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A rare case of cerebral tuberculosis and paraneoplastic encephalitis

Abstract

Voltage gated potassium channel (VGKC) antibodies are seen in many conditions including limbic encephalitis. It typically involves medial temporal lobe, and in rare instances, bilateral cerebellar lobes. Patients can present with seizures and often with alerted mental status and hallucinations. Cerebral tuberculosis (TB)tends to prefer posterior fossa and patients typically present with headache, seizures, and confusion. However, there is no particular association between VGKC encephalitis and disseminated tuberculosis. Presence of both may limit treatment options for paraneoplastic encephalitis. We present a case of a young female with disseminated TB who was also found to have atypical radiographic presentation of TB encephalitis/meningitis and VGKC antibody concerning for paraneoplastic encephalitis. The patient received treatment with steroids and immunoglobulin therapy along with treatment for disseminated tuberculosis. Overall, treatment of paraneoplastic encephalitis is limited in the presence of disseminated TB and a multidisciplinary approach should be used and clinical improvement should be monitored.

Keywords: paraneoplastic encephalitis, neuromyotonia, mphohematogenous dissemination

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Introduction

Disseminated tuberculosis (TB) is when two or more noncontiguous sites result fromly mphohematogenous dissemination of the mycobacterium tuberculosis. Extrapulmonary involvement occurs in one fifth of cases whereinvolvement of central nervous system (CNS) is seen in 5-10% of extrapulmonary TB cases and 1% of all TB cases.[1] Some of the risk factors include children, human immunodeficiency virus (HIV), malnutrition, recent measles in children, alcoholism, malignancies, and use of immunosuppressive agents in adults.[1] Symptoms usually include vague illnesses lasting 2-8 weeks prior to development of meningeal irritation, malaise, anorexia, fatigue, fever, myalgia, and headache.[1] CNS involvement commonly manifests as leptomeningitis with exudates that is more pronounced in interpeduncular fossa and in some instances as tuberculoma in the posterior fossa and cerebellum.[2] The World Health Organization (WHO) treatment guidelines for TB meningitis are based on pulmonary TB treatment with 2 months of rifampicin, isoniazid, pyrazinamide, ethambutol (RIPE), followed by 10 months of rifampicin and isoniazid. Magnetic resonance imaging (MRI) is modality of choice for monitoring benefits of treatment. Corticosteroids reduced mortality in non- HIV patients with a lack of evidence in HIV patients.[3]

Conversely, paraneoplastic encephalitis is a rare disorder triggered by an abnormal immune system response to a neoplasm. Paraneoplastic encephalomyelitis which is a multifocal inflammatory process, is most common, affecting limbic and brainstem structures.[4] In brainstem encephalitis, CSF may be inflammatory (pleiocytosis), and/or show high proteins with oligoclonal bands.[5] It is usually life threatening and it rarely responds to treatments. Voltage gated potassium channel (VGKC) antibodies are seen in many conditions including limbic encephalitis. Patients commonly present with seizures and psychiatric symptoms. It typically involves medial temporal lobe and in rare instances, bilateral cerebellar lobes.[4] Voltage gated potassium channel (VGKC) paraneoplastic syndromes include neuromyotonia, limbic encephalitis and morvan syndrome and patients may have underlying myasthenia gravis or thymoma and rarely small cell or adenocarcinoma lung cancer.[6] It responds well to plasma exchange, intravenous immunoglobulin (IVIG) or a pulse steroid with oral taper.

However, there is no association between VGKC encephalitis and disseminated tuberculosis. Presence of both makes the treatment options limited for paraneoplastic encephalitis. We present a case of a young female with disseminated TB and VGKC antibody, who was also found to have radiographic presentation concerning for TB and paraneoplastic encephalitis..

Case presentation

A 26 year-old female with history of irritable bowel syndrome and family history of colon cancer in the mother and breast cancer in the sister presented with encephalopathy and abdominal pain. Patient was in a study abroad program in China one month prior to this presentation and initially showed behavioral changes with worsening hygiene and increased religiosity upon arrival which was unlikely for her. She was noticed to have increased fatigue, lethargy, nausea, vomiting, and non-intentional weight loss of over fifty pounds. She also had progressive lower extremity weakness and deteriorating mental status. She had abdominal pain and was found to have abdominal ascites. Neurologic exam results showed significant disorientation, slower speech and processing of commands, vertical and horizontal gaze nystagmus, 1/5 bilateral lower extremity and 4/5 bilateral upper extremity strength, generalized decreased sensation to light touch in distal lower extremities and bilateral dysmetria on finger to nose.

Investigation

She had extensive workup for a deteriorating neurologic exam and mental status with significant weight loss. She had mildly elevated inflammatory markers including c-reactive protein (2.86mg/dL, ref <0.50) and erythrocyte sedimentation rate (68 mm/hr, ref<32). The electroencephalogram showed diffuse slowing without any epileptiform discharges or seizures. The cerebrospinal fluid (CSF) showed 2 cells (ref 0-5/uL), 48 glucose (ref 40-75mg/dL) and 31 protein (ref 15-45 mg/dL) with negative cytology and cultures and polymerase chain reaction (PCR) was negative for mycobacterium TB. CSF angiotensin converting enzyme (ACE) was within normal limits and CSF paraneoplastic panel was unremarkable. Serum voltage gated potassium antibody, however, was elevated (207pmol/L, ref<31).Magnetic resonance imaging of the brain showed bilateral

cerebellum and thalami edema with cerebellar folia enhancement concerning for cerebral tuberculosis and paraneoplastic encephalitis (Figure 1). Imaging of the spine was unremarkable.

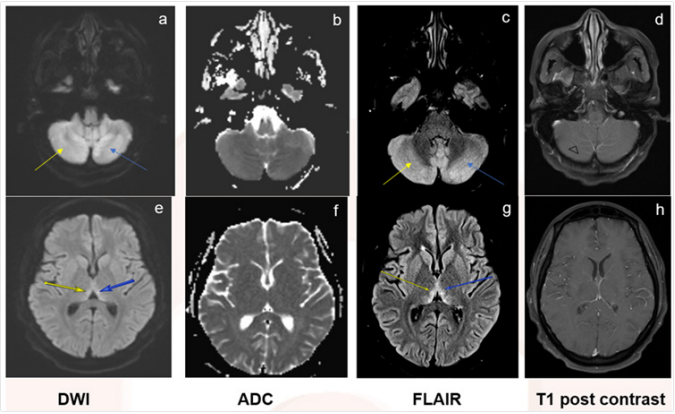

Figure 1 Shows hyperintensity in the bilateral cerebellum and thalami concerning for edema (a-c, e-g,) and cerebellar folia enhancement (g,)..

She also had systemic workup given presence of ascites and weight loss. Computed tomography (CT) for chest, abdomen, and pelvis with and without contrast showed mediastinal lymphadenopathy with small partially loculated pleural effusion on the left and partially loculated ascites with enhancing thickened peritoneum. Paracentesis revealed fibrinous material with mature lymphocytes and scattered histiocyte and mesothelial cells, bronchoscopy with bronchioalveolar lavage (BAL) had positive PCR for mycobacterium tuberculosis and lymph node biopsy showed caseating granuloma. She had negative quantiferon gold test.

Autoimmune workup including rheumatoid factor, citrullinated peptide (CCP) IgG, antinuclear antibody (ANA) with reflex, C3/C4, antineutrophil cytoplasmic antibodies (ANCA) and anti-sjogren's A/B was nonrevealing. Serum ACE was elevatedat179 (ref14-82U/L).

Infectious workup was alsonegative for HIV, acute hepatitis, influenza A and B. Cancer screening markers including Cancer Antigen (CA) 19-9 and carcinoembryonic antigen were normal with elevated CA 125 (126U/mL, ref<46).

Differential diagnosis

The differential diagnosis of her deteriorating neurologic exam included meningitis/encephalitis, autoimmune condition such as rheumatoid arthritis, pulmonary and cerebral sarcoidosis and cancer. Workup for autoimmune conditions was nonrevealing and presence of caseating granuloma in the lymph node biopsy made sarcoidosis unlikely despite elevated ACE. Even though workup for cancer with pan-scans was nonrevealing, given the presence of mildly elevated CA 125 and serum VGKC antibody concerning for paraneoplastic encephalitis, cancercould not be ruled out.

Treatment

The patient was suspected to have TB and paraneoplastic encephalitis given the constellation of findings in the workup. She was treated with intravenous immunoglobin (IVIG) for 5 days, intravenous methyl prednisolone for 5 days with slower taper over 8 weeks and was started on RIPE treatment.

Follow up and outcomes

The patient had improved clinically at her 3 months follow up. She had completed her rehabilitation and was able to perform her daily routine with assistance. She was able to move around the house using her wheel chair with improved but still significant lower extremities weakness. She had poor insight and recall about her hospital stay. MRI of the brain at this time showed mild persistent signal abnormality in the cerebellar hemispheres and thalami with decreasing enhancement and CT for abdomen showed resolution of enhanced peritoneal thickening. She refused to have further gynecological tests for cancer screening in her outpatient follow up with the gynecologist.

Discussion

Tuberculosis and paraneoplastic encephalitis are difficult to differentiate when present simultaneously. They both can affect posterior fossa and can cause similar clinical presentations.

In TB encephalitis, sensitivity of CSF culture of the detection of acid-fastbacilli (AFB) is about 50% and imaging shows meningeal enhancement in the basal cisterns and less commonly, cerebellar involvement.[5] This could explain the absence of CSF AFB detection in our presented patient and given positive AFB PCR from peritoneal sample, there was still concern for disseminated TB with CNS involvement.

In VGKC encephalitis, MRI will show characteristic abnormalities in about 60% of the patients with hippocampal high signal where the majority is bilateral and 15% of the time unilateral.[7] EEG shows generalized slowing with or without an ictal focus.[7] CSF abnormalities are uncommon, and antibodies are not always detectable in CSF.[7] Tumor workup is indicated in these patients, especially for thymoma and small cell lung cancer, which is present less than 10% of the time.[7] This is a monophasic illness and with treatment, antibodies are undetectable, and relapse is uncommon.[7] As seen in our patient, VGKC was not detected in the CSF sample, however serum VGKC antibody was positive. Our patient also did not reveal any presence of cancer even though screening marker CA 125 was elevated. However, given elevated serum VGKC antibody, clinical presentation in the setting of abnormal brain MRI, there was concern for superimposed paraneoplastic encephalitis.

Lastly, treatment of paraneoplastic and TB encephalitis differs. Paraneoplastic encephalitis is usually treated with immunomodulatory therapy with plasma exchange, IVIG or steroids.[7,8] On the other hand, TB meningitis/encephalitis is treated with RIPE and steroids.[3] However, presence of disseminated TB may limit the use of plasmapheresis as a treatment option for paraneoplastic encephalitis. Plasmapheresis can deplete immunoglobulins for several weeks, making one immunodeficient.[9] Hence, in the setting of disseminated TB with CNS involvement, a suppressed immune system might make it worse. Therefore, it is important to take a multidisciplinary approach to creating an effective treatment plan in these complex cases as seen in our case.

Conclusions

Disseminated TB with CNS involvement and paraneoplastic encephalitis can have similar clinical and radiographic features. Presence of both may limit the treatment of paraneoplastic encephalitis. However, the multidisciplinary approach should be utilized, and clinical improvement should be monitored when formulating treatment plan.

Conflict of interest

The author declares no conflict of interest.

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