“The Worst Headache of My Life”
A Diagnostic Dilemma

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History

68 yo woman c/o "worst headache of [her] life" after 3 wks of intermittent HAs.

No neurologic deficits, seizures, CP, trauma


PMH: HTN, Hyperchol
Meds: Atenolol, Triamterene/HCTZ, Lipitor. NKDA
SH: Recent Travel across US, Lives alone
Febrile, Elevated WBC, Hypertensive (195/116).

Tox screen, LP (2 RBCs, 0 WBCs), cardiac enzymes wnl
EKG ? Inferior MI

CXR showed b/l interstitial infiltrates, probable cardiomegaly c/w CHF

High on DDx: stroke, Subarachnoid Hemorrhage (SAH)
? hemorrhage in pt with HTN and “worst HA of her life”
Our patient: no intraparenchymal or extraaxial hemorrhage

No increased attenuation in our patient’s CSF, Sylvian fissure, basal cisterns or ventricular system.
Head CT Findings

Head CT: Edema
Largely Right Posterior

Some loss of gray-white differentiation and hypodensity in R occipital lobe.

Subcortical white matter hypodensities.

No midline shift, No hydrocephalus.

Broad Differential: Tumor, Infection, Inflammation
ED Course

- Pt intubated on propofol.
- Neuro exam: Comatose, non-focal
- Fundoscopic Exam: Disc Margins blurred.
- C/w CT findings of edema.
- Head MRI per radiology recommendation 5 hours after arrival
MRI

- MRI showed focus in R posterior region
- Additionally, multiple cortical and subcortical enhancing lesions bilaterally in cerebral hemispheres and cerebellum
- Gray and white matter
Enhancing Lesions

- Magnevist (Gadolinium-DTPA complex) is highly hydrophilic
- Brain uptake only if hydrophobic Blood Brain Barrier disrupted
- Enhancement on post-Gadolinium T1 images compared with T1 pre-Gadolinium images
Our patient’s T1 Axial Images Pre and Post Gadolinium
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Multiple bilateral enhancing cerebellar lesions
Our patient’s T1 Axial Images Pre and Post Gadolinium

More cerebellar enhancing lesions
T1 Axial Images
Pre and Post Gadolinium

PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium

Temporal Lobe apparently spared, enhancing lesions in occipital lobe.
T1 Axial Images
Pre and Post Gadolinium

Pre

Post

PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium

Pre

Post
T1 Axial Images
Pre and Post Gadolinium

Pre

Post

Basal Ganglia and Thalamus spared  PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium
T1 Axial Images
Pre and Post Gadolinium

PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium

Corona Radiata (and optic radiation) relatively spared
T1 Axial Images
Pre and Post Gadolinium

Pre
Post
Question of a watershed distribution (Middle Cerebral and Anterior Cerebral Arteries)
Possible watershed distribution in Parietal lobes bilaterally
T1 Axial Images
Pre and Post Gadolinium

Pre

Post

PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium

Pre

Post

PACS, BIDMC
T1 Axial Images
Pre and Post Gadolinium

Pre
Post

PACS, BIDMC
T1 Gadolinium Findings

- Multiple enhancing nodular lesions predominantly in occipitoparietal region bilaterally (R>L)
- Lesions in frontal lobe
- Temporal lobe, Basal ganglia, and Brain Stem spared
- Possible watershed distribution (MCA, ACA)
Fluid-Attenuated Inversion-Recovery (FLAIR)

- Strong T2 weighting + CSF suppression
- High lesion to tissue contrast
- Spin-echo technique
- Possible CSF pulsation artifact
- High sensitivity for MS, SAH
Fluid-Attenuated Inversion-Recovery (FLAIR)

Prominent hyperintensity in posterior distribution, R>L c/w Edema
Fluid-Attenuated Inversion-Recovery (FLAIR)

- Possible Edema in posterior region
Hyperintensity points to Acute Ischemia

Diffusion Weighted Images (DWI) measures the diffusion of water molecules. (Brownian Motion)

2 pulses tag and catch Hydrogen.

1st pulse dephases spins

2nd pulse rephases the spins if no net movement. If between pulses, there is net movement, signal is attenuated

In acute ischemia, blood flow is lowered. Sodium enters cells, followed by H2O-> cytotoxic edema. Water movement now restricted within cell membranes.

Image from www.brooklyn.cuny.edu/bc/ahp/ChemInvest
Diffusion Weighted Image (DWI)

Right posterior parietal region raised question of small associated infarction.

However, may be an artifact of T2 shine through. High T2 weighting may yield this apparent lesion on DWI and may represent the strong lesion seen on T2.
Gradient Echo (GRE)

T2 weighted technique sensitive to magnetic field inhomogeneity, such as created by paramagenetic materials.

Hypointense lesion may represent hemosiderin from small hemorrhage. No evidence of lacunar infarcts c/w HTN hemorrhages.
Magnetic resonance angiography
MRA

MRA showed a complete Circle of Willis. No aneurysms or other vascular abnormalities seen.

Images derived from Time of Flight based on blood flow

ACA=Anterior Cerebral Artery, MCA= Middle Cerebral Artery, PCA=Posterior Cerebral Artery, ICA = Internal Carotid Artery
MRI Impression

Innumerable nodular enhancing foci predominantly in watershed distribution in cerebrum and cerebellum with edema. Primarily parietal, occipital, and frontal lobes. Possible small posterior parietal area of new infarction with minimal hemorrhage.

T1 sagittal post-Gadolinium
Differential Diagnosis

- Hypertensive Leukoencephalopathy
- Multiple Sclerosis
- Neurosarcoid/other granuloma
- Small Vessel Vasculitis
- Acute Disseminated Encephalomyelitis (ADEM)
- Infectious Encephalitis
Hypertensive Encephalopathy

Pro
- Patient was hypertensive (195/116 in ED)
- Possible subacute presentation
- MRI classically shows primarily posterior lesions in gray and white matter.
- FLAIR and DWI show lesions with edema

Con
- Lesions normally not enhancing
- Centrally located, usually spares calcarine cortex/sulcus
- Rarely involves Cerebellum
Multiple Sclerosis (MS)

Pro
• Multiple lesions, enhancing seen also on T2, FLAIR

Con
• Single attack
• Plaques usually periventricular or in corpus callosum
• MS plaques normally ovoid
• Large number of lesions for initial presentation

Image from www.splweb.bwh.harvard.edu
Neurosarcoidosis

Pro
Presents with Multiple White Matter Lesions

Can affect any part of the CNS

Con
Unlikely, but possible, without lung involvement on CXR

Neurosarcoidosis usually in base of the brain and midline, affecting hypothalamus and pituitary

May include space occupying lesions

www.medscape.com
Brain Biopsy

On Hospital day #3, our patient had a brain biopsy to evaluate for vasculitis or other unknown etiology

Biopsy showed:
Subacute Encephalomyelitis
Infectious(Viral) vs Immunologic(MS, ADEM)
Cytology negative for malignancy
ADEM

• Acute demyelination after viral infections or vaccine
• Usually in children
• Often mistaken for MS, but has resolution of symptoms
• Causes include (zoster, measles, rubella, HSV, coxsackie, echo, polio, CMV, EBV, VZV, influenza, and parainfluenza, Japanese Encephalitis Vaccine). As well as Mycoplasma pneumoniae, Listeria, Streptococcus, and typhus.

T1 images post gado
www.med.ege.edu.tr
ADEM and MRI

ADEM results in perivascular edema, inflammation, and demyelination.?

MRI: Multifocal, asymmetric white or gray matter lesions
Lesions resolve with time
Lesions can be enhancing, associated with edema, and found in b/l hemispheres, cerebellum, and basal ganglia

MR Spectroscopy shows promise in determining chemical composition of lesions to differentiate from MS

www.emedecine.com
Viral Encephalitis

- Clinical Encephalitis (Elevated WBC, fever, recent travel)
- Persons with cerebrovascular disease (HTN, Hypercholesterolemia) are at increased risk of viral encephalitis
Causes of Viral Encephalitis

- Herpes Encephalitis
- West Nile Virus
- St Louis Encephalitis
- Western/Eastern Equine Encephalitis
- Influenza
- HIV
- Enterovirus
- Measles, Subacute Sclerosing Panencephalitis
- Herpeseviridae (EBV/CMV/HHV6/HHV7)
- Progressive Multifocal Leukoencephalopathy
- Japanese Encephalitis
- Nipah Virus
- ?Von Economo
Treatable Encephalitis

- HSV
- HIV
- CMV, EBV, HHV6, HHV7
- Influenza
- Vaccine for Japanese Encephalitis

- Question of whether steroid treatment (often for cerebral edema) is harmful for viral encephalitis
Unlikely HSV Encephalitis

- Classically Temporal Lobe (spared in our patient)

- Medial temporal and frontal lobe first affected due to intracranial spread from meningeal branches CN V.

- Insular cortex (sparing lentiform nucleus). Limbic system spread and later pontine involvement

- Edema, then Hemorrhage and Necrosis.

- Most common encephalitis in US

West Nile Virus

- Close to 10,000 cases in US with >20% Mortality
- Mostly Western States
- MRI shows diffuse lesions with enhancement, but often targets substantia nigra (unlike our patient)
- St Louis Encephalitis closely related, seen in Southern US

Solomon 2004. NEJM. 351 (4): 370
Equine Encephalitis

- Eastern, Western, Venezuelan
- Rare (8 cases/yr in US of Eastern and Western)
- Eastern in MA
- Multiple enhancing lesions common
- Usually in Basal Ganglia, Thalami as seen in this pt

NEJM. 1997.336:1867-1874
Immunocompromised Disease

- Patient not immunocompromised
- Lesions rarely enhancing given immunocompromise and lack of inflammation
- HIV results in atrophy, large ventricles
- PML is demyelinating
- CMV, EBV, HHV6, HHV7
Exotic Encephalitis

- Japanese Encephalitis, Nipah, Murray Valley
- No known domestic transmission
- South East Asia (Nipah recently emerged from pig virus; Murray Valley in Australia and Papau New Guinea)
- Result in punctate central lesions, predominantly in Thalami (JE) and Basal Ganglia (both)
- Infection often unrecognized until Parkinsonism sequelae
The Verdict

- Most likely ADEM
- Cause infectious, post-infectious, or autoimmune
- Exacerbated by HTN
- ADEM precipitant unknown
- If Viral possibly West Nile, St Louis, Eastern Equine, or Enterovirus given travel history, lack of immunosuppression, and MRI, but radiologic presentation is not classic
Patient’s progress

• Pt placed on IV steroids in Neuro ICU
• Pt improved neurologically, began nodding replies
• Extubated after 3 days
• Discharged after 2 weeks to long term care
• A+Ox3, speech fluent. Residual mild L hemi-neglect, distal lower extremity weakness.
• Sister reported possible URI/Earache prior to HA which may represent ADEM precipitant or viral prodrome
Useful References

• Huk, WJ et al. MRI of Central Nervous System Diseases. 1989. Springer-Verlag, NY
• Greenfield’s Neuropathology. Editors Graham and Lantos. 1997. HDI, NY
• Martin K, C Franco-Paredes. Lancet 2002. 360, 9342; 1286
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