Recent Advances in Neurology
Clinico-Pathologic Conference

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Key Elements of the History

- Headache: posttraumatic?, meningeal irritation?, increased ICP?
- Visual Changes: migraine?, ICP?, occipital cortex?, TPO junction?
- Diffuse localization: memory, language, motor, possible temporal lobe seizures
- History of smoking

Key Elements of the Examination

- Not delirious: 7 digits forward
- 3 D words and 13 animals in 60 seconds
- Shuffling, wide-based gait
- Bilateral UMN signs: spastic UEs
- No clear meningeal signs
Normal Pressure Hydrocephalus (NPH)

- Lots of shunts placed for neurodegenerative conditions: AD, PSP most common
- Radiologic reports do us no favors
- We feel you have to prove it’s not “H”
  - Exclude inflammatory conditions
- We use 72-hour lumbar drains with timed/videotaped gait in highly selected pts
  - Data remains extremely problematic

Thoughts from Initial Imaging

Description

- Left-sided abnormalities, but examination and history clearly indicate more diffuse involvement
  - Bilateral pyramidal and extrapyramidal signs
  - Memory problems, gait perhaps all due to hydrocephalus
- Clearly leptomeningeal involvement, perhaps explaining hydrocephalus
  - Surprisingly few meningeal signs

Inflammatory vs. Non-Inflammatory

- Enhancement on MRI certainly pushes towards inflammatory
- We rarely perform LP without sending OCBs and IgIndex
  - Helpful in vasculopathy/vasculitis, toxic/metabolic vs. whatever, myelopathy vs. myelitis
- Although CSF acellular here, the elevated IgIndex puts the case squarely in the inflammatory camp
What’s Going on Here?

- 67 year-old man presents with progressive headache, visual changes, gait disturbance
- Signs of hydrocephalus on exam along with focal involvement of left side and cortical irritation
- Workup suggests a progressive process involving meninges and brain parenchyma (likely vascular involvement given DWI lesions)
- Clearly inflammatory, but no obvious systemic involvement

Our Approaches to These Types of Difficult Cases

- 1. Always distinguish inflammatory vs. non-inflammatory
- 2. CSF analysis can be helpful if sent for a broad range of tests, some of which are underutilized
- 3. Biopsy early with path consultation pre-op
- 4. Always obtain meninges as part of the biopsy
- 5. Never, never, never give steroids!!!

Is Biopsy Safe and Useful?

- Review of UCSF experience of 171 patients biopsied for rapidly deteriorating neurologic conditions over a 10-year period
- HIV and brain tumors (except lymphoma) excluded
- Sensitivity for diagnosis was 65%, specific treatment started in around 40%
- Complications from the procedure were rare (1-5% depending on definition)
Carcinomatous Meningitis

• Difficult to diagnose in some cases
• Low glucose and high protein common in CSF
• Hydrocephalus common (60%)
• Cranial and spinal nerve abnormalities
• Although it complicates 3-8% of all cancers and can be the presenting sign in 1-3%, isolated meningitis without systemic primary on PET/CT is case report-able

Atypical Infections: TB

• Difficult to diagnose
  – One of our more common “answers” on difficult-to-diagnose cases
  – Low glucose more reliable than high protein
  – Look for systemic disease: ppd, chest CT, consider bronchoscopy
  – CSF AFB cultures very insensitive (high-volume better, dependent on lab techs)
  – CSF TB PCR has emerged in last decade with disappointing results

Atypical Infections: Cocci

• Common in central California
  – “Valley Fever”

• Meningitis (can be focal) with hydrocephalus very common presentation
• Low glucose, variable cellularity
• PET and chest imaging helpful to exclude active systemic disease, but often not present
• Once a patient has pulmonary disease, fluconazole FOR LIFE
• Diagnose with CSF complement-fixing Abs or immunodiffusion tests for IgG and IgM
CNS Vasculitis

- Step-wise progression
- Parenchymal disease with strokes is the most common prominent abnormality
- Quite inflammatory CSF the rule
- Moves very quickly (days to weeks)
- Almost always has systemic involvement outside of the CNS

SARCOID

versus

LYMPHOMA

Progressive Neurological Syndrome with Suspicion for CNS Lymphoma

↓ HD 1
Contrast enhanced brain MRI
Contrast enhanced spine MRI
SEROLOGIES (CBC, Coag, HIV, Beta 2 microglobulin, LDH, SPEP, F/E)

↓ HD 2
Lumbar puncture, provided imaging shows no risk of herniation
Send CSF for:
- Cell count and diff
- Protein, glucose
- Igg index
- Oligoclonal Bands (with serum)
- Cytology
- Flow Cytometry
- EBV PCR

↓ HD 3
Whole Body PET CT
Ophthalmology consult – IR lamp examination & fluorescin angiogram

↓ HD 4
Lymph node/tissue biopsy if + on PET
OR
BMBx
OR
Vitreal sampling
OR
Repeat lumbar puncture, send CSF for:
- Cytology
- Flow cytometry
- Antithrombin III
- Immunoglobulin heavy chain rearrangement

↓ HD 5
Brain or meningeal biopsy

CSF Biomarkers for Lymphoma

- Would be a tremendous advance for neurologists and save a good amount of diagnostic confusion and CNS tissue sampling
Neurosarcoidosis

- Neurologic manifestations of sarcoid may be underestimated
  - 5% estimated in clinical series
  - 15% in autopsy studies of sarcoid patients
- Isolated neurosarcoidosis is thought to be a rare disease (prevalence unknown)
  - Spend most energy looking for systemic tissue to biopsy

Search for a Difficult-to-Diagnose Disorder

- Systemic disease
  - Chest CT
  - PET
  - Serum ACE
  - Eye and skin examination
- CSF Studies
  - Low glucose with pleocytosis
  - CSF ACE is worthless

Low CSF Glucose Differential

- 1. Bacterial Meningitis
- 2. Fungal Meningitis
- 3. TB Meningitis
- 4. Carcinomatous/Lymphomatous Meningitis
- 5. Sarcoid

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CNS Vasculitis: Misbeliefs

- Most (>80%) of cases don’t progress step-wise
- Meningeal disease occurs commonly and is prominent/isolated in ~5-20%
  - Target biopsy to include leptomeninges always
- CSF may be only mildly inflammatory, but it is abnormal 85-90% of the time (include OCBs and IgIndex)
- Usually subacute over months
- Isolated disease without systemic involvement not unusual

Vasculopathy vs. Vasculitis

- Terminology important due to treatment implications of autoimmune CNS vasculitis
- “Vasculitis” should be proven with...
  - 1. Inflammatory CSF (Including Ig Index, OCBs)
  - 2. Gadolinium enhancement
  - 3. Pathological specimens
- No great estimates but likely around 60% to 40% in favor of “-opathy” in the literature
  - Our recent experience more like 75/25

Cerebral Vasculitis

Diagnosis: Our Approach

- Vasculopathy vs. Vasculitis
- Search for evidence of systemic involvement
  - Both for clinical and pathologic diagnosis
- Rarely treat empirically because it means empiric prednisone and cyclophosphamide
- Don’t utilize angiography that frequently
- Frequently biopsy

My Diagnosis:

Primary CNS Vasculitis: Granulomatous Angiitis of the CNS