Double problems with double vision: How neuroradiologic and pathologic clues decipher rare from common neuroophthalmologic disease

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64-Year-Old Female

- CC: “constant double vision”
  - Progressive for 2 months
  - Binocular with oblique images
  - Worse in downgaze and better in upgaze
  - Slightly worse in the morning
  - No pain or vision loss
Binocular Double Vision

- From ocular misalignment
  - Resolves by closing EITHER eye

Etiologies:
- Breakdown of congenital misalignment
- Cranial Nerve Palsy (CN3,4,6)
  - Congenital, trauma, ischemia, mass
- Extraocular muscle damage
  - Thyroid eye disease, inflammation, trauma
- Myasthenia Gravis
- Orbital mass
- Skew deviation
Additional History

**PMHx / POHx**
- Colonic cancer (3 years prior)
  - S/p hemicolecotomy
  - “Adenocarcinoma with mucinous features”
  - Last colonoscopy normal

- Childhood amblyopia OD
  - Patched OS for “crossing”

**Social Hx**
- Smoked cigarettes for > 15 years (quit 1995)
Examination

- **VA (cc)**
  - 20/20 OD
  - 20/15 OS

- **Normal**
  - Pupils
  - Intraocular pressure
  - Visual fields
  - Slit lamp exam
  - Dilated fundus exam
Extraocular Motility

Partial limitation of elevation and depression, right eye
Full motility, left eye
Ocular Alignment:

- Right hypertropia, resolves in upgaze.
- Exotropia.
Examination cont’d

- Remainder of cranial nerves
  - Normal
  - Normal orbicularis strength
- No Cogan’s lid twitch
- No eyelid fatigability
External Appearance

Exophthalmometry:
21 mm / 21 mm (base 96 mm)
What is the most likely diagnosis?

- **Thyroid-associated orbitopathy**
- Orbital pseudotumor
- Myasthenia gravis
- Partial third nerve palsy

**PLAN:**
- Thyroid function panel
- Thyroid stimulating immunoglobulins
- Orbital ultrasound
- Acetylcholine receptor antibodies
Thyroid Associated Orbitopathy (TAO)

- Pathophysiology unknown
  - Not related thyroid hormone level
  - Likely autoimmune/crossreactive antigen

- Eyelid features
  - Retraction, lag

- EOM/orbital features
  - EOM thickening
  - Orbital fat inflammation
  - Proptosis
Lab Work

- **Thyroid function tests**
  - T3 / T4 normal
  - TSH = **6.12** (0.40-5.50 mIU / L = NL)

- **Thyroid stimulating immunoglobulins (TSI)**
  - TSI = 115 % (NL = < 125 %)

- **Acetylcholine receptor binding ab**
  - Negative
Orbital Ultrasound

- Massively thickened right inferior rectus
  - Diameter = 9.3 mm
  - Left IR = 5.2 mm
  - Low reflectivity
- Remaining extraocular muscles mildly enlarged and hyper-reflective
TAO - Orbital Ultrasound

B scan showing enlarged SR/levator complex

A scan showing SR/levator complex with high internal reflectivity
Further Evaluation

- Atypical features on Ultrasound prompted additional imaging
Case presentation - Radiology

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Next step?

A. Perform a lumbar puncture.
B. Perform a biopsy.
C. Start steroids for management of TAO.
D. Observational management of TAO without optic neuropathy.

Internal debate:
To biopsy or not to biopsy
Case presentation - Pathology

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Assistant Professor of Clinical Pathology & Laboratory Medicine
Right Inferior Rectus Biopsy
Immunohistochemistry

Chromogranin (+)  Synaptophysin (+)  Pancytokeratin (+)
Immunohistochemistry

Chromogranin (+)  Synaptophysin (+)  Pancytokeratin (+)

Diagnosis: Neuroendocrine tumor
Thyroid associated ophthalmopathy
Adenocarcinoma of the Colon
Second malignancy?

- Biopsy not consistent with colonic adenocarcinoma
  - Chromogranin and Syntaptophysin (+)
  - Cytokeratin 20 and CDX2 (-)

- Prior pathology from 2004 reviewed
  - Consistent with original report
    - “Adenocarcinoma with mucinous features”
Staging

- **CT chest / abdomen / pelvis**
  - Left lower lobe lung
    - 2.5 cm nodule
  - Two parenchymal liver lesions
    - 1.5 cm and 3.4 cm
    - Suspicious for metastasis

- **Biopsy: liver and pulmonary lesions**
  - Neuroendocrine tumor
Bronchial carcinoid tumor with metastasis to the right inferior rectus muscle and liver
Discussion: Extraocular Muscle Thickening

- Large retrospective series 1976-1997
  - **Thyroid orbitopathy:** 94.3% (1651/1750 cases)
- Other causes (99 cases)
  - Inflammatory = 45 cases (45.5%)
  - Vascular = 24 cases (24.2%)
  - Neoplasms = 20 cases (20.2%)
  - Metastases = 12 cases
    - 7 melanoma, 3 breast CA, 1 bowel adenocarcinoma
    - 1 carcinoid
  - Other: Amyloid, Neurofibromatosis, Infection
Identifying the Wolves Among Sheep

- Irregular borders
- Heterogenous enhancement
- Ultrasound reflectivity
  - TAO = high reflectivity
  - Malignancy = low reflectivity
Carcinoid Tumor

- Neuroendocrine malignancy
  - Arises from chromaffin cells
  - 0.5% of all malignancies
  - 10% produce serotonin syndrome
  - Sites of origin:
    - GI (65%) > Pulmonary (25%) > Unknown (10%)
- Generally benign
  - Unless spread observed clinically
Carcinoid Metastases to the Eye

- Choroidal metastases
  - More common than orbital metastases
  - Bronchial carcinoid

- Orbital metastases
  - \( \approx 4-5\% \) of all orbital mets
  - GI carcinoid
  - Known carcinoid at diagnosis: 12/15 (80%)
  - Median survival: 108 months (n=13)
  - Predilection for extraocular muscles
    - Single EOM enlargement in 50%
Patient Follow-up

- **Ocular**
  - External beam radiation (EBR) to right IR
  - Cumulative dose = 50.4 Gy over 28 fractions
  - Restrictive right hypotropia after EBR
  - 18 PD LHT in primary gaze
    - Underwent RIR and LSR recession

- **Systemic**
  - Radiographic growth of liver and lung lesion
  - Cyber knife to liver and lung
  - Chemotherapy (somatostatin analogue)
  - Succumbed to malignancy in 2 years
Pearls

- Thyroid associated ophthalmopathy
  - Most common cause of EOM enlargement

- Red flags for metastasis to the EOM
  - Clinical Characteristics
    - Location, laterality
    - History of malignancy
  - Imaging characteristics
    - Reflectivity, borders, enhancement

- Carcinoid tumor metastasis
  - Predilection for EOM within orbit
Thank You