Spinal cord compression in mucopolysaccharidosis

Agnes Chen, MD
K30 Case Study
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9 year old girl with MPS I

- Diagnosed at age 2
- Intravenous enzyme replacement therapy since dx
- Over the last two months has started tripping and falling
- Mother notes intermittent “tremors” of both legs
- Increased toe-walking
- Last week, numbness in arms and legs which went away after 30 minutes
- Denies bowel or bladder symptoms
Physical exam

- VSS, Height: 102cm, Weight: 24.5kg, BMI: 23.5, OFC: 60cm
- HEENT: facial features of mucopolysaccharidosis, moderate corneal clouding, hearing aids in both ears, gingival hypoplasia, large tongue
- Neck: short, limited range of motion, no TTP
- Chest: CTAB, RRR, nl S1, S2
- Back: slight kyphosis, no scoliosis
- Abd: soft NT, ND, no HSM
- Ext: symmetric shortening, joint widening, flexion contractures in fingers
Neurological exam

- Alert, talkative, cooperative, oriented x3
- CN: PERRL, EOMI, full visual fields, no facial weakness, large tongue which is midline
- Motor: increased tone in both legs, spastic in nature, mild decrease in strength in both legs
- DTRs: 3+ at biceps, triceps and knees, several beats of clonus at both ankles
- Sensation: intact to light touch and pinprick, no level
- Coor: No dysmetria on finger to nose
- Gait: toe-walking, spastic gait
Imaging

- MRI: Upper cervical spinal stenosis with cord compression, partial occipitalization of C1
- Flex-ex x-rays: 4mm of motion between C1 and C2

- Severe, diffuse cervical cord compression with signal change
- Odontoid dysplasia
- Dural thickening
Intrathecal enzyme replacement vs. neurosurgical intervention

- **Proposed surgery:**
  - Suboccipital craniectomy
  - C1-C2-C3 decompressive laminectomy
  - Possible duraplasty
Cardiology pre-op eval

- 1st degree heart block with PR of 250ms
- Mildly thickened mitral and aortic valves
- EF: 67%, moderate posterior wall and septum thickening
- Dobutamine echo: no infarct or ischemia with excellent ventricular function
- Holter: normal, no dropped beats
- Overall good function but concern for the development of advanced AV block at the time of anesthesia
What causes the spinal cord compression in mucopolysaccharidosis?

- Bony vertebral abnormalities
- Thickening of spinal ligaments
- Thickening of the meninges
- Intrathecal enzyme replacement would theoretically only treat the last cause
“Standard of care” is decompressive laminectomy

- Only about 20 published cases
- MPS patients are risky surgical candidates:
  - Airway: very distorted anatomy, many reports of emergent tracheostomies
  - Lung: obstructive and restrictive disease
  - Cardiac: arrhythmias, valvular and coronary artery disease
- Two case reports of recurrence of surgery
- One case report of cervical myelopathy presenting at age eight, after receiving a bone marrow transplant at age 2
Intrathecal enzyme replacement therapy for MPS I: animal data

- **Alpha-L-iduronidase activity (units/mg protein)**
  - Normal = 15.4
  - 1 mg dose (n=13)
  - 0.46 mg dose (n=2)

- **Glycosaminoglycans (µg/mg dry weight)**
  - Untreated MPS I
  - Normal

Locations:
- Cervical
- Thoracic
- Lumbar
Challenges with intrathecal enzyme replacement therapy for spinal cord compression in MPS

- Thickening of extradural components is probably a major contributor to compression; this is not expected to respond to IT ERT
- Long-standing glycosaminoglycan storage can lead to permanent tissue damage and fibrosis, which may not respond to therapy
- Early treatment and prevention of damage may be more achievable, but would require very long-term controlled studies
Spine MRI as an outcome measure

- MRI can’t distinguish between dural thickening and extradural thickening
- May not be sensitive enough to assess effects of intrathecal enzyme replacement
Due to rapid progression of her symptoms, parents opted for decompressive surgery.