Normal pressure Hydrocephalus and Alzheimer Disease: Comorbidities and shunt response.

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March 11th, 2016
Case

- CC: Confusion, behavioral issues and gait abnormalities

- 76-year-old gentleman with 2 week history of confusion, gait instability and incontinence.

- PMH positive for Alzheimer’s dementia, but otherwise healthy

- independent with ADLs and needing minor help from his wife for IADLs

- now oriented to person only, voiding in the hallways of his house and needing one person assist for ambulation.

- Vitals signs, physical exam unremarkable except physical therapy assessment revealing a decreased ambulatory cadence, with broad base gait and unsteadiness needing one-person contact assist on admission
Case

- Negative lab work up

- Non contrast CT head: “mild cerebral volume loss and mild periventricular and central white matter change consistent with chronic microvascular disease with no acute intracranial abnormality”

- Neurology input upon seen CT: enlargement of the lateral, 3rd, and 4th ventricles

- Gamma cysternogram: There was minimal migration of the radiopharmaceutical over the convexities consistent with type 4 pattern of activity associated with normal pressure hydrocephalus.

- Ventriculoperitoneal shunt placed 2 months after discharge. There were no reported complications from surgery, and he is now able to ambulate at baseline. Urinary incontinence has resolved. His mentation is reported to be back at baseline and he was able to return to work.
Normal Pressure Hydrocephalus (NPH)

- Clinical hallmark: dementia, gait dysfunction, in urinary incontinence in the context of enlarged ventricles and a normal CSF opening pressure.

- No clinical picture or diagnostic test has definitely teased out idiopathic normal pressure hydrocephalus from other dementias, and the gold standard for diagnosis remains clinical improvement with CSF shunting.

- Gait disturbance:
  - progresses from balance difficulties, to shortened stride length
  - the most frequent symptom in normal pressure hydrocephalus.
  - 89% of patients with NPH had abnormal gait, whereas 79% were demented and 44% had urinary incontinence.
  - The absence of gait disturbance or the onset of gait disturbance after onset dementia predicts poor shunt response.

- Urinary incontinence:
  - responds well to shunting, however is a poor independent predictor of shunt outcome
  - PPV to shunt response: 31 to 33%
  - PPV to complete triad: 65 to 74% with 82% NPV

- Currently there are no tests with high enough sensitivity and specificities to be recommended over automatic shunt insertion in cases of suspected NPH.
The Evans index on CT:
- the ratio of the maximum width of the frontal horns to the maximum width of the inner table of the cranium
- NPH = index greater than 0.3; but ratio varies with the age and sex
- can be an indicator of NPH and easily followed with serial CT scans
- Some clinicians may require a high ratio preoperatively despite the ratio not correlating with the clinical improvement after shunt placement.

MRI:
- greater sensitivity for identifying CSF flow effects.
- Small study: abnormal magnetic resonance flux and improvement of function post shunting with a predictive accuracy 88%.

Brain glucose metabolism:
- PET-fluorodeoxyglucose studies had a sensitivity of 89% and specificity of 82% in differentiating healthy controls from NPH patients,
- however this study could not predict shunt outcome.
- Also there was not a specific pattern in glucose metabolism found amongst patients.
CSF dynamic study, or Tap test:
- drainage of 40-50 mL of CSF from the lumbar cistern or the ventricles simulating shunt placement.
- acute improvement of gait with CSF drainage
- external lumbar CSF drainage (ELD): 18 patients
  - 5 days lumbar drain
  - sensitivity and specificity of 100%.
  - This was limited simple study but it may prevent patient from being exposed to an unnecessary operation if the clinical improvement post shunt is uncertain.

Meta-analysis study:
- isotope cysternography, hydrodynamics tests, and neurocognitive testing plus lumbar puncture all performed less than automatic shunt insertion.
- A three-day external lumbar drainage (ELD): only test that theoretically could provide outcome better than those for automatic shunt insertion.
- The ELD sensitivity and positive predictive value are high, meaning a high likelihood of shunt success.
- However specificity and negative predictive value of ELD are much lower. 22% of patients who had received a shunt despite negative test findings showed some improvement, a rate similar than that for automatic shunt surgery.
Now adding Alzheimer’s to the mix

- Golomb et al:
  - follow 56 cognitively impaired patients who received ventriculoperitoneal shunts for a diagnosis of idiopathic normal pressure hydrocephalus.
  - cortical biopsies obtained during surgery:
    - CERAD diagnosis of definite Alzheimer’s disease: 7; probable 9; possible disease in 7 patients (23/56)
  - Alzheimer’s disease + patients:
    - significantly higher global deterioration scale and lower Mini mental status examination scores.
    - greater gait dysfunction (slower velocities and higher ambulatory index score)
    - Both Alzheimer’s disease positive and Alzheimer’s disease negative patients exhibited statistically significant improvements in gait velocity and ambulatory index scores.
  - Neither the mini mental status examination nor global determination scale scores improved significantly with shunting.
Now adding Alzheimer's to the mix

- Hamilton et al:
- 37 patients with NPH, small prospective study
- Cortical biopsy (Amyloid B plaques, neuritic plaques, neurofibrillary tangles)
- 25 (67.6%) demonstrated evidence of one or more Alzheimer’s disease pathologic marker
- Moderate to severe tau and amyloid B pathology:
  - More severe baseline impairment and poorer performance post operatively on symptom severity scales and measures of cognition.
  - Also, in sharp contrast to individuals with less severe pathology, patients with moderate to severe pathology failed to demonstrate any improvement in gait, cognition, in incontinence at four-month follow-up.
Shunting

- A meta-analysis study: significant complications
- 6% permanent neurological deficits or death
- 22% require additional surgery.
- Long-term outcome rate were approximately 20 to 30%.
- This indicates the normal pressure hydrocephalus is more than simply a disorder of CSF production and absorption, and then by manipulating the CSF dynamics, perhaps were enabling the marginal brain to function at higher level
Conclusion

- Alzheimer’s disease:
  - common in patients with normal pressure hydrocephalus
  - prevalence increases in proportion to the severity of dementia.
  - more cognitively impaired and exhibited a disproportionate level of gait dysfunction
  - their improvement after shunt placement was comparable with patients with negative biopsies at the 2 month post op follow up
  - However no improvement at 4 month post shunting for moderate to severe Alzheimer’s patients was seen

- For the future:
  - Measures of cortical tau and amyloid B as biological markers derived from CSF
  - may prove useful for signifying the presence of Alzheimer’s disease as a comorbid condition.
  - **NPH is a treatable cause/ worsening of dementia**
Conclusion

- Patients with NPH and Alzheimer’s disease would be expected to progressively worsen with the passage of time.

- Patients with mild Alzheimer’s disease whom otherwise good candidates for shunt surgery would benefit from such procedure, whereas the benefits beyond the 4-month post op mark for patients with moderate to severe Alzheimer’s disease are much less supported.

- Recommendations for shunt insertion even if tests are negative or questionable in the case of high clinical suspicion for NPH until further research produces screening test with higher and negative predictive values.
References


