Plexiform Tumor of the Orbit
Anat Stemmer-Rachamimov, MD
Department of Pathology
Massachusetts General Hospital
Harvard Medical School

Disclosure of Relevant Financial Relationships
USCAP requires that all faculty in a position to influence or control the content of CME disclose any relevant financial relationship WITH COMMERCIAL INTERESTS which they or their spouse/partner have, or have had, within the past 12 months, which relates to the content of this educational activity and creates a conflict of interest. Dr. Anat Stemmer-Rachamimov declares she has no conflict(s) of interest to disclose.

CLINICAL HISTORY
- 34 year old man was referred to oculoplastic service for evaluation of right orbital mass
- Patient had a lump on his forehead when he was 7 years old. Pathology diagnosis was neurofibroma
- Age 16 developed headaches, nausea and protrusion of right eye.
- Imaging: bilateral vestibular schwannomas and an orbital tumor
- Diagnosed with NF2 (9 years after presentation)

- Resection of Left vestibular schwannoma.
- Age 19- Left vestibular schwannoma regrew and necessitated second surgery and radiation.
- Right eye proptosis worsened and visual acuity was compromised.
- Several skin lesions on arms were noted
- Family history negative for neurofibromatosis.
EXAMINATION

- Examination (age 34) shows a large exophytic mass in the right orbit extending into the eyelids which appear expanded.
- There is no light vision or extraocular movements on the right side.
- There is a subcutaneous mass extending the entire length of the forehead to the vortex of the scalp (5.0x4.0 cms).

T1 weighted post gadolinium
Enhancing lesion centered in the right orbit.
Ant: infiltrates lids and may extend to nasal ala
Post: widens orbital fissure and displaces optic nerve, scallops the chiasm (which is not expanded)

Clinical diagnosis: meningioma

T1 weighted Pre gadolinium
Multi nodular appearance; classic for nerve sheath tumors (plexiform neurofibroma)
NO cystic component or fluid levels
Laterally, remodels the bone (slow growing)
Compresses the globe.

Pathology
- Exenteration specimen
- Multiple lobules of yellow, soft, myxoid tumor
- Globe is compressed
- Tumor extends and expands the eyelid

Microcopy
- Large tumor attached to sclera and extending to eyelid
- Multinodular
- Replacing and extending nerves and nerve twigs
DISCUSSION

• The tumor is a plexiform schwannoma – an uncommon variant

• This patient has a syndromic tumor – NF2.

Plexiform

• Definition
  • Tumors that diffusely involve and expand the nerve. Often multinodular.
  • Gross appearance of rope (plexiform); when multiple nerves are involved – bag of worms
  • Most common/classic example is plexiform neurofibroma

Plexiform Schwannoma

• First described in 1978 (Harkin et al)
• Berg et al - series of 97 cases
• How common (Berg et al - series of 97 cases):
  • 4.3% of all schwannomas
  • 15% of cutaneous schwannomas
  • 23% each involving head and neck; limbs, trunk
  • 3% large nerves/plexus;3% visceral (deep)
  • 1 case of cranial nerve involvement
  • Association with NF – 15%, much higher in pediatric tumors (45%)

• Most plexiform schwannomas are superficial (cutaneous, subcutaneous) – 90%

• Deep plexiform schwannomas often arise in the context of NF (NF2 or schwannomatosis)

• Most plexiform schwannomas show cellular schwannoma growth pattern (67%!). The rest have conventional pattern.

• In one series (Mayo clinic) 6 cellular plexiform schwannomas in childhood were misdiagnosed as MPNST
Schwannoma or Neurofibroma?

- Different risks for malignant transformation
- Different criteria for diagnosis of malignancy
- When multiple - different forms of NF:
  - Neurofibroma : NF1
  - Schwannomas : Schwannomatosis OR NF2

NF2

- AD
- Incidence - 1:40,000, Newer data 1:25,000 (Evans, 2006)
- 50% are “de novo”:
- Germline mutation in the NF2 gene
• Benign tumors:
  • Schwannomas: vestibular, cranial nerves, peripheral, cutaneous
  • Meningiomas
  • Ependymomas

• Non tumoral manifestations:
  • Meningioangiomatosis
  • Ocular abnormalities
  • Polyneuropathy

Ocular manifestations in NF2

• Presenting symptom in 10% (Ragge)
• CATARACT: (81%, early, specific; Parry)
• Retinal hamartomas
• Combined pigment epithelial and retinal hamartomas
• Chroidal hamartomas
• Ocular motor abnormalities
• Epiretinal membranes
• Optic nerve sheath meningiomas

Ragge et al; Am J Ophthalm, 1993
Parry et al; Am J of Med Gent, 1994

Clinical criteria for the diagnosis of NF2

• Bilateral VS
  OR
• First degree family with NF2 AND
  • unilateral VS <30 yrs OR
  • 2 NF2 associated lesions

Presenting symptoms in NF2

• Adult
  • Hearing loss
  • Tinnitus
  • Balance dysfunction

• Pediatric
  • Weakness, neuropathy
  • Symptoms of other cranial nerves
  • Ocular symptoms

• Diagnosis often lags 7 years after initial presentation

Schwannoma/meningioma

S100
EMA

schwannomatosis

• Syndrome characterized by multiple peripheral schwannomas.
• NO VS.
• Often associated with pain
• Cranial nerve involvement is rare
• Age of presentation: adults (40s)
• Non tumor manifestations are absent (no ocular involvement to date)
• Minority is familial (15%)
  - AD
• Most cases are sporadic (85%)
• Genetic risk is low
• Many cases are segmental (30%)

Clinical distinction from NF2
• Distribution of schwannomas
• Age of presentation
• Lack of non-tumor manifestations
• Pain
• Segmental distribution
  Different germline mutation – SMARCB1, LZTR1

Post operative with prosthesis

Acknowledgments
Scott Plotkin, NF clinic, MGH

Thank you!

Important Information Regarding CME/SAMs
The Online CME/Evaluations/SAMs claim process will only be available on the USCAP website until September 30, 2017.
No claims can be processed after that date!
After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.