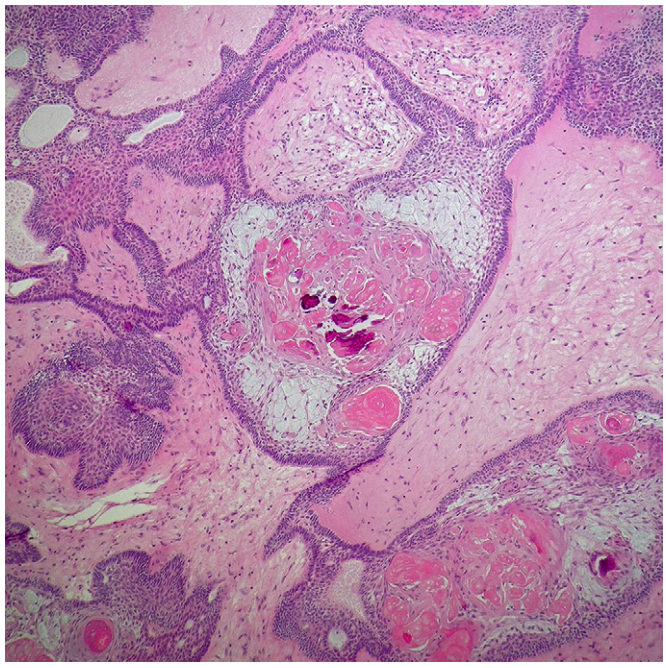

FIGURE 3. Photomicograph of the specimen showing interconnected foci of eosinophilic anucleate squamous cells (some with calciferation) compressing the "wet keratin" component that are surrounded by palisaded epithelial cells and looser "stellate reticulum" areas (100× original magnification).

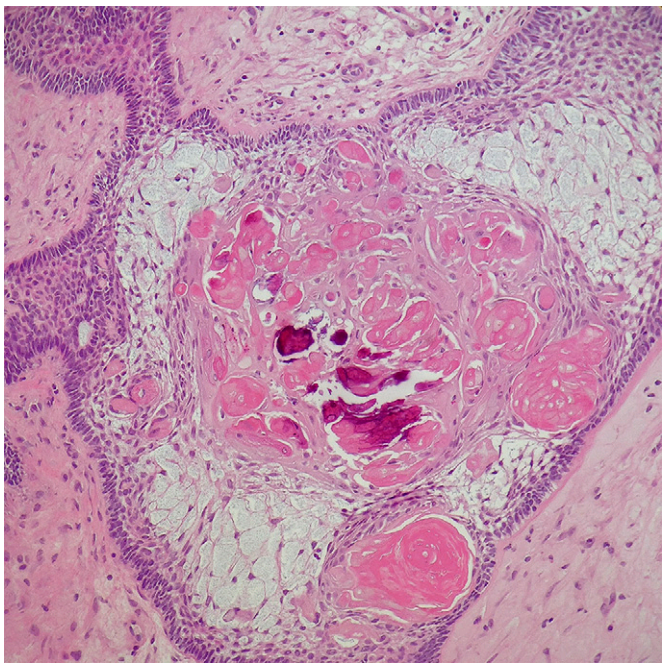

FIGURE 4. Photomicograph of the specimen showing eosinophilic anucleate squamous cells (some with calcification) comprising "wet keratin" component that are surrounded by palisaded epithelial cells and looser "stellate reticulum" areas (200× original magnification).

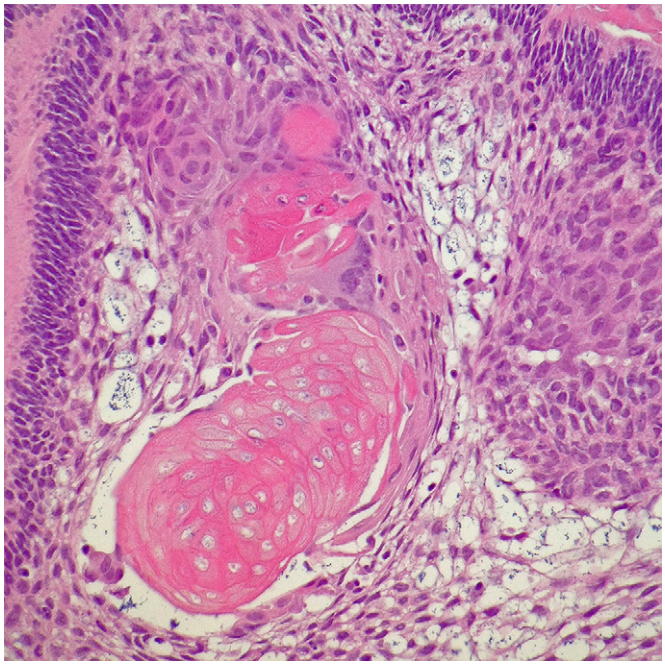

FIGURE 5. Photomicograph of the specimen showing eosinophilic anucleate squamous cells (some with calcification) comprising "wet keratin" component that are surrounded by palisaded epithelial cells and looser "stellate reticulum" areas (200× original magnification).

Because of its slow growing nature, symptoms are often present for a year or more before the diagnosis is made.[7] Symptoms include headache and nausea which are nonspecific manifestations of intracranial pressure.[8] Visual symptoms are frequent, often as a direct result of pressure on the optic chiasm. Patients of about 40 to 87% were also present with at least one hormonal deficit[9,10] to include growth hormone, gonadotropin, thyroid-stimulating hormone, and adrenocorticotropic hormone. Diabetes insipidus is frequently associated with craniopharyngiomas, presenting preoperatively in 17 to 27% of patients.[10,11] Endocrine testing, especially adrenal and thyroid function, is indicated before treatment as many patients patient with craniopharyngioma will have at least partial hypopituitarism.

The diagnosis of craniopharyngioma is usually made by the presence of a mass on MRI or computed tomography. The most common localization is suprasellar with an intrasellar portion; only 20% will be exclusively intrasellar.[3] Common radiological clues are the combination of solid, cystic, and calcified tumor components.

Treatment of craniopharyngiomas remains controversial and includes two basic approaches consisting of either aggressive surgery in an attempt to achieve complete resection or a conservative surgical approach with adjunctive radiation therapy to treat residual disease.[12] The goal of surgery is to first establish diagnosis, alleviate mass-related symptoms such as compression of the optic pathways, and finally to remove as much tumor as safely possible. Depending on the location of the tumor, a transcranial or transsphenoidal approach can be performed. Several small retrospective studies have suggested rates of obesity and diabetes insipidus may be lower in patients treated with more conservative surgical approaches.[13,14] Current radiation therapy techniques allows for great treatment precision and conformity.

Treatment complications include neurologic, visual, endocrine, and vascular abnormalities. Common neurologic complications include impaired intellectual functioning,[15] sleep disorders and disruption of circadian rhythm,[16,17] and behavioral problems.[18] Visual deficits before treatment may be exacerbated by treatment. In the majority of treated cases, panhypopituitarism is present and is manifested by hypogonadism, hypothyroidism, adrenal insufficiency, and growth hormone deficiency.[19] Hypothalamic damage can cause disabling obesity because of disturbance in energy management. This is exacerbated by marked daytime sleepiness and disturbances in circadian rhythm.[20] Other endocrine complications include disorders of temperature regulation and diabetes insipidus. A variety of vascular abnormalities including cavernomas and aneurysms can follow radiation.[21] Moyamoya syndrome, a radiation-induced cerebrovascular condition predisposing to stroke, has been described.[21,22] A retrospective series of 123 patients with craniopharyngioma treated with multimodality therapy found 14 patients had experienced transient ischemic attack or stroke.[19]

There are no evidence-based guidelines for follow-up after initial therapy. Management should include neuroimaging with annual MRI, annual visual field testing, and monitoring of endocrine function. Recurrent disease is most frequently local. Management of recurrent tumor is difficult as scarring from previous operations or radiation treatment decrease the possibility of successful excision. Perioperative morbidity and mortality is increased with a second surgery, so radiotherapy options should be considered in a recurrence.[23,24]

The long-term prognosis in craniopharyngioma patients is affected by both the tumor itself and treatment received. Overall mortality rates are three to five times higher than those of the general population.[25,26] Tumor size is likely a prognostic factor as increased survival rates have been shown in tumors with a diameter smaller than 3 cm.[27] Some studies also described a more favorable prognosis when tumors lack calcification especially in adults.[27,28] In a series of 121 cases, the 10-year survival rate following presentation was 90% when nontumor related deaths were excluded.[23] However, late mortality may be increased in patients without tumor progression and may be related to complications of treatment. In a series of 41 patients treated over a 37-year period, there were 9 deaths overall. Four occurred more than 10 years after presentation, and the causes were uncontrolled diabetes insipidus, pontine infarction, panhypopituitarism, and liver failure.[29] Other causes of late mortality include hypothalamic insufficiency, hormonal deficiencies, cerebrovascular disease, and seizures.

CONCLUSION

The above case highlights the importance of performing a complete eye examination in patients presenting with ocular complaints. Although the initial urgent care provider elicited a good history which indicated injury to the cornea as the most likely explanation to the visual changes, a more serious disease was the cause to the patient's symptoms. Even without access to advanced diagnostic tools such as a slit-lamp or formal visual field testing, a complete eye examination can be done. Assessing distant visual acuity and confrontational visual fields allowed for the prompt diagnosis and treatment of this patient with craniopharyngioma. Every clinician should develop a systematic approach to the eye examination to avoid missing pertinent signs that can help reach the correct diagnosis.

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