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Letter to the Editor: New Observation

Neuro-Behcet's Presenting as a Tumefactive Brainstem Mass

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A 33-year-old male of West-African descent was diagnosed with Behcet's disease based on international criteria[1] following a 4-year history of aphthous ulcerations in the scrotal, scalp and oral area, uveitis, polyarthralgia, and mild right hemiparesis. Brain MRI at diagnosis revealed a small T2-weighted (Figure 1A) and fluid-attenuated inversion recovery (FLAIR, Figure 1B) hyperintensity at the level of the left olivary nuclei accounting for his hemiparesis. He briefly trialed apremilast with no significant improvement.

Two years later, he presented with 10 days of generalized headaches, horizontal binocular diplopia, ataxia, a low-grade fever, and new genital/oral ulcers. On examination, he had bilateral limitation in eye abduction, dysarthria, right-sided spasticity/hyperreflexia/residual weakness, truncal ataxia, and a wide-based gait. An enhanced brain MRI redemonstrated the left medullary hyperintensity (not shown). Additionally, a large enhancing, centrally necrotic, parenchymal lesion of the right pons extending to the medulla (Figure 1C–H) with moderate mass effect was noted. T1-weighted imaging revealed a large hypodense gadolinium-enhancing lesion (Figure 1C and D). T2-weighted and FLAIR imaging demonstrated ring-like patchy enhancement with a central area of necrosis (Figure 1E and F). There was an increased signal on diffuse-weighted imaging (Figure 1G) with a central area of hypointensity on apparent diffusion coefficient (ADC) imaging (Figure 1H).

He had an elevated erythrocyte sedimentation rate at 50 mm/hour (reference range 0–15) and C-reactive protein at 16.8 mg/L (reference range <3.0). A rheumatologic workup including extractable nuclear antigen, antinuclear antibody, rheumatoid factor, double-stranded DNA, and anticyclic citrullinated peptide was negative. His infectious serology was negative for hepatitis C, human immunodeficiency virus, human T-cell lymphotropic virus, syphilis, and strongyloides. His labs were consistent with remote cytomegalovirus (CMV) and Epstein–Barr virus (EBV). His hepatitis-B surface antigen and antibody were negative; while his hepatitis B core antibody was positive. Our Infectious Disease colleagues attributed his test result to a previous infection, based on the Centers for Disease Control and Prevention guidelines. Of note, less common interpretations of our patient's hepatitis serology include false positives, a low level of chronic infection, and a resolving acute infection for which he had no clear symptoms. Our patient also tested positive for latent tuberculosis (TB, QuantiFERON-TB®). His cerebrospinal fluid (CSF) revealed lymphocytic-predominant pleocytosis with 11.10^6 cells/L (reference range 0–5). He had high CSF levels of interleukin-6 (44.8 pg/ml, >85% the reported reference range) commonly seen with parenchymal neuro-Behcet disease (NBD).[1] His CSF MitogenDx® encephalitis and paraneoplastic panels were negative, as was flow cytometry for acute leukemia/lymphoma. His CSF bacterial and fungal culture were negative, as was testing for mycobacterium, enterovirus, parechovirus, herpes simplex virus, varicella zoster, CMV, EBV, and polyomavirus. Stool cultures were negative for parasites. A CT chest revealed no disease activity. Considering the patient's history and negative work-up, his presentation was believed to be parenchymal NBD. He received intravenous methylprednisolone 1 g daily for 3 days, followed by prednisone 60 mg (with taper) and azathioprine 150 mg daily. In light of his immunosuppression, our Infectious Disease colleagues suggested treatment of his latent TB with isoniazid 300 mg and pyridoxine 25 mg daily, and tenofovir 300 mg daily to prevent hepatitis-B reactivation. He rapidly and significantly improved with steroids and an MRI 1-week later revealed a resolution of enhancement on T2-weighted/FLAIR imaging (Figure 2A and B). There was near complete lesion resolution by 3 months (Figure 2C and D), and at 12 months, the patient was clinically stable.

Neurological involvement in Behcet's ranges from 5% to 40% among studies, typically occurring 2–4 years after disease onset.[1] Parenchymal NBD includes brainstem, myelopathy, cerebral, optic neuropathy, or multifocal syndromes. Nonparenchymal syndromes include cerebral venous thrombosis, acute meningitis, and intracranial hypertension. Brain lesions in parenchymal NBD are typically hypo to iso-intense on T1-weighted imaging and ADC, hyperintense on T2/FLAIR, and enhancing; similar to our patient.[1] Rarely, parenchymal NBD presents as a brain mass, mimicking a primary brain tumor. Males are more often affected, presenting with headaches and pyramidal dysfunction; with the thalamus and basal ganglia as frequent lesion locations.[2,3].Tumefactive NBD is rare and has only been reported a handful of times.[2–6] Imaging in tumefactive NBD demonstrates areas of T2 hyperintensity and diffuse contrast enhancement

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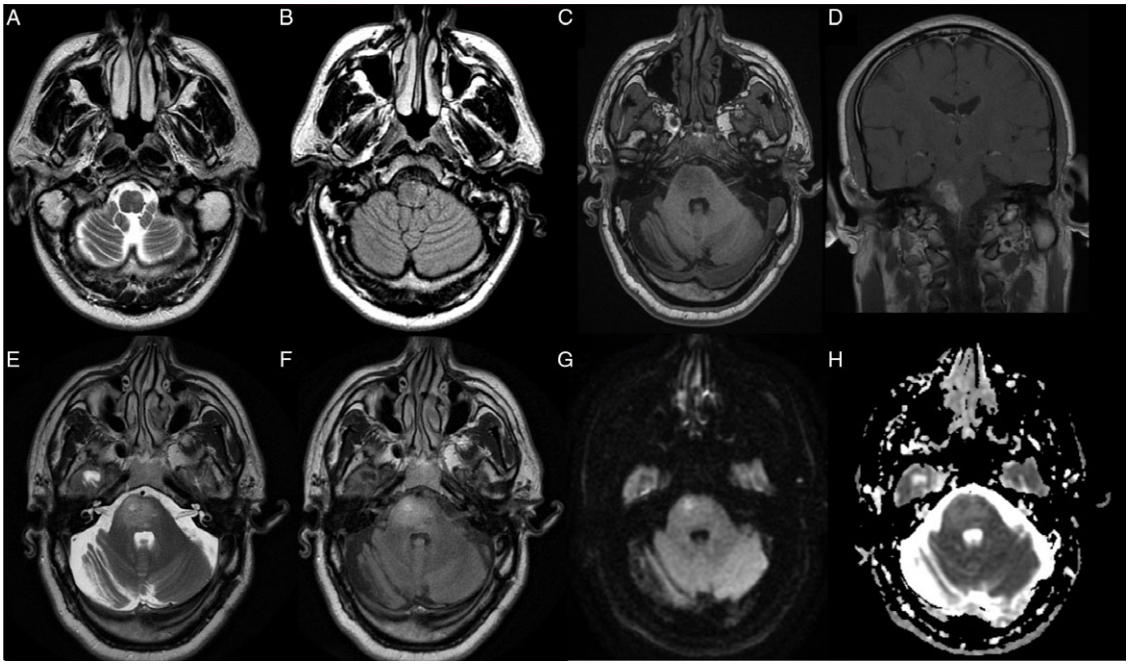


Figure 1: MRI at diagnosis revealed a small area of hyperintensity on T2-weighted imaging (A) and fluid attenuation inverse recovery imaging (FLAIR, B) at the level of the left inferior olivary nuclei. On representation, MRI revealed a large parenchymal lesion of the right pons on T1-weighted imaging (C), with enhancement visible in the coronal view (D). This was also observable in the axial view on T2-weightd imaging (E), FLAIR (F), diffusion-weighted imaging (G), and apparent diffusion coefficient imaging (H).

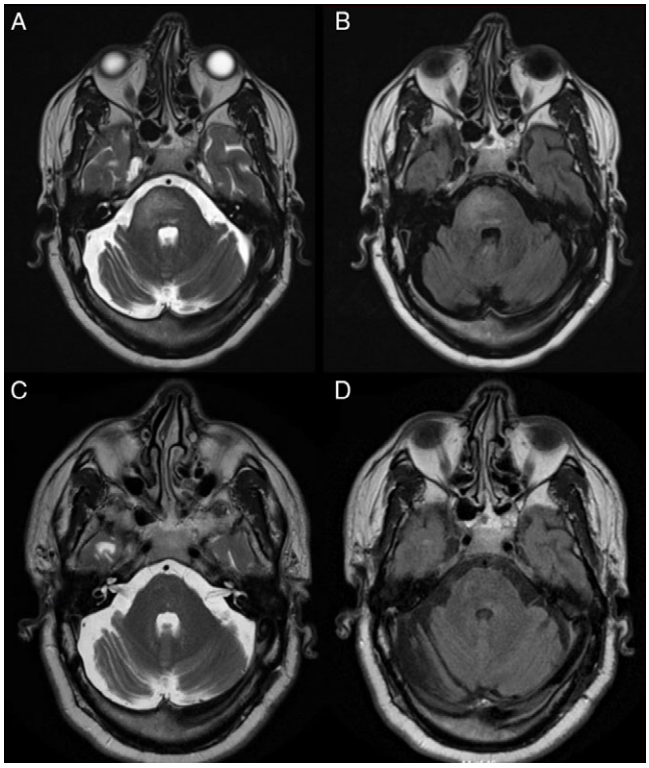


Figure 2: The patient was treated with 5 days of intravenous steroids, with an MRI 7 days after initial presentation revealing a marked decrease in enhancement on T2 weighted imaging (A) and fluid attenuation inverse recovery imaging (FLAIR, B). At 3 months, there was near complete lesion resolution on T2-weighted imaging (C) and FLAIR (D).

suggesting edema; consistent with our patient's imaging.[7] The main radiologic differential includes glial lesions, lymphomas, or infectious and granulomatous lesions.

There are several features of our case, aside from its rarity, that makes it noteworthy. First is the insidious development of mild brainstem signs and symptoms associated with a relatively large pontine lesion.

Second, this case presented a diagnostic challenge. Our patient had established Behcet's based on international criteria[1] and his neurologic symptoms were attributed to NBD after an extensive negative workup. His imaging was in keeping with previously reported findings for parenchymal NBD[1,7]; and his CSF lymphocytic pleocytosis and IL-6 elevation were consistent with NBD.[1] Additionally, a hallmark of tumefactive NBD is an adequate clinical and radiological response to intravenous high-dose steroids as seen in our patient. It is important to note that tumefactive NBD can be difficult to distinguish from a ring-enhancing neoplasm or abscess radiographically; however, his infectious/neoplastic workup was negative and these disease entities typically have a T2-hypointense rim with surrounding edema.[7]

Third, our patient tested positive for latent TB and previous hepatitis B infection although neither entity was thought to be the cause of his presentation. Hepatitis B does not typically cause lesions in the brain, and he had no clinical findings to suggest active tuberculosis infection. Although tuberculomas can present as a tumefactive mass, these are extremely rare, occur in immunocompromised hosts, and typically cause leptomeningeal enhancement[8] which our patient did not have. Further, our patient's astounding and rapid clinical response to steroids guided us away from a primary central nervous system infection. Although neither infection is inherently associated with Behcet's disease, long-term

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immunosuppression to treat NBD is concerning for the reactivation of opportunistic diseases. Our patient was empirically treated for both diseases. Prior to our patient's infectious diagnosis, he trialed 1 month on Apremilast, a phosphodiesterase-4 inhibitor. To our knowledge, this drug has not been associated with an increased risk of opportunistic infections.

In summary, we present a case of NBD mimicking a brain mass that posed a significant diagnostic challenge. A high index of suspicion for clinical Behcet's and a spectacular response to steroids are invaluable in diagnosis and helped this patient avoid biopsy. Additionally, the reactivation of comorbid latent infections should always be considered in long-term management of immunosuppressed patients.

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