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Polymorphous low-grade adenocarcinoma with cavernous sinus involvement presenting as third nerve palsy

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ABSTRACT

Purpose: Polymorphous low-grade adenocarcinoma is a tumor of the salivary glands that typically localizes within the oral cavity. We present a case of isolated third cranial nerve palsy as the initial presentation of polymorphous low-grade adenocarcinoma involving the left cavernous sinus in a patient status post glaucoma surgery.

Observations: A 68-year-old woman status post glaucoma drainage device implantation in her left eye presented with an isolated left third nerve palsy ten weeks postoperatively. Differential diagnoses included microvascular ischemic neuropathy, postoperative ptosis, and compressive mass. MRI revealed a left cavernous sinus mass, and subsequent excisional biopsy revealed a diagnosis of polymorphous low-grade adenocarcinoma.

Conclusions: There are few cases reporting polymorphous low-grade adenocarcinoma originating from and extending beyond the nasopharynx. This report emphasizes an unexpected neuro-ophthalmic manifestation of this salivary gland tumor.

1. Introduction

Isolated third cranial nerve palsy is a neuro-ophthalmologic presentation that can be secondary to a number of etiologies, including compressive masses. Polymorphous low-grade adenocarcinoma (PLGA) is a tumor of the minor salivary glands that classically presents as an intraoral painless mass of the hard palate, tongue, upper lip, or tonsils.[1] Extraoral presentations of PLGA are rare. We report a case of PLGA presenting as a left cavernous sinus mass causing third nerve palsy in a patient status post glaucoma surgery.

2. Case report

A 68-year-old female status post glaucoma drainage device (GDD) implantation in her left eye (OS) presented for a follow-up at the glaucoma clinic at the ten-week post-operative mark. The patient's prior post-operative course had been unremarkable. She reported a new five-day history of worsening left upper lid ptosis and retro-orbital headache. She denied changes in visual acuity, weakness, fever, dysphagia, sense of smell, or voice.

Her past medical history was remarkable for hypertension, hyperlipidemia, and a forty-year history of uncontrolled type 2 diabetes on insulin complicated by neuropathy and nephropathy.

The patient had a past ocular history of bilateral primary open angle glaucoma that was more severe in the left eye as well as proliferative diabetic retinopathy. Her past ocular surgical history included a superotemporal GDD implantation OS four years prior, an inferonasal Baerveldt GDD implantation ten weeks ago, bilateral panretinal photocoagulation for proliferative diabetic retinopathy, and cataract surgery OS.

The patient underwent an uncomplicated inferonasal GDD implantation OS ten weeks prior with good subsequent IOP control. Her 10-2 Humphrey Visual Field testing showed a defect consistent with her glaucoma (Fig. 1) with corresponding superior and inferior thinning of the retinal nerve fiber layer (RNFL) on optical coherence tomography (OCT) (Fig. 2). Visual acuity was essentially unchanged from her preoperative baseline and varied between 20/60 to 20/80.

Upon examination, she was found to have severe left upper eyelid ptosis (margin reflex distance of −4 mm) with hypotropia and exotropia in primary gaze and impaired supraduction, infraduction, and adduction past the midline. No relative afferent pupillary defect was noted, though efferent function of both pupils was impaired from past surgery. Visual

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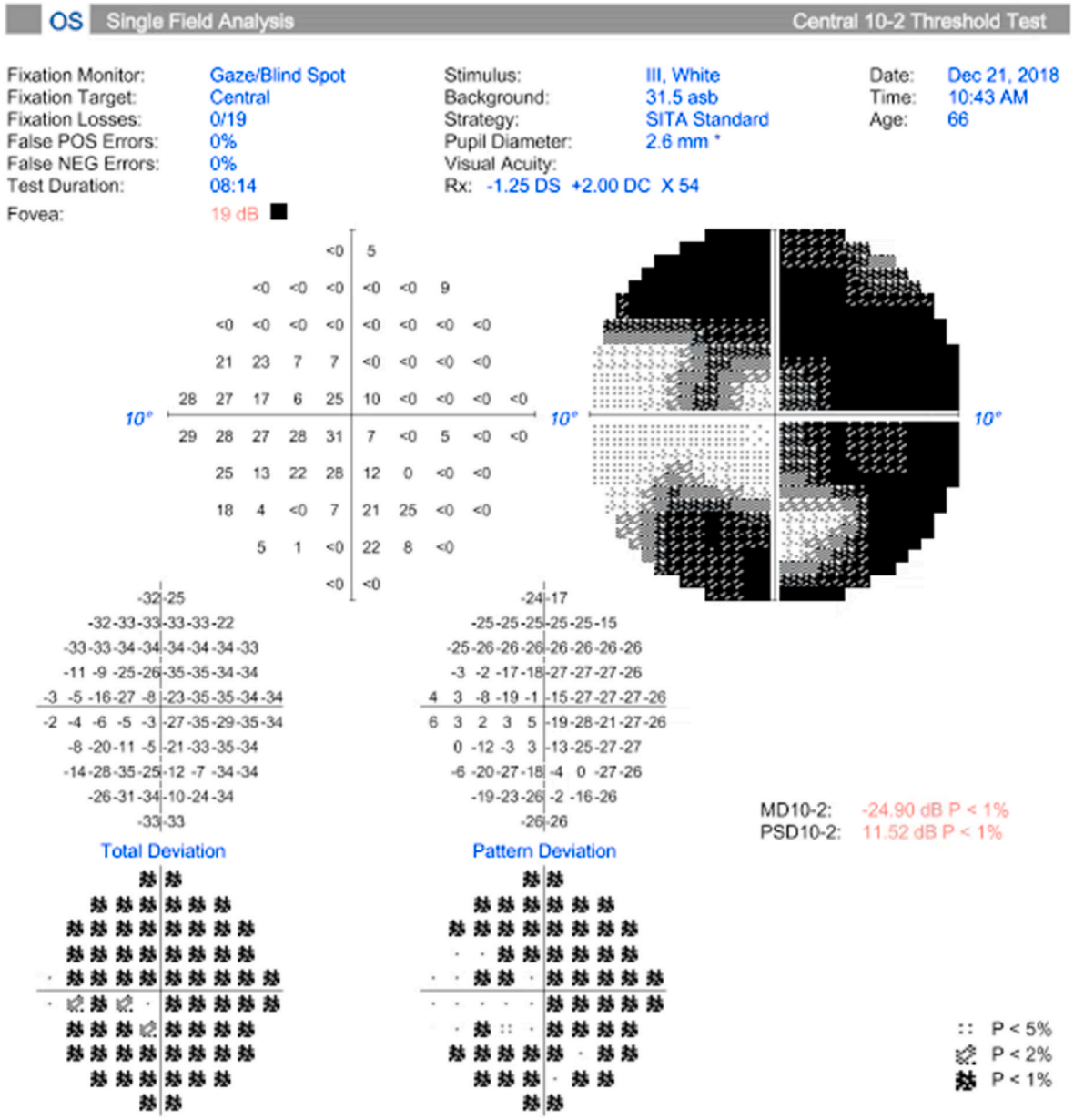

Fig. 1. Humphrey Visual Field 10-2 SITA Standard of the left eye showing advanced glaucoma at a) first presentation to glaucoma clinic and b) most recent clinic encounter.

acuity was 20/70 and IOP was 7 mm Hg. Corneal sensation was intact. No exophthalmometry was performed at the time. Given an isolated palsy of cranial nerve III, inability to adequately evaluate pupillary involvement, and concern for an acute vascular process such as an aneurysm or stroke, the patient was sent to the emergency department for urgent imaging and further evaluation. Brain magnetic resonance imaging (MRI) and computed tomography (CT) of the head revealed a 3.4× 2.3 × 3.6 cm left cavernous sinus mass which extended laterally into the sphenoid wing, medially across the midline, anteriorly into the left sphenoid sinus, superiorly past the clivus, and inferiorly into the left nasopharynx, eroding the skull base (Figs. 3 and 4). The remainder of her neurologic exam was unremarkable, and otolaryngology exam showed no suspicious masses or mucosal lesions of the oral cavity.

Ten days after presentation, she underwent an excisional biopsy and resection of the skull base by neurosurgery and otolaryngology. Histopathology revealed a low-grade adenocarcinoma with small bland nuclei and minimal pleomorphism. The tumor shows variable growth patterns including tubular (Fig. 5A), cribriform (Fig. 5B), and solid (Fig. 5C). No overt biphasic epithelial-myoepithelial pattern, squamous differentiation, or chondromyxoid matrix is identified. By immunohistochemical staining, the tumor was positive for CK7 with diffuse staining showing no suggestion of luminal-abluminal distinction (Fig. 5D). The tumor was p63 positive and p40 negative (Fig. 5E and F). A p63 positive and p40 negative immunophenotype has been reported to be very helpful in distinguishing polymorphous low grade adenocarcinomas from other salivary gland neoplasms with morphologic overlap such as

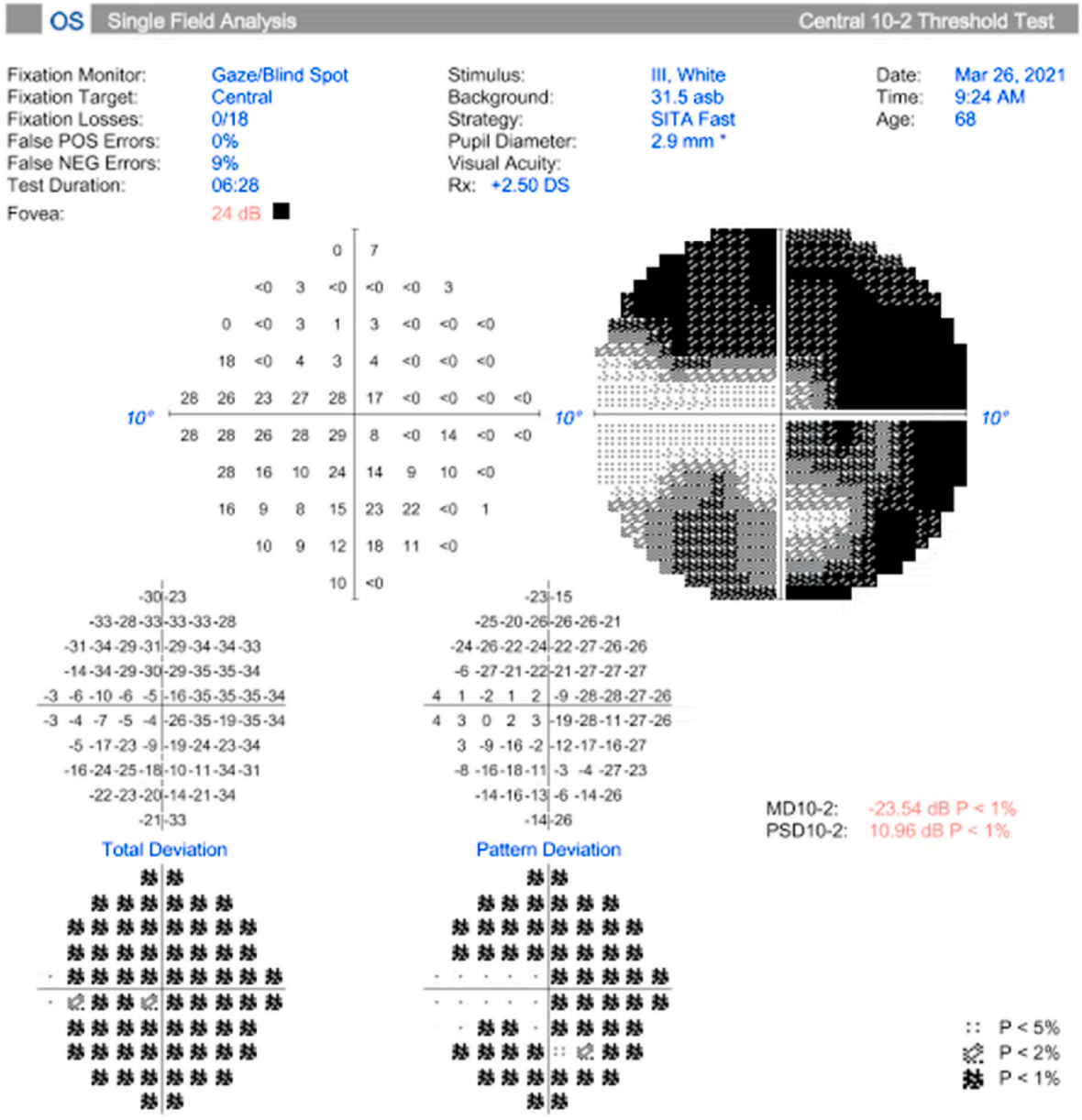

Fig. 1. (*continued*).

adenoid cystic carcinoma and pleomorphic adenoma.[2] Overall, given the morphology and immunophenotype, the findings were most compatible polymorphous low grade adenocarcinoma (PLGA).

Further surgical resection was not recommended due to tumor involvement of the third cranial nerve and apposition to a carotid aneurysm. Upfront external beam radiation therapy followed by stereotactic boost was recommended. The patient received 56 gy in 28 fractions with volumetric modulated arc therapy (VMAT) based planning and daily image-guided radiation therapy (IGRT). MRI brain at this time revealed a stable size and distribution of the tumor. Subsequently, the primary tumor was boosted with an additional 12 Gy in 4 fractions, for a total cumulative dose of 68 Gy, using a stereotactic technique that spared normal brain, brainstem, and optic structures. Given the risk of cancer recurrence and morbidity of treatment, the patient will be followed by an oncologist for a minimum of 5 years.

3. Discussion

PLGA is a rare, malignant tumor of minor salivary glands that typically presents as an asymptomatic mass within the hard palate of the oral cavity.[3] Most commonly it presents in the sixth or seventh decade of life with a 2:1 predilection for females.[4] High rates of perineural invasion have been reported.[5] The 10-year relative survival is 98.8%, and complete surgical resection is the preferred treatment of choice.[6] To our knowledge, there are four previously reported cases of PLGA arising from the nasopharynx; of these only two cases extended beyond the nasopharynx (Table 1).[7–10] In our patient, the tumor likely arose from salivary gland tissue in the nasopharynx and ascended along the vidian nerve before invading the cavernous sinus. These prior cases presented with a variety of clinical symptoms ranging from ringing or fullness of the ear, epistaxis, nasal obstruction or headache.[9] Our case is the first to report a cranial nerve palsy as the initial presentation of PLGA arising in

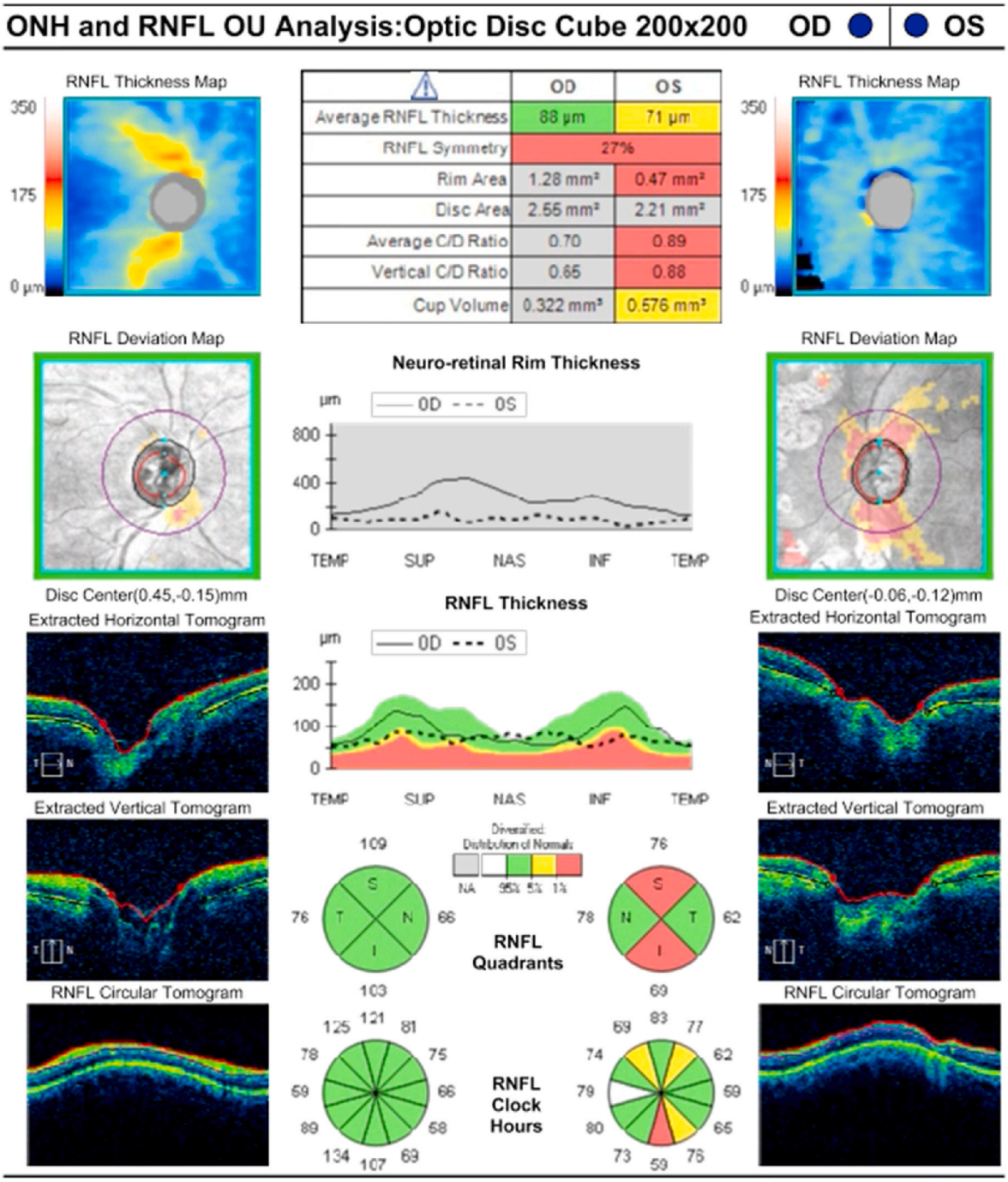

Fig. 2. OCT corresponding to earliest visual field testing (Fig. 1a) shows superior and inferior RNFL thinning of the left eye.

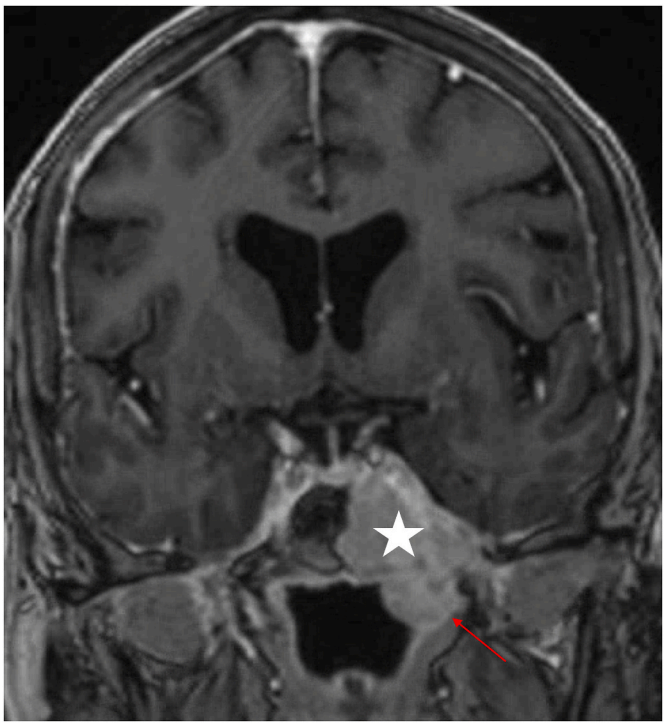

Fig. 3. Contrast-enhanced coronal T1 MRI showing a lobulated enhancing lesion in the left cavernous sinus that extends laterally into left sphenoid wing, medially across midline, anteriorly into the left sphenoid sinus and inferiorly into the left nasopharynx (red arrow), eroding the skull base. The mass encases and narrows the petrous segment of the left internal carotid artery and effaces the left foramen ovale and rotundum. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

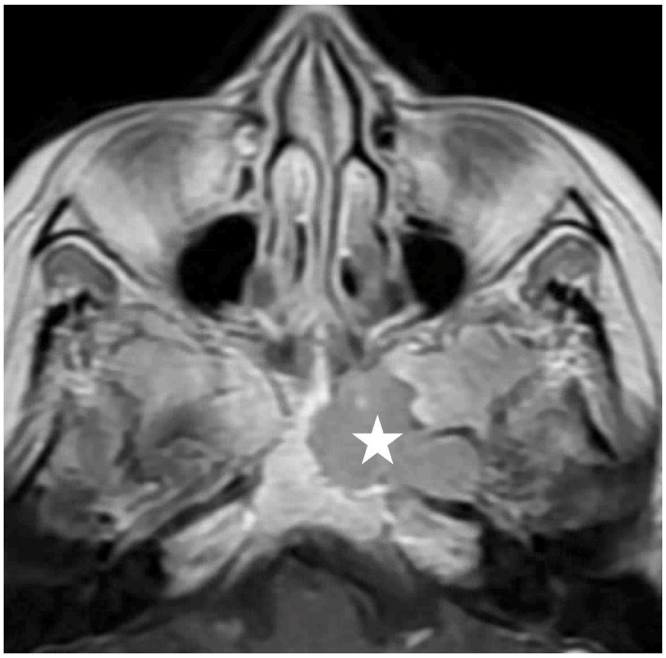

Fig. 4. Contrast-enhanced axial T1 MRI. The left cavernous sinus lobulated enhancing lesion extends laterally into left sphenoid wing and medially across midline.

the nasopharynx, emphasizing that ophthalmologists may be among the first physicians to encounter patients with symptomatic intracranial tumors.[11,12]

Our case was seen in clinic for a ten-week post-operative follow up after GDD implantation. Ptosis is a known postoperative complication following routine intraocular surgery.[13] In glaucoma surgeries, ptosis can occur due to compression by the lid speculum and increased manipulation of the conjunctiva or eyelid to expose the bulbar surface of the globe.[13–15] A previous study by Roddy et al. reports that the rate of ptosis in GDD patients is significantly higher at three months post-operatively.[14] Assessing extraocular movements during routine follow up is therefore important in distinguishing between postoperative ptosis and a cranial nerve palsy.

Cavernous sinus syndrome is a common sequelae of intracranial tumors and presents with multiple cranial neuropathies, proptosis, chemosis, ophthalmoplegia, or Horner syndrome.[16]

Our patient presented with only isolated involvement of the third cranial nerve and no other symptoms of cavernous sinus syndrome were noted, emphasizing the insidious growth of PLGA. Acquired third nerve palsies are classified as either pupil-sparing or pupil-involving. A common cause for pupil-sparing third nerve palsy is microvascular ischemia from diabetic neuropathy, while common causes for pupil-involving cranial nerve palsies are compressive lesions such as aneurysm of the posterior communicating artery or tumor.[17,18] Of note, in a fair number of cases, compressive lesions do not result in pupillary abnormalities.[19]

Imaging guidelines are nuanced for patients older than 50 years old with cranial nerve palsy.[20] Current guidelines suggest that close observation is appropriate in patients who are older than 50 years of age, have known risk factors for third nerve palsy, and present with no pupillary abnormalities.[21,22] However, pupillary abnormalities are not uncommon after eye surgeries and limit reliable assessment of pupillary involvement.[23] Further, pupillary constriction and dilation are less dynamic in patients with known diabetic neuropathy.[24] Neuroimaging should therefore be considered in this subset of patients, regardless of the presence of known risk factors for an ischemic cranial nerve palsy. The involvement of multiple cranial nerves would likewise necessitate neuroimaging.[22]

4. Conclusion

There are few cases reporting PLGA originating from the nasopharynx. Here, we report a case of a 68-year-old woman in which a third cranial nerve palsy was the presenting sign of a malignancy originating from the nasopharynx and involving the cavernous sinus.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

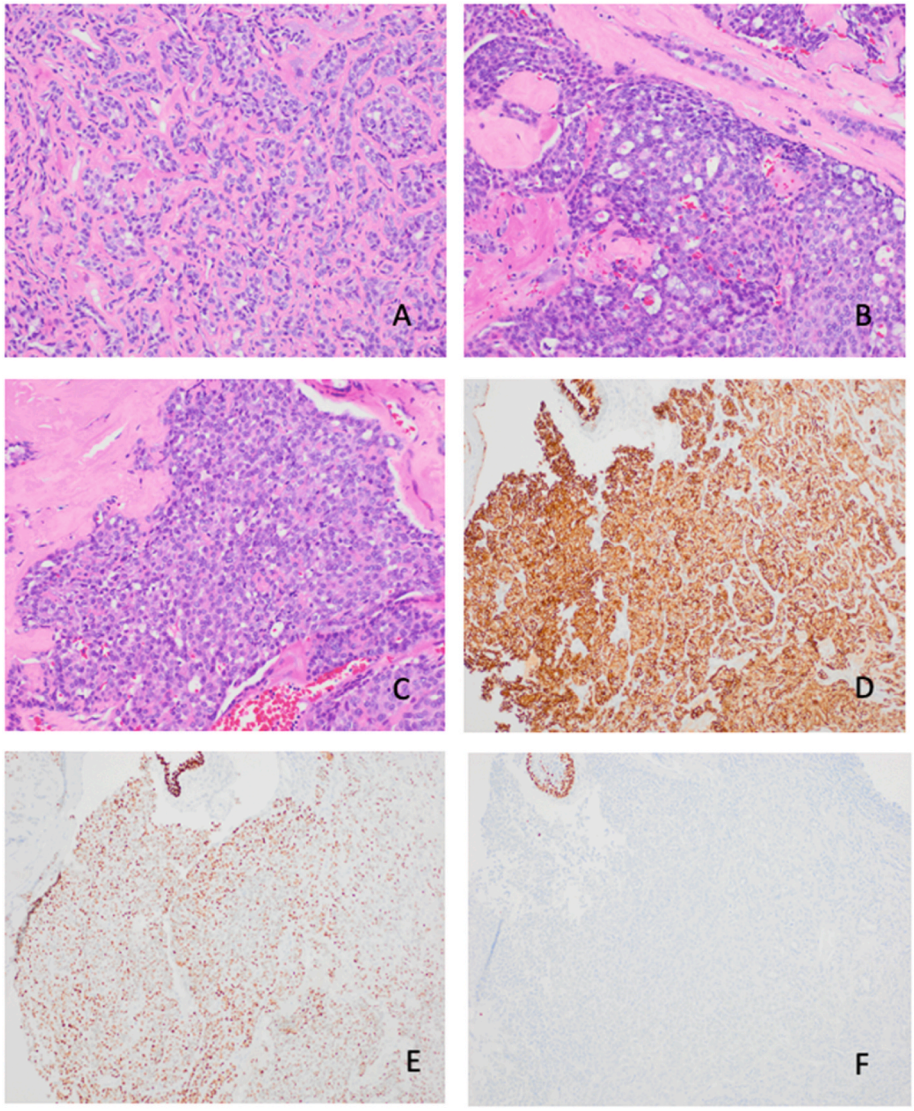

Fig. 5. A: Tubular pattern (H&E, 200x); B: Cribriform pattern (H&E, 200x); C: Solid pattern (H&E, 200x); D: Tumor is positive for CK7 immunostain (10x); E: Tumor is positive for p63 immunostain (10x); F: Tumor is negative for p40 immunostain (10x).

Table 1
Prior cases of extraoral presentation of polymorphous low-grade adenocarcinoma.

Prior cases	Location of tumor spread
Wenig et al., 1989	Nasopharynx
Lengyel et al., 2000	Nasopharynx with intracranial involvement through the paraclival skull base
Wei et al., 2008	Nasopharynx
Turri-Zanoni et al., 2016	Nasopharynx with intracranial spread to the infratemporal fossa and parapharyngeal space

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None.

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