Posterior Reversible Encephalopathy Syndrome (PRES)

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44-year-old man with a history of metastatic renal cell carcinoma s/p debulking operation. Now with recurrent mass in left renal bed and metastasis to abdominal lymph nodes and lungs.

Currently on Sutent (multiple RTK inhibitor) and Gemzar (nucleoside analogue).

Presents with headache, fatigue, “word finding difficulties” and fluctuating mental status including periods of agitation and inability to recognize family. He is noted to have new onset hypertension (160s / 100s from a baseline of 130-140s/70-80s).
Differential diagnosis

- The acute onset of mental status changes has a long differential diagnosis.

- In the absence of an obvious cause, several emergent conditions should be ruled out by head imaging:
  - Hemorrhage
  - Mass effect (midline shift, herniation, increased ICP)
  - Ischemia / infarction

- Non-contrast CT is the first-line test for assessing intracranial hemorrhage (seen as hyperdensity) and mass effect…
Patient RF: Baseline and current head CT

8 months ago

Present

Bilateral, white-matter hypodensity with no mass effect
Patient RF: Lesions on MRI and CT

MRI (FLAIR)

Lesions are T2-hyperintense.

CT
There are multiple high signal lesions bilaterally in the white matter of all four lobes, but most predominant in parietal cortex.
Patient RF: Summary

- Multiple, bilateral, hyperintense subcortical white-matter lesions on T2-weighted MRI.
- Parietal >> occipital, frontal, and temporal involvement.
An abbreviated differential: T2-bright white matter

- **Neoplastic** - glioma, lymphoma, gliomatosis cerebri, metastasis
- **Vascular** - arterial or venous thrombosis, anoxia, vasculitis, amyloid angiopathy
- **Demyelination** - MS, ADEM, acute hemorrhagic encephalomelitis, Schilder’s disease, Marburg disease, concentric sclerosis
- **Dysmyelination** - leukodystrophies, PKU, MSUD
- **Infection**
  - **Viral** - HIV, VZV, JC (PML), measles (SSPE), rubella
  - **Bacterial** - Lyme, neurosyphilis
  - **Parasitic** - toxoplasmosis
- **Inflammatory** - neurosarcoid, SLE, Behcet’s, Sjogren’s, Wegener’s, polyarteritis nodosa, scleroderma
- **Hydrocephalus** - early and normal-pressure
- **Trauma** - diffuse axonal injury
- **Seizure**
- **Toxic** - radiation therapy, antineoplastics, immunosuppressants, drugs of abuse, environmental exposures
- **Posterior Reversible Encephalopathy Syndrome (PRES)**
- **Other genetic** - NF2, Hurler’s syndrome, mytonic dystrophy
Narrowing the differential for patient RF

- Neoplastic - metastatic renal cell cancer
- Ischemia/infarction
- Infection - PML
- Posterior Reversible Encephalopathy Syndrome (PRES)
- Toxic - secondary to chemotherapy (Sutent, Gemzar)
Typical appearance of brain metastasis on MRI

- Most common tumors to metastasize to the brain (in decreasing frequency): lung, breast, melanoma, renal and colon.

- Appearance on MRI
  - Multifocal, classically at gray-white junction
  - T1 isotense or mildly hypointense. Hemorrhagic necrosis may be hyperintense.
  - T2-hyperintense (tumor and surrounding vasogenic edema)
  - Exhibit mass effect, distortion of brain architecture.
  - Enhancing: solid, nodular or irregular ring pattern. Nonenhancing lesions are less likely to be metastasis.
Companion patients #1-3: Brain metastasis on post-gadolinium T1W-MRI

Solid enhancing lesion with surrounding edema¹.

Multiple, ring enhancing lesions¹.

Single enhancing lesion with central necrosis, surrounding edema and sulcal effacement².

2. http://www.nature.com/bjc/journal/v89/n2/fig_tab/6601116f1.html
Patient RF: C- and C+ MRI

Lesions do not enhance.
Patient RF: Summary

- Multiple, bilateral, hyperintense, subcortical white-matter lesions on T2-weighted MRI.
- Parietal >> occipital, frontal, and temporal involvement.
- Mild sulcal effacement.
- Nonenhancing.
Diffusion-weighted MRI is sensitive for ischemia within minutes of the cerebrovascular event, presumably secondary to cytotoxic edema.

Appearance on MRI
- Lesions confined to a vascular territory, though multiple emboli can produce multifocal disease.
- Bright on diffusion-weighted imaging (DWI)
- Anything that is T2-hyperintense (e.g. cerebral edema) can falsely elevate signal on DWI (“T2 shine through”).
- To eliminate the effect of T2 signal, an Apparent Diffusion Coefficient (ADC) is calculated. Ischemia is dark on ADC imaging.
Companion patient #4: Right MCA stroke on MRI

DWI

ADC

PACS, BIDMC
Patient RF: possible ischemia on DWI and ADC MRI

DWI

ADC

PACS, BIDMC
Patient RF: Summary

- Multiple, bilateral, hyperintense, subcortical white-matter lesions on T2-weighted MRI.
- Parietal >> occipital, frontal, and temporal involvement.
- Mild sulcal effacement.
- Nonenhancing.
- Questionable areas of ischemia/infarction.
Infection: PML

- Progressive multifocal leukoencephalopathy - a subacute demyelinating disorder.
- Secondary to reactivation of latent JC virus in the setting of impaired cell-mediated immunity. (80% AIDS, 13% hematologic malignancy, 5% post-transplant immunosuppression)
- Symptoms: commonly weakness, speech disturbance, headache. Any focal neurologic sign is possible. 10% have seizures.
- 1-year survival if HIV+: 50% if treated with HAART, 10% if untreated
- Appearance on MRI:
  - Multiple T2-hyperintense periventricular and subcortical white matter lesions.
  - Typically do not enhance or exhibit mass effect.
  - Rarely show diffusion restriction.
Companion patient #5: PML on MRI (FLAIR)

A good fit for patient RF’s imaging, however less likely clinically. PML rarely seen secondary to anti-neoplastic agents. RF was not leukopenic (WBC 4.1).

www.emedicine.com/radio/topic573.htm
Posterior Reversible Encephalopathy Syndrome (PRES)

- Also called Reversible Posterior Leukoencephalopathy Syndrome.
- Presents with headache, altered consciousness, visual disturbances and/or seizures typically in the setting of new-onset hypertension.
- Associated with acute hypertensive encephalopathy, eclampsia and cytotoxic / immunosuppressive drugs (including Sutent).
- Etiology unclear, thought to be secondary to endothelial damage in the setting of hypertension and failure of cerebrovascular autoregulation with subsequent vasogenic edema. The posterior circulation is more sensitive to the effects of hypertension.
Appearance on MRI

- Multifocal T2-hyperintensities
- Favors parietal and occipital cortex (nearly 100% of cases), but can involve other cortex, thalamus, basal ganglia, cerebellum and brainstem.
- Variable presentation on diffusion weighting imaging. Ischemic changes on DWI/ADC are associated with worse prognosis.
- Can exhibit subcortical “gyral” enhancement secondary to breakdown of the blood-brain barrier.
- Mass effect associated with edema
Companion patient #6: PRES on MRI (FLAIR)

http://www.mypacs.net/cgi-bin/repos/mpv3_repo/wrm/repo-view.pl?cx_subject=1775907&cx_repo=mpv4_repo
PRES can resolve rapidly

- **Treatment**
  - Control hypertension
  - Discontinue cytotoxic drugs
  - Antiepileptics if seizing

- If treated, most patients exhibit complete neurologic recovery within ~2 weeks accompanied by resolution of the radiologic lesions.

- Resolution is not always complete. Predictors of poor prognosis include larger area of involvement and evidence of ischemia/infarction on MRI.
Companion patient #7: Resolution of PRES on MRI

PRES can resolve rapidly once the causal insult is removed.
Patient RF’s course

- Patient RF’s chemotherapy was withheld and his blood pressure tightly controlled. His symptoms resolved after ~3 days. Repeat MRI at 5 days was unchanged. He was discharged after 1 week and has not had a recurrence of symptoms for the last 7 months despite being restarted on Sutent.

- He has not had follow-up head imaging.
Patient RF: Summary

- Multiple, bilateral, hyperintense white-matter lesions on T2-weighted MRI.
- Parietal >> occipital, frontal, and temporal involvement.
- Mild sulcal effacement.
- Nonenhancing.
- Questionable areas of ischemia/infarction.

- Dx: PRES secondary to hypertension and/or Sutent toxicity with possible secondary ischemia.
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