A 40 Year old Woman with a History of HIV and Lupus Presents with Right Sided Weakness

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Resident Presenters: Asher Albertson & Andrew Findlay
Financial Disclosures

• Dr. Naismith consults for: Acorda, Alkermes, Bayer, Biogen, EMD Serono, Genentech, Genzyme, Novartis, and Teva
• Asher Albertson: No Disclosures
• Andrew Findlay: No Disclosures
Dr. Robert Naismith

• BS: Case Western Reserve University- 1994
• MD: Case Western Reserve University- 1998
• Neurology Residency: Washington University - 2002
• Neuroimmunology Fellowship: Washington University- 2004
Fashion Forward Teaching

• Dr. Naismith wore his famed sport coat all through residency- a trend some of the current residents have begun emulating.

  -Because of his dressing style, he was frequently confused for an attending.

• Dr. Naismith is an ”amazing” cook. He considered becoming a chef- but ultimately chose medicine as he thought the hours would be better.

  -This has lead many in his division to question his judgement.

• Dr. Naismith roasts his own coffee beans making the space outside of his office a favorite for passing through.
Chief Complaint

• “I’ve started having trouble moving my right side.”
History of Present Illness

• This is a 40 year old woman with a history HIV/AIDS, discoid lupus, hepatitis C, and vitiligo who presents with several months of worsening right arm and right leg weakness.

• 4 months prior to presentation she began noticing that her right foot was “clumsy”. Over the following weeks this progressed to R arm and hand clumsiness. Symptoms finally progressed to overt arm and leg weakness. She then began falling.

• Outside of a vague “tingling” sensation- she denied sensory complaints.
Additional Questions?

- Diagnosed with HIV 18 years ago
- Mostly non-compliant-but **three weeks prior had restarted HAART therapy.**
- Last CD4 Count and Viral Load were 2 years prior.
  - CD4 Count: 42 cells/mcl
  - Viral Load: 32,000 copies/ml
- Currently compliant for 3 weeks on antibiotic prophylaxis
- No subjective fevers or chills

- No difficulty speaking or swallowing
- No headache
- No Shortness of breath
- No change in bowel or bladder function
- No systemic pain
• **Past Medical History**
  1. HIV/AIDS
  2. Hepatitis C
  3. Discoid Lupus
  4. Depression

• **Social History**
  • Denies alcohol use
  • Smokes 1 pack per day
  • Smokes marijuana weekly
  • Distant history of IVDU
  • Not currently working
  • Lives alone in St. Louis

• **Family History**
  • The patient denied any significant family history of neurologic illness, malignancy, or autoimmune disease

• **Travel History**
  • No recent travel outside Missouri

• **Allergies**
  • Bactrim
  • Ciprofloxacin
  • Azithromycin
  • Latex

• **Medications**
  • **HAART**
    • didanosine 400 mg Q day
    • lamivudine 300 mg Q day
    • atazanavir 200 mg Q day
    • raltegravir 400 mg BID

  • **Prophylaxis**
    • rifabutin 150 mg Q day
    • dapsone 100 mg Q day

  • **Other**
    • Percocet 5/325 Q6 PRN pain
Review of Systems

Constitutional: Negative
HEENT: Negative
Skin: Negative
Cardiovascular: Negative
Respiratory: Negative
Gastrointestinal: Negative
Genitourinary: Negative

Neurologic: Weakness and Falls
Muskuloskeletal: Some pain from falls
Hematologic: Negative
Lymphatic: Negative
Endocrine: Negative
Psychiatric: Significant anxiety and depression
What will you be looking for on examination?
General Examination

• Vital Signs:
  • Temperature: 36.7° Degrees C
  • Respiration: 18 Breaths/Min
  • Heart Rate: 57 Beats/Min
  • Blood Pressure: 118/52 mmhg

• Constitutional:
  • Thin/frail appearing woman in no apparent distress

• HEENT:
  • White plaques throughout oropharynx

• Respiratory:
  • Clear to auscultation bilaterally

• Cardiovascular:
  • Regular rate and rhythm, No murmurs, rubs, or gallops

• Abdominal:
  • Soft, non-tender, non-distended, normal bowel sounds

• Extremities:
  • No deformity, swelling, or evidence of trauma

• Skin
  • Multiple areas of hypopigmentation

• Psychiatric
  • Very anxious throughout the exam
Neurologic Exam

- Mental Status:
  - Awake, alert, oriented to person, place, and location.
  - 5 Quarters in 1.25, Presidents to Clinton, months backward

- Language:
  - Able to name and repeat simple and complex words and phrases.

- Cranial Nerves
  - 2-12 Intact
  - Normal fundoscopy
  - No dysarthria, droop, abnormal eye movements, facial weakness, or sensory change

- Motor:
  - R arm with pronator drift and slow FFM.
  - R tricep and Deltoid 4-/5
  - R leg with spastic catch on flexion and extension
  - R iliopsoas: 4-/5.
  - R knee extension 4+/5 and flexion: 4-/5.
  - Ankle dorsiflexion 4-/5 and plantar flexion: 4+/5

- Sensory:
  - Intact to pinprick, vibration, and proprioception in all 4 extremities.

- Coordination
  - No dysmetria on L FNF. R FNF limited by weakness.
  - No dysmetria on L to R heal knee shin.
  - R to L heal knee shin limited by weakness

- Reflexes:
  - 3+ in bilateral biceps, brachioradialis, triceps, patella, and ankle.
  - 3 beats of clonus in the right ankle.
  - R toe up-going

- Gait
  - Hemiparetic gait with right sided weakness requiring partial assist
Localization and Broad Differential Diagnosis
Diagnostic Tests

- Serum Labs
- CT Head
- Lumbar Puncture
- Brain MRI
- Whole Body PET
- Ultrasound Consult
- Neurosurgery Consult
Laboratory Data

HIV Viral Load: 35,200 Copies/ml
CD4 Count: 21 cells/mcl
Urine Histoplasma Antigen: Negative
Blood Cultures: No growth
Urine Cultures: No growth

UDS: Positive for opiates

Beta-2 Microglobulin: 4.2 (1.1-2.5)
LDH: 240
Immunofixation: No monoclonal peak
ANCA: Negative
ANA: Negative
ENA: Negative
Non-contrast Head CT
Brain MRI

Dr. Thomas Madaelil
Department of Radiology
Imaging DDx

• PML
• Lymphoma
• CMV
• HIV Encephalitis

What is a U-fiber?
Lumbar Puncture

Protein: 20 mg/dl
Glucose: 48 mg/dl
Nucleated Cells: 0 cells/mcl
Red Blood Cells: 21 cells/mcl

Oligoclonal Bands: 0
CSF Flow Cytometry: Pending
CSF Cytology: Pending
CSF VDRL: Negative
CSF JC Virus: Negative

CSF EBV: Inconclusive
CSF HSV: Negative
CSF VZV: Negative
CSF CMV: Negative
CSF Cryptococcus: Negative
CSF Toxoplasmosis: Negative

CSF Acid Fast Culture: No Growth
CSF Fungal Culture: No Growth
CSF Aerobic Culture: No Growth
Ultrasound Guided Lymph Node Biopsy

- Mixed Lymphoid Population
- Non Diagnostic
Brain Biopsy

Dr. Richard Perrin
Department of Pathology
Large atypical cells... ...proliferating

Also many small T-cells
B-cell lymphoma (EBER negative)
Microglial encephalitis?!

No viral inclusions; No multinucleated cells; Negative for HSV I&II, CMV...
Diagnoses:

Brain, left neocortex, biopsy:

- B-cell lymphoma with robust gliosis and microglial nodules
- Scattered cell nuclei positive for JC virus
Follow up

- The patient was treated with high dose Methotrexate and Rituximab.
- She was discharged to intensive inpatient rehabilitation.
- She followed up with radiation oncology and ultimately underwent 5 cycles of treatment with high dose methotrexate and rituximab.
- Admitted for new onset seizures several months ago.
  - At that time the right upper extremity had severe contracture and there was worsening weakness in R lower extremity.
  - She unfortunately missed a subsequent follow up appointment.
CNS Lymphoma

• Primary CNS Lymphoma
  • Variant of extra-nodal NHL
  • Involves brain, leptomeninges, eyes, spinal cord, or nerve without evidence of systemic disease

• Secondary CNS Lymphoma
  • Systemic NHL involving CNS - 10% of NHL cases
  • Leptomeninges and epidural space often involved
Primary CNS Lymphoma Epidemiology

- 4% of newly diagnosed primary CNS tumors
- AIDS patients
  - Incidence: 2-6%
  - Mean age at diagnosis: 43
- Immunocompetent patients
  - Incidence: 1000 fold less than AIDS patients
  - Mean age at diagnosis: 55
Primary CNS Lymphoma
Predisposing Factors

• Immunodeficiency
  • Iatrogenic, congenital
  • HIV: CD4 count, viral load
  • Strong relation to EBV in patients with HIV

• Autoimmune disorders
  • RA, SLE, MG, Sjogren’s
    • Disease or therapy related
Clinical Presentation

Clinicopathological Entities

- Intracranial lesion(s)
- Diffuse leptomeningeal or periventricular lesions
- Vitreous / Uveal deposits
- Intramedullary spinal cord lesion
- Neurolymphomatosis

Symptoms At Onset

- Focal neurologic deficits (70%)
- Altered cognition (43%)
- Seizures (14%)
  - More common in HIV patients
- Signs of increased ICP
  - Less common in HIV patients
- Ocular symptoms (4%)
- B symptoms (80%)
Evaluation of Primary CNS Lymphoma

- **MRI** with contrast
- **CSF** analysis
- **Slit lamp** examination of both eyes
- **Biopsy**
  - Stereotactic brain biopsy
  - Vitreal biopsy
- **Evaluate for systemic disease**
  - CT/PET of chest, abdomen, pelvis

Diagnosis requires histopathology
MRI Features

- Well defined focal or multifocal lesions.
  - Poorly defined in 15% of cases.

- Location:
  - Supratentorial and involve white or grey matter
  - In contact with subarachnoid / ependymal surfaces
  - Can cross corpus callosum

- Contrast:
  - High grade tumors – intense homogenous enhancement
  - Immunocompromised cases - Irregular and inhomogenous enhancement

- Mass effect but limited vasogenic edema.
CSF Analysis

- **Cell count:** Lymphocyte predominant pleocytosis
- **Protein:** Elevated
- **Glucose:** Normal. Low with leptomeningeal involvement.
- **Cytology:** 26% sensitive in HIV seronegative cases. Serial CSF samples may increase sensitivity. Unclear sensitivity in HIV associated cases.
- Flow Cytometry
- Toxoplasmosis serologies
- EBV PCR
Slit Lamp Exam

- Yellowish-white infiltrates at the sub-retinal pigment epithelium

- Intraocular Biopsy
  - Vitrectomy with cytology, flow cytometry
    - 64% sensitive, 100% specific in cases with vitreous involvement
Stereotactic Brain Biopsy

- Histopathology Subtype: diffuse large B cell lymphoma
- Lymphoid infiltrate along perivascular spaces and surrounding parenchyma
- Occasionally invade blood vessel walls
- Histopathology of 27 cases of primary CNS lymphoma revealed 6 positive for JC virus (Valle 2004)

- Corticosteroid impact on diagnosis:
  - Tumor shrinks in days
  - Lesion no longer enhances
  - Biopsy with necrotic non-diagnostic tissue
Treatment

• HIV/AIDS associated Primary CNS Lymphoma
  • High dose methotrexate + corticosteroids + antiretroviral therapy
  • Addition of rituximab is feasible in patients already on antiretroviral therapy
  • Radiation therapy
    • Limited survival benefit and significant morbidity
Prognosis

• Immunocompetent Primary CNS Lymphoma
  • Untreated: 1.5 months
  • Chemotherapy + Radiation: 30-60 months
  • 5 year survival: 30%

• AIDS associated Primary CNS Lymphoma
  • Untreated: 1-3 months
  • Chemo + steroids + antiretroviral therapy: 12-18 months
Thank You!

Dr. Naismith
Dr. Perrin
Dr. Madaelil
Dr. Ances