AMSER Case of the Month
August 2020

2-year-old with Neurofibromatosis type I with Headache

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Patient Presentation

• HPI: A 2 year old girl with NF type I confirmed by genetic testing presents to the neurology clinic with a h/o of HA for 9 months. HA can wake her up from sleep. Onset varies. No modifying factors. No vomiting, photophobia, phonophobia.

• PMHx: NF type 1, + genetic testing.

• PSHx- bilateral ear tubes

• Fam Hx: Paternal Grandfather with DM, Twin brother healthy
Exam

• Gen – well appearing child
• Head and Neck- atraumatic, normocephalic, neck supple
• Eye- VA Fixes and Follows
  • Left eye polar cataract outside of visual axis
• CV- nl S1, S2, no murmurs
• Lungs- CTAB
• GI-Soft NT, ND
• Skin- café au lait spots, no axillary/inguinal freckling, no fibromas
• Neuro-CN 2-12 grossly intact, normal gait, DTR 2+, no abnormal movements
• What Imaging Should We Order?
# ACR Appropriateness Criteria


<table>
<thead>
<tr>
<th>Procedure</th>
<th>Appropriateness Category</th>
<th>Relative Radiation Level</th>
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Axial T2/FLAIR: Non-enhancing foci of increased signal in the cerebellar white matter.

Coronal T2/FLAIR: Inc signal in the right inferior aspect of medulla/cervical cord, appears expansile → attention on follow-up imaging.
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Abnormality in upper cervical cord on Brain MRI → Follow-up Cervical Spine MRI
Ordered by neurologist
Follow-up MRI Brain and C-Spine Labeled

3 yrs old

Coronal T2: Focal enlargement of R optic nerve - 6 mm diameter = SMALL OPTIC NERVE GLIOMA

Sagittal Cervical Spine T2 Stir: Partially visualized paraspinal masses - likely PLEXIFORM NEUROFIBROMAS
Vision Problems?

Eye Exam:
  • VA 20/30 OU with glasses
  • Visual Field testing Full
  • Optic Disc: sharp, pink, normal cup
  • Left anterior polar cataract—not in visual axis
  • No Lisch Nodules
### ACR Appropriateness Criteria

**Variant 6:** Visual loss, *intraocular mass*, optic nerve, or pre-chiasm symptoms. Initial imaging.

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Follow-up MRI Orbits Unlabeled

4 yrs old

Axial T1 POST GAD
Axial T1 Post Gad: R optic nerve larger than L without discrete enh mass. Tortuosity of both optic nerves seen.

4 yrs old

Follow-up MRI Orbits labeled
### ACR Appropriateness Criteria

**Variant 4:**

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Plexiform neurofibromas only partially visualized on C-spine MRI → Follow Up Thoracic spine MRI

Ordered by neurologist
Follow-up MRI Thoracic spine Unlabeled

4 yrs old

Axial T2
Follow-up MRI Thoracic spine labeled

4 yrs old

Axial T2: Fully visualized right paraspinal mass = Plexiform neurofibroma
Follow-up Brain MRI Unlabeled

4 yrs old

Axial T2 flair
Axial T2
Axial T1 Post Gad
Follow-up Brain MRI Labeled

Axial T2 flair: large focus of inc signal in L globus pallidus

Axial T2: large focus of inc signal in L globus pallidus

Axial T1 Post Gad: non-enhancing focus in R superior cerebellar peduncle

Multiple new foci of spongiform and vacuolar changes consistent with NF1

4 yrs old
Case Timeline Summary

• 2.5 yo child with NF1 with secondary HA → Brain MRI
  • FASI (focal areas of signal intensity) found in cerebellum and inf medulla/cervical cord

• 3 yo-Known brain lesions and nondiagnostic cervical lesion → Follow up Brain and Cervical MRI
  • NEW Optic nerve glioma
  • NEW Plexiform neurofibromas that are incompletely characterized

• 4 yo Known Brain lesions, orbital tumor, and paraspinal masses → Follow up Brain, Orbital, Thoracic MRI
  • Optic nerve glioma unchanged
  • Plexiform neurofibromas unchanged
  • NEW FASI lesions involving globus pallidus and cerebellar peduncle
Diagnosis

• Sequelae of Neurofibromatosis type I
  • Optic nerve glioma
  • Spongiform and vacuolar changes in brain
  • Plexiform neurofibromas in the spine
Radiographic Findings for NF1

• FASI- focal areas of signal intensity
  • Most common finding in NF1
  • Areas of inc T2 signal commonly in basal ganglia (often *globus pallidus*), thalamus, brainstem, cerebellum
  • Pathologically spongiform myelinopathy or vacuolar change of myelin
    • Vacuoles filled with water → T2 signal hyperintensity
  • Unclear role in NF1 spectrum of disease

• Optic Pathway Glioma
  • Decreased vision
  • Mass effect with proptosis
  • Hypothalamus involved → polyuria, polydipsia, sexual precocity, endocrine dysfunction

• Plexiform Neurofibromas
  • Pathognomonic for NF1
  • Benign tumor of peripheral nerves
  • High potential for malignant transformation
Case Discussion

• Epidemiology: affects 1:2500-3000 individuals
  • 50% inherited, 50% de novo mutation

• Clinical Dx: 2 or more required (most dx by 1yr of age)
  • 6 or more café au lait spots in one year
  • 2 or more neurofibromas or one plexiform neurofibroma
  • Optic pathway glioma
  • Bony dysplasias
  • Two or more iris hamartomas (Lisch nodules)
  • Axillary or inguinal freckling
  • First degree relative with NF1 with above criteria

• Loss of gene product neurofibromin on chromosome 17q11.2 → Neoplasm due to inactivation of tumor suppressor gene
Treatment and Prognosis

• Combination of supportive and surgical therapies. NO single treatment exists
• Overall life expectancy half of non-affected individuals
• Optic nerve gliomas require resection \(\rightarrow\) loss of vision in affected eye
Resources


• Nguyen R et al: Characterization of spinal findings in children and adults with neurofibromatosis type 1 enrolled in a natural history study using magnetic resonance imaging. J Neurooncol. ePub, 2014


• https://radiopaedia.org/articles/focal-areas-of-signal-intensity-brain-1?lang=us

• https://radiopaedia.org/articles/optic-pathway-glioma?lang=us

• https://radiopaedia.org/articles/plexiform-neurofibroma?lang=us