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Psychotic Features and Behavioral Dysregulation in a Patient with Tumefactive Multiple Sclerosis

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Background

- Multiple sclerosis (MS) is a chronic demyelinating disease, classically characterized by lesions disseminated in time and space[1]
- Tumefactive multiple sclerosis (TMS) is a rare variant of MS, with a prevalence of approximately 3 per 1,000,0000 individuals[2]
- Radiologic characteristics of TMS[3]
  - Lesions >2 cm
  - Possible associated mass effect, edema
  - Open-ring enhancement
- TMS may mimic lesions of neoplastic, vascular, infectious, and inflammatory etiology[3-5]
- Clinical presentation is dependent upon location and size of lesions[6-8]
  - Mass-effect symptoms
  - Higher cortical deficits
  - Motor symptoms
  - Sensory symptoms
  - Cerebellar symptoms
  - Brainstem symptoms
  - May also be asymptomatic
- Relationship between MS and psychiatric disorders such as mood, anxiety, substance use, and less commonly psychotic disorders has been well studied[9-13]
- However, there is sparse literature on the psychiatric manifestations of TMS

Case Presentation

- 42-year-old African American woman with a chart documented psychiatric history of schizoaffective disorder depressive type
  - Diagnosed with schizoaffective disorder 9 years prior to admission at an outside hospital
  - Last hospitalized 6 years prior
  - No hallucinations of paranoia in 3 years
  - She self-discontinued haloperidol and divalproex for at least 15 months, as she felt better
- Presented to Kingswood Psychiatric Hospital initially for mood instability and irritability
  - CBC, CMP, TSH were within normal limits
  - Urine drug screen and urine pregnancy test were negative
  - No psychosis present throughout initial hospitalization
  - Improved on divalproex and was discharged on this alone
- Readmitted 2 weeks later with fears that she was pregnant
  - CBC, CMP, were within normal limits
  - Urine drug screen and urine pregnancy test were negative
  - Psychotic symptoms on encounter
    - Affect was out-of-sync
    - Appeared to be responding to internal stimuli
    - Disorganized speech (dysphonia with abnormal prosody)
    - Disorganized behaviors (repeatedly flicking her juice bottle, laying down unprompted, walking around partially dressed)
    - Loose-tangential thought process
  - No improvement after olanzapine and paliperidone were sequentially trialed
  - Developed signs suspicious for catatonia, though did not meet DSM-V criteria
    - Bush-Francis Scale
      - Verbigeration (1)
      - Grimacing (1)
      - Stereotypies (1)
      - Staring (1)
    - No response to lorazepam challenge
    - In order to avoid exacerbating potential catatonia, paliperidone was discontinued and aripiprazole was initiated[14]
  - Sudden development of neurological deficits: Right upper extremity weakness, dysphagia, expressive aphasia, urinary incontinence, gaze deviation and eye fluttering
    - Concern for vascular, infectious, or neoplastic etiology
    - Sent to HF Main

Imaging

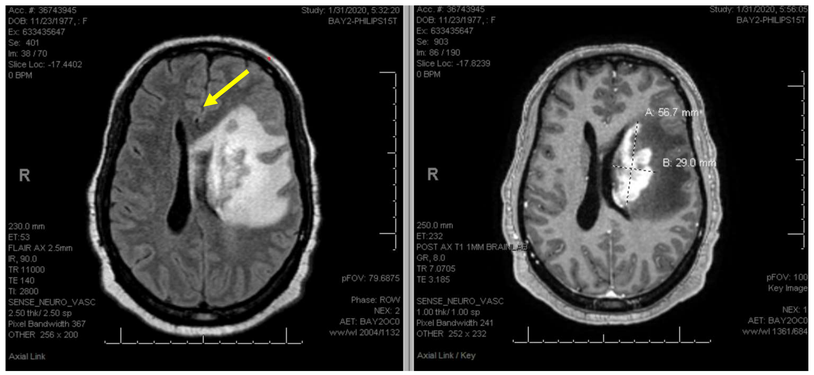

FIGURE 1. MRI brain 1/31/20. Shown above are axial T2-weighted FLAIR (left) and post-contrast T1-weighted (right) images. Note the extensive vasogenic edema surrounding the diffusion restricted mass and rightward subfalcine herniation (arrow). Findings initially were highly suspicious for lymphoma, metastatic disease, or high-grade astrocytoma.

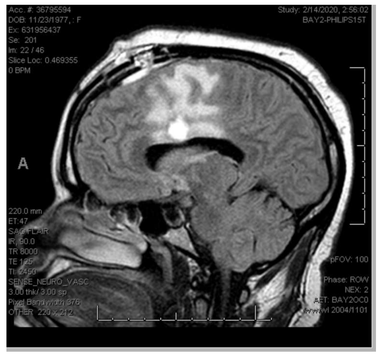

FIGURE 2. MRI brain 2/14/20. Shown above is a sagittal T2-weighted FLAIR image following the craniotomy and 5-day course of methylprednisolone. Clinically, patient was noted to have improvement in right upper extremity weakness, gaze deviation and eye fluttering, expressive aphasia, and psychotic behavior.

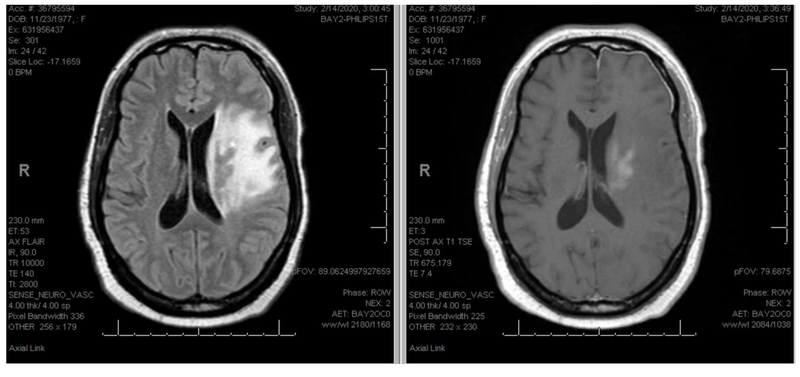

FIGURE 3. MRI brain 2/14/20. Shown above are axial T2-weighted FLAIR (left) and post-contrast T1-weighted (right) images. Note the improvement in vasogenic edema and mass effect-associated herniation following the craniotomy and 5-day course of methylprednisolone.

Case Work-up and Management

- **<u>Imaging</u>**
  - CT Head: Vasogenic edema predominantly in the left frontal lobe and basal ganglia concerning for an underlying intra-axial mass lesion
  - MRI Brain: Enhancing diffusion restricted mass in left frontal lobe extending to body of corpus callosum; extensive vasogenic edema and mass-effect with rightward subfalcine herniation
  - MRI Cervical, Thoracic, Lumbar spine: Negative for spinal lesions
  - CT Abdomen Pelvis: Negative for malignancy
- **<u>Further Neurological Work-Up</u>**
  - cEEG: No epileptiform activity
  - Paraneoplastic, vasculitis panels negative
  - CSF studies: IgG index 0.8; Protein 41.4 g/L, RBC<3/cu mm, WBC<3/cu mm, Glucose 92 mmol/L; Negative for oligoclonal bands, HSV 1/2, HIV, fungal culture, cryptococcus, CMV, VDRL, VSV, and EBV; CJD panel collected and pending
  - Underwent left frontal craniotomy with biopsy
    - Frozen section: Preliminary lymphoma
    - Pathology: Reactive T cell population with tumefactive demyelinating features
- Received 5-day course of methylprednisolone; vasogenic edema and psychotic behavior improved
- Divalproex and aripiprazole were reinitiated at lower doses: 500 mg divalproex and 10 mg aripiprazole
- Continued to have intermittent fluctuations in confusion and aphasia
  - Interval development of hyponatremia, which was gradually corrected with fluid restriction, salt tablets, discontinuation of home thiazide diuretic
  - Discharged on high dose oral prednisone for one month
- Follow-up Neurology appointment 4/1/20: No neurological deficits; no aggression or psychotic behaviors noted by patient or her sons
  - Patient advised to continue gradual taper of oral prednisone and to follow-up with her psychiatrist

Discussion

- No MRI brain images in our system from the time she was initially diagnosed with schizoaffective disorder
  - MRI 3 years prior to most recent admission showed cerebral atrophy, which may occur very early in the course of MS, independent of demyelination[15]
- Patient was found to have developed other neurological symptoms *after* her initial schizoaffective disorder diagnosis, which may have been potentially related to an underlying demyelinating process
  - Urinary incontinence
  - Dysphagia
  - Memory loss
- Management in TMS includes steroids[16], agents known to cause neuropsychiatric complications[17]
- Steroid responsive enhancing lesions represent a flare[12]
  - It is possible that our patient's behavioral dysregulation and psychotic features were secondary to a TMS flare
- Improvement in psychosis may have been confounded by presence of aripiprazole
  - Aripiprazole has been found to be efficacious in treatment of MS-related psychosis[18,19]
- Mood and anxiety disorders predate onset of clinical MS symptoms by up to five years[20,21]
- Psychosis also found to occur before onset of MS symptoms[12,20,21]
- Overall, this case demonstrates that psychiatric symptoms, including psychosis and possibly aggression, may be also be part of the TMS prodrome

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