A young woman with blurry vision and an abnormal brain MRI

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History of Presenting Illness

- A 27-year-old, right-handed Caucasian woman presented to the UCSF Multiple Sclerosis Center with an 18-month history of bilateral blurry vision that worsened with movement.

- Two months after symptom onset, she began experiencing episodic vertigo and unsteadiness that was provoked by riding in the car.

- A few months later, she began to notice gait imbalance that was exacerbated by exercise or stress as well as episodes of arching her back while in the shower.

Initial Evaluation: Ophthalmology

- Six months prior to her UCSF visit, she was evaluated by an ophthalmologist, was diagnosed with pars planitis, and was treated with topical triamcinolone.

- Subsequently, she developed new urinary hesitancy without change in her bowel habits.

- A few months later, she was treated with high-dose oral dexamethasone for five days without a dramatic impact on her visual or neurologic symptoms.

- The patient also sought the opinion of an outside neurologist, who sent her to UCSF Multiple Sclerosis Center after an initial evaluation raised the suspicion for a demyelinating disorder.

- In the month prior to her UCSF evaluation, she noted episodic numbness and tremor in her hands, and her legs felt wobbly when standing for long periods.
Past Medical History
- Lifelong depression; anxiety
- Headaches
  - began at age 23; + nausea
  - increased frequency over past two years
  - last up to two days; relieved by sleep
- Recurrent nephrolithiasis
- Pars planitis

Medications
- Escitalopram (Lexapro) 20mg daily
- Treated with antidepressants since childhood
- Ages 24 to 26: Bontril (phendimetrazine) for weight loss

Family History
- Mother: Hashimoto’s thyroiditis; bipolar; pancreatic cancer
- Maternal cousin: “colitis”
- Maternal grandfather: essential tremor
- Paternal cousin: multiple sclerosis
- Paternal aunt: Crohn’s disease

Social History
- Lives in the Central Valley; no recent travel
- College student
- Drug/alcohol use:
  - Cigarettes– <1 pack per day for 10 years
  - Alcohol– rare
  - Marijuana– frequently
  - High school–2 cans of Dust-off (difluoroethane);
    -LSD, opium for ~3 months
  - Ages 23 to 26–cocaine (snorted)
**Examination**

Cranial nerves:
- Visual acuity: 20/30 OD; 20/70 OS
- Fundi: normal
- Pupils: briskly reactive; no APD
- Sensation: slightly decreased temperature sensation on left face

Motor: mildly increased tone in lower extremities; trace hip flexor weakness bilaterally

Sensory: reduced temperature and pinprick sensation on left arm and leg

Cerebellar: mild postural>intention tremor in right>left upper extremity; mild bilateral dysmetria on finger-to-nose, heel-to-shin

Reflexes: 2+ in upper extremities; 3+ at patellae; 5 to 6 beats of bilateral ankle clonus; Babinski’s sign present on left

Gait: mild difficulty with tandem

Romberg’s sign: absent

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**Neuro-opthalmology Exam**

- Decreased color vision bilaterally
- Decreased low-contrast visual acuity
- Normal retinal nerve fiber layer thickness

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**Discussion**
Serologic Tests
- Normal/negative from outside hospital:
  - Lyme
  - ESR
  - Vitamin B12
  - Thyroid-stimulating hormone (TSH)
  - Angiotensin converting enzyme (ACE)
  - HIV

Evaluation at Outside Hospital
- Lumbar puncture #1:
  125 red blood cells, 0 white blood cells, protein 35, glucose 52

- Lumbar puncture #2 (~5 days later):
  1 red blood cell, 11 white blood cells, protein 37, glucose 53; >5 oligoclonal bands, IgG index 0.7; negative cytology, VDRL, myelin basic protein, Lyme

Neuro-imaging
Differential Diagnosis of Diffuse White Matter Disease

- Metabolic disorder
  - Adrenoleukodystrophy
    - X-linked; 80% sensitivity of VLCFAs in females; adrenomyeloneuropathy in adults
  - Metachromatic leukodystrophy
    - in adults: behavioral change; neuropathy; posturing; late tetraparesis
  - Krabbe’s
    - late-onset: optic nerve pallor, pes cavus, slowly progressive tetraparesis, neuropathy
Metachromatic Leukodystrophy

Krabbe’s Disease

Pelizaeus Merzbacher

- Mitochondrial disorders
  - Pelizaeus-Merzbacher
    - In adults: spastic paraplegia, impaired cognition
  - Leukoencephalopathy with neuroaxonal spheroids
    - In adults: sporadic; primarily presents with cognitive decline; asymmetric on MRI; pathology with spheroids and pigmented glia
Adult-onset leukoencephalopathy with neuro-axonal spheroids

Differential Diagnosis, continued

- Toxic exposure
  - Heroin (heated; “chasing the dragon”)
  - Toluene
  - Cocaine
  - Amphetamines?
  - Methotrexate, other chemotherapeutic agents

Chronic toxic exposure

Cocaine
Differential Diagnosis, continued

- Malignancy- intravascular lymphoma
  - extranodal large B cell lymphoma
  - lymphocyte proliferation within vessels
  - often preferentially involves CNS, skin
  - can present with relapsing-remitting or progressive symptoms
  - “Largest” series with CNS disease: 1/7 +
    CSF cytology
  - Median survival 12 months; 14-32% 3-year survival; only 30% diagnosed antemortem

Intravascular Lymphomatosis

Differential Diagnosis, continued

- Infectious
  - Progressive multifocal leukoencephalopathy (PML)
  - HIV
  - Subacute sclerosing panencephalitis (SSPE)
HIV Encephalopathy

Further Normal Testing
- Methylmalonic acid, homocysteine, folate, ANA
- Nerve Conduction Study/EMG
- Consultation by uveitis clinic: no signs of prior or current inflammation to suggest pars planitis
- Very long chain fatty acids, ABCD1 gene mutation
- Arylsulfatase level, lysosomal storage disease screen
- Urine heavy metal screen, toxicology screen

SSPE

Repeat Lumbar Puncture
Red blood cells: 6169
White blood cells: 63 (50% lymph; 40% PMNs; 10% monos)
Protein: 58
Glucose: 56
Gram stain, culture: negative
Viral PCRs, AFB: negative
Cytology, flow cytometry: normal
Amino acids: normal
Oligoclonal bands: 1
IgG index: 0.7
**Additional Imaging**

- Spinal cord imaging: normal
- MRS: elevated choline peak

**Clinical Course**

- The patient reported worsening in the time between her initial visit and the completion of the workup, some of which was confirmed on clinical examination.

- Given the worsening and the increased pleocytosis in the CSF, brain biopsy was recommended.

**Biopsy**

**Axonal Damage and Gliosis**
Vacuolation

Other Stains

- LFB, PAS, neurofilament stains offered no additional information

Diagnosis?