Title: Grave’s Disease...Pseudotumor Cerebri...Don’t Settle for What is in Front of You—Look Behind the Eyes!
Authors: Muen Yang OD, Joan K Portello OD MPH MS FAAO

Abstract: Grave’s disease and chronic papilledema may have similar signs as orbital cavernous hemangioma. This report discusses the diagnosis and management of a patient who has all three conditions with the first two masking the latter.

I. Case History
- Patient demographics: 48 year old Caucasian female.
- Chief complaint: Pt presented for routine eye exam without particular complaints. Upon questioning, patient reported rare diplopia in primary gaze but it “resolved instantly” when she focused.
- Ocular, medical history: Patient was suspect for Grave’s Ophthalmopathy related to thyroid cancer which was removed in 2004. Patient had chronic asymptomatic papilledema secondary to pseudotumor cerebri (PTC) diagnosed 15 years ago. Patient had hypertension that is well-controlled with medications.
- Medications: Synthroid, Losartan, Metoprolol, Amlodipine.
- Other pertinent information: Swelling of the left upper and lower lids, which the patient thought might be related to a robotic hysterectomy in 2011.

II. Pertinent findings
At initial exam 2 years ago:
- Clinical:
  - BCVA: OD 20/20, OS 20/20
  - EOM/pupils: mild restriction of elevation and abduction OS. PERRL (−)RAPD OU.
  - Stereoscopy/color test: both within normal limits.
  - Tonometry: OD 19mmHg, OS 24mmHg with Goldmann appplanation tonometry.
- Physical:
  - External: lid retraction (Dalrymple’s sign) with symmetrical mild proptosis OU.
  - Pt is obese.
  - Biomicroscopy: Left superior and inferior lids are swollen. Open angles OU. Other elements of the anterior segment are unremarkable.
  - Dilated fundus exam: C/D ratio 0.25 OU. Elevated rim tissue with indistinct borders (-)hemes OD/OS. Macula, periphery, vasculatures, vitreous are unremarkable.

At subsequent exam 1 year ago:
- Clinical:
- BCVA/pupils: same as previous findings, WNL.
- EOM: 4+ restriction of up/lateral gaze OS.
- Tonometry: increased asymmetry OD 18mmHg, OS 26mmHg with Goldmann.

- Physical:
  - Biomicroscopy/Dilated fundus exam/External: same as previous findings.
  - Humphrey VF SITA Standard 24-2: OD-increase in an inferior nasal step/arcuate defect, OS increase in an nasal defect.

Patient was referred to OMD, then was seen by multiple neuro-ophthalmologists. The report is as follow:
- Proptosis OD 23mm < OS 26mm. Retropulsion OD normal, OS resistant. CT scans of the orbits and MRI of the brain showed a well circumscribed mass in the left intracanal space: it wrapped around the optic nerve, collapsed the optic sheath, and had a mass effect on the medial rectus muscle. OMDs were uncertain whether the mass was longstanding or recent. A biopsy was indicated.
- Dilated fundus exam confirmed bilateral disc edema. OCT showed thickened RNFL OU. MRI/CT showed a partially empty sella and distended optic nerve sheath OU, findings that are consistent with papilledema. Cerebrospinal fluid yielded 44cmH2O.
- EOM showed limitation in elevation, depression, and abduction of OS; with bilateral lids retraction, these findings confirmed Grave’s ophthalmopathy although EOM restriction can also be attributed to the orbital mass OS.

Patient returned for optometric exam this year:
- BCVA: OD 20/20, OS reduced to 20/40+
- Pupils: 2+ APD OS
- Tonometry: OD 14mmHg, OS 24 mmHg

Pt reported that she refused any type of ocular surgery; she was strongly advised to return to the neuro-ophthalmologist.

III. Differential diagnosis
- Primary: Orbital cavernous hemangioma, Grave’s ophthalmopathy, chronic papilledema from PTC.
- Others: Lymphoma, metastatic lesion, sarcoidosis.

IV. Diagnosis and discussion

General
- Orbital cavernous hemangioma is the most common primary benign orbital tumor in adults, with a predilection for females in the 4th-5th decades.\(^1,2\) It is a unilateral vascular malformation originating possibly from the arterial side; it presents as an oval, well-circumscribed tumor commonly located laterally in the muscle cone.\(^1,3\) Most of the lesions grow over time (over 50% of pts) and pregnancy seems to accelerate the process.\(^4\) Clinical signs include gradual axial proptosis that concurs with mild vision loss,
visual field defects and disc edema due to compression on the optic nerve.\textsuperscript{1,2} Choroidal folds and increase in hyperopia may occur.\textsuperscript{2}

- Grave’s ophthalmopathy is an autoimmune disease associated with thyroid dysfunction, where antibodies cause periorbital swelling and inflammation of extraocular muscles (EOM); subsequently the enlarged EOMs can compress the optic nerves, causing VF defects, elevated IOP, possible reduced VA, and occasionally disc edema. Because involvements are bilateral but asymmetric, a (+)RAPD may be present. When EOMs become fibrotic restricted motility develops, commonly affecting the inferior rectus, medial rectus, and superior rectus, resulting in restriction of elevation, abduction, and depression respectively.\textsuperscript{1} Proptosis and lid retraction are common signs.\textsuperscript{5}

- Pseudotumor cerebri is the increase of intracranial pressure without identifiable lesion of the brain and the composition of cerebrospinal fluid (CSF) is normal.\textsuperscript{6} It occurs typically in overweight women from age 15 to 45 and is marked by an opening pressure of lumbar puncture $>250\text{mmH}_2\text{O}$.\textsuperscript{6} Common symptoms include severe headaches, vomiting, altered consciousness, transient visual obscuration, and diplopia from 6 CN palsy.\textsuperscript{1} MRI shows distended optic nerves but the hallmark sign is papilledema, which is bilateral swelling of optic nerve head that result in enlarged blind spots. At the chronic stage, the discs remain elevated. VF can show nasal defect, arcuate scotomas, and general constriction due to axonal damage.\textsuperscript{6}

**Present case study**

- This case’s uniqueness resides in the fact that the patient had 3 concurrent conditions; their main clinical signs overlapped so that Grave’s disease and papilledema potentially masked the presence of the cavernous hemangioma until further testing was performed.
- Chronic papilledema induced VF defects which can mimic tumor-related field loss. Pre-existing disc edema complicated the detection of possible new tumor-induced swelling.
- EOM restriction and proptosis are common in both Grave’s ophthalmopathy and cavernous hemangioma; since patient had a known history of thyroid disease with corresponding signs (lid retraction/lid swelling), one would naturally associate these signs to Grave’s rather than suspecting a tumor. In addition, Grave’s disease and hemangioma can both be compressive in nature: the visual affectations caused by each would be difficult to distinguish.
- The unilateral increase in IOP may be due to the tumor pressing on the globe. Furthermore, since IOP can also show an increase in Grave’s disease, the practitioners were uncertain if the hemangioma was present at the initial visit, although the unilaterality suggest causes other than thyroid ophthalmopathy. The new onset of decreased VA and RAPD OS may indicate that the tumor is compressing the optic nerve, which could be a sign of growth.

**V. Treatment, management**

- Cavernous hemangioma is generally discovered by chance with a CT or MRI.\textsuperscript{1} For most cases, observation with repeated imaging and VFs to monitor progression suffices.\textsuperscript{7}
• Surgical removal by orbitotomy is indicated if the patient is symptomatic, has major VF deficit at initial visit, presents evidence of growth or compressive neuropathy. The surgery is uncomplicated and generates good result; visual field defects can return to normal after tumor removal, and the resection does not always have to be complete. For the present case, surgery was recommended since patient shows signs of progression and possible compressive neuropathy. However, at last exam patient refused surgery.

• Treatment for Grave’s disease includes smoke cessation, antithyroid drug, radioactive iodine treatment, and thyroidectomy. If ophthalmopathy is important, intravenous immunosuppressor should be considered followed by orbital, muscle, or lid surgery if necessary. Presence of compressive neuropathy should receive urgent treatment with intravenous steroid and orbital decompression surgery. For the present case, the patient’s EOM restrictions and decreased VA are most likely caused by the tumor rather than Grave’s disease, therefore previously discussed treatments do not apply for her. She is advised to continue Synthroid and artificial tears are given to treat dryness caused by lid retraction and proptosis. If she develops constant diplopia, prism will be used.

• For papilledema, although patient was asymptomatic, Diamox was prescribed for 5 months due to suspicion for flare-up. This medication reduces CSF production which will decrease intracranial pressure. Weight loss was recommended, since without it papilledema is likely to persist chronically even after medical treatment. Other treatments found in the literature are corticosteroid to stabilize an acute presentation, serial lumbar punctures, or surgical procedures such as optic nerve decompression or CSF diversion shunts if condition is severe. These options do not apply to this patient because her papilledema is neither acute nor severe.

VI. Conclusion
• Patients with multiple co-existing conditions should be followed more frequently to monitor change. Special attention needs to be allocated to rapid/sudden alteration.
• Clinical signs of one disease can potentially mask another condition. Even though every finding is consistent with Grave’s disease and chronic papilledema, any worsening should be considered suspicious especially if it is unilateral. Prompt referral for imaging to rule out neoplasm is important.

Sources


