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Typical Sounding Atypical Diagnostic Conundrum -- A Rare Case of Mycobacterium Avium Complex (MAC) Presenting with Multiple Cranial Nerve Involvement

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Typical sounding atypical diagnostic conundrum -a rare case of Mycobacterium Avium complex (MAC) presenting with multiple cranial nerve involvement

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ABSTRACT

Background: MAC infections rarely cause symptomatic systemic infection in immunocompetent healthy individuals. This case brings to light a rare such presentation that gives us a learning point about keeping a strong pre-clinical suspicion for this condition in patients whom lung imaging reveals suspicious cavitary lesions. Starting empiric therapy while awaiting culture results may be considered after weighing risks and benefits in order to achieve the morbidity and mortality associated with the disease

Case report: A 54 year-old white male presented for evaluation of progressively worsening vertigo, imbalance, vertical diplopia, facial diplegia, bilateral hyperacusis followed by hearing loss, dysphagia, and dysarthria together with unintentional 40 pound weight loss, headache, neck stiffness, and productive cough over 5 months. His neurological exam showed multiple cranial nerve abnormalities. Contrast enhanced MRI head showed mild thickening and enhancement of cranial nerves V, VII, and VIII bilaterally. Biopsy of a cavitary left upper lobe lung lesion noted on CT chest and PET scan along with specimen culture surprisingly revealed Mycobacterium avium complex (MAC). Despite starting treatment, he died 6 weeks after discharge from presumed disseminated MAC. This rare case of MAC in an immunocompetent individual presenting with only multiple cranial neuropathies has not been previously reported.

Conclusion: MAC related CNS infections are very unusual in immunocompetent patient. Our case highlights one such unique presentation of an immunocompetent male who presented with multiple cranial nerve palsy that was ultimately diagnosed to be secondary to MAC infection. Given its rarity, it is very likely to lead to a delay in diagnosis and this could further delay treatment and poor outcome as in our patient. More extensive reporting of this rare CNS MAC infection in immunocompetent individuals could help understand the disease presentation better and might aid in earlier diagnosis and initiation of treatment.

Case report

A 54 year-old white male farmer who lived with birds with history of smoking, chronic obstructive pulmonary disease and restless leg syndrome developed symptoms of vertigo, dizziness, lightheadedness and gait instability of 5 months duration. He then developed abnormal movement of his eyes described as “rolling up” of his eyeballs, by which he meant that one eye had deviated upwards from hypertropia. About 2 weeks later he noticed hyperacusis initially in the right ear and then left, followed by sequential bilateral hearing loss. He then lost the ability to blink, lift his eyebrows, or smile on both sides of his face. He slowly noted changes in his voice. Over this time, he lost 40 pounds and developed headaches, neck stiffness and cough with greenish sputum. He denied any focal weakness or sensory symptoms.

On examination, he was alert and oriented and had trouble talking due to inability to move his lips. Cranial nerve exam showed right trochlear nerve palsy resulting in a right hypertropia, bilateral lower motor neuron facial nerve palsy, bilateral hearing loss, and poor gag reflex. Likely fourth nerve was involved from infiltration of infection in the subarachnoid space as with other cranial nerves. His-dysarthria and dysphagia were likely secondary from multiple cranial nerve involvement including 5,7,9 and 10 evidenced by impaired facial movements, labial

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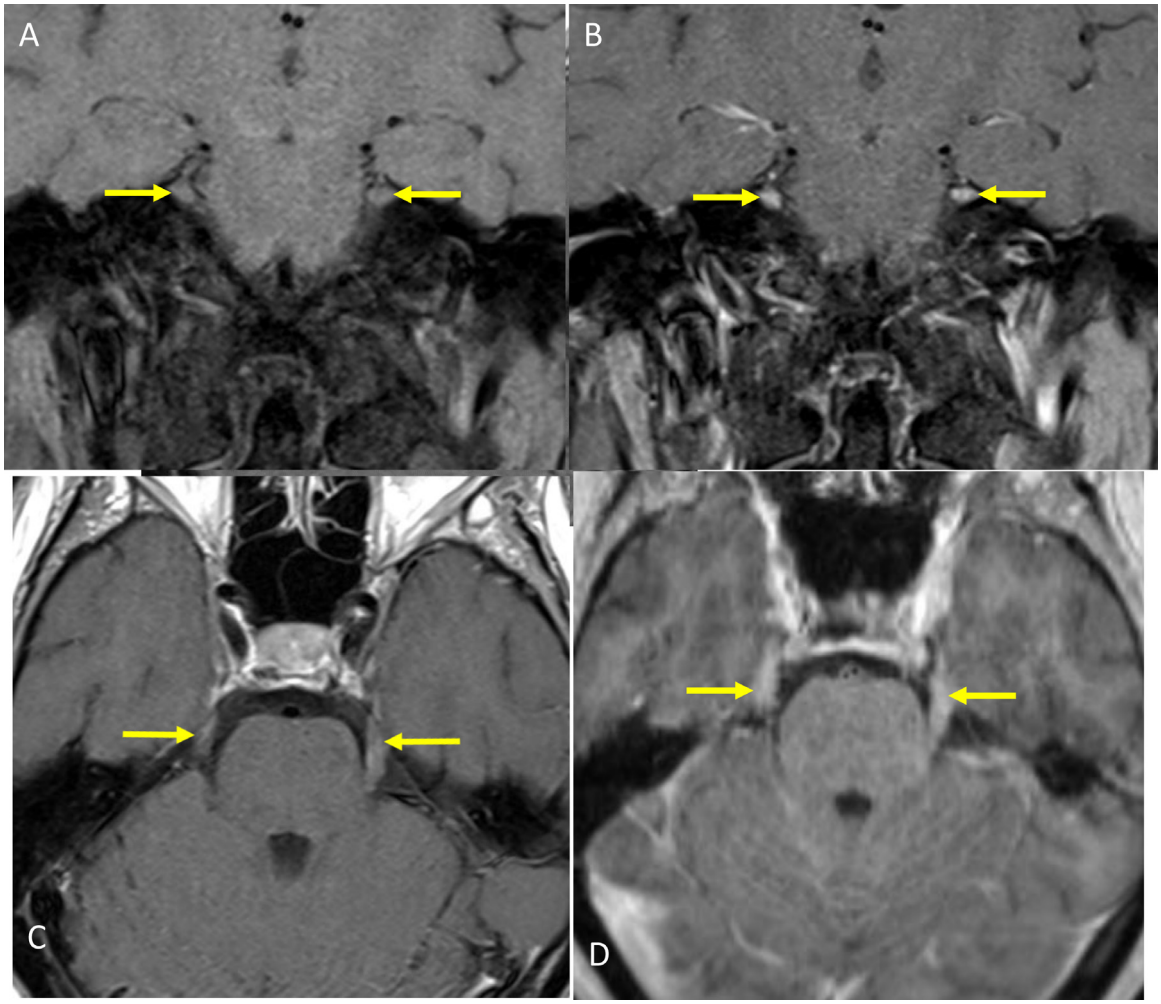

Fig. 1. Pre-contrast (A) and post-contrast (B) coronal T1-weighted images with fat-saturation and axial post-contrast T1-weighted image (C) and axial T1-weighted post-contrast MPRAGE image (D) show enhancement of the cisternal portions of the 5thth cranial nerves extending into the porus trigeminus bilaterally. (arrows).

strength and range of motions, impaired seal around mouth, reduced laryngeal elevation, pharyngeal contraction, and reduced clearance which resulted in profound pyriform sinus residue that patient was unable to clear using multiple strategies.

The patient's vertigo was not positional and worsened after Epley's maneuver tried before he presented to us, suggesting that it was central in origin. Ocular exam was normal. The rest of his neurologic exam including motor, sensory, coordination, and gait were normal. Plantars were down going on both sides.

Review of his outside hospital labs showed elevated ESR at 58 and CRP of 4.38. Other labs including serum calcium, angiotensin converting enzyme, ANA, ANCA, Anti-neuronal IgG, Voltage-gated *K*+ channel antibody, serology for Histoplasma, HIV 1&2, Mycobacterium PCR, Pneumocystis jiroveci antigen, Aspergillus antigen, Hepatitis panel, Beta (1,3)-D-glucan, Lyme and West Nile serology, atypical fungal markers, and syphilis was negative.

Contrast enhanced MR head and MRA head though reported as normal initially, when repeated showed contrast enhancement within the bilateral CN V,VII, and VIII (Fig. 1 and 2). No meningeal enhancement was seen. There were no lesions affecting the base of the brain.

The neuroimaging showed enhancement of the cisternal portions of the 5thth cranial nerves extending into the porus trigeminus bilaterally but no trigeminal neuropathy on exam. Though there was clinical involvement of cranial nerves 9 and 10 this was not evident on neuroimaging.

Computed tomography of the chest showed a left lung cavitary lesion. Besides malignancy, neurosarcoidosis and vasculitides such as granulomatosis with polyangiitis remained in the differential. CT abdomen and pelvis was unrevealing. Bronchoalveolar lavage with transbronchial biopsy showed lympho-histiocytic infiltration with abundant blood, but no malignant cells or fungi, and negative acid-fast stain. Electromyography and nerve conduction study showed mild diffuse sensory motor neuropathy. The patient underwent lumbar puncture which was significant for nucleated cell count of 16 with lymphocyte (50%) monocyte (48%),neutrophil 2%, protein 438 and glucose 29. Cerebrospinal fluid gram stain, culture, acid fast stain, Lyme and West Nile serology and paraneoplastic antibody markers, were negative.

A initial presumptive diagnosis of sarcoidosis was made and he was initiated on 5 days of IV Methylprednisolone 1 gram daily followed by oral prednisone on tapering doses besides Amoxycillin and Clavulanate.

A PET scan revealed a large left upper lobe cavitary lesion with hypermetabolic consolidation at the pleural side of the lesion which was highly suspicious for malignancy, but atypical infection and granulomatous disease with intensely hypermetabolic mediastinal and left hilar lymph nodes could not be excluded. The PET did not show any intracranial activity.He was continued on oral prednisone. Biopsy of the cavitary lesion showed granulomatous inflammation with extensive caseation and filamentous acid-fast organisms. Subsequently his acid-fast culture obtained from sputum grew Mycobacterium avium intracellulare (MAC) at 2 weeks following discharge. He was started on Rifampin, Isoniazid,

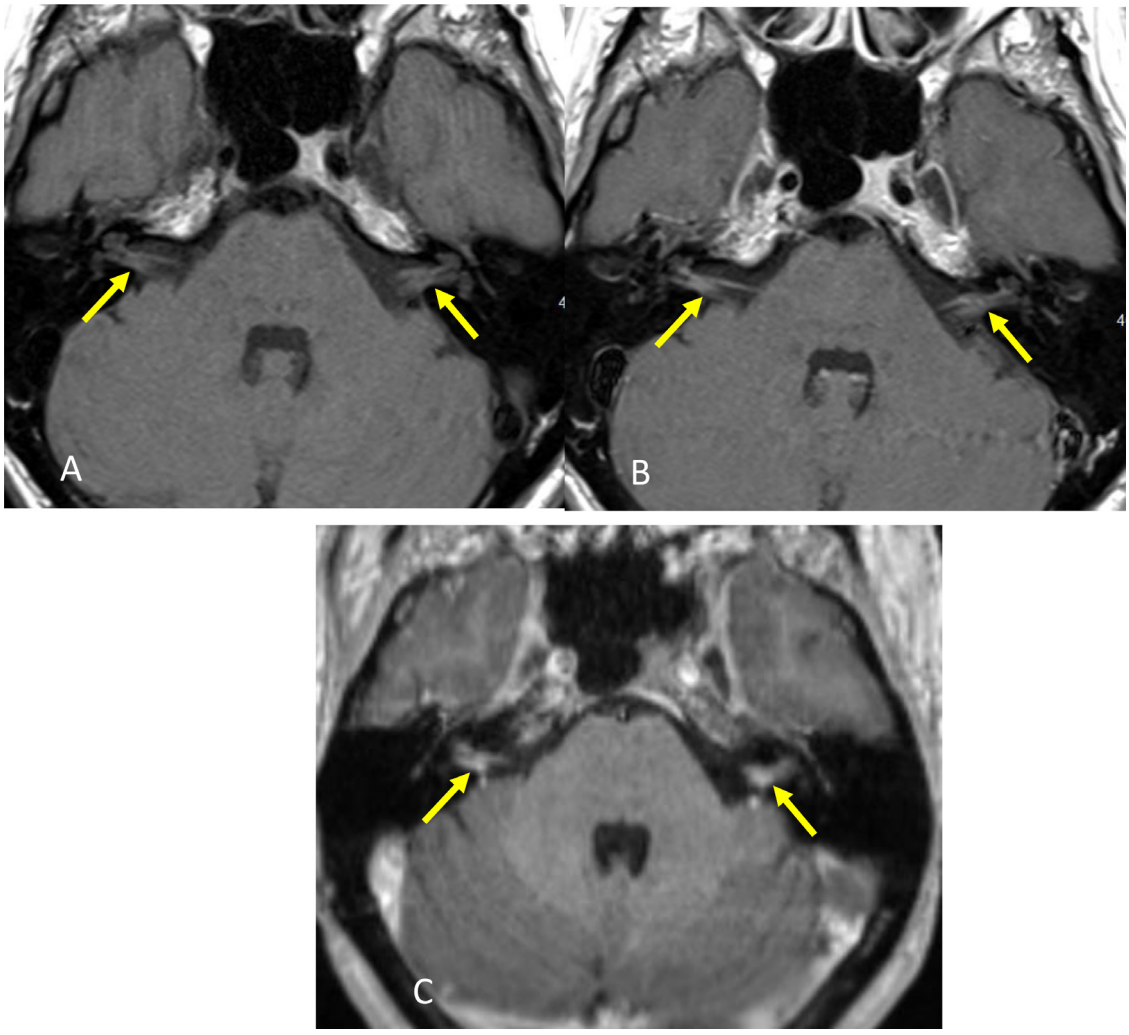

Fig. 2. Pre-contrast (A), post-contrast (B) axial T1-weighted images and axial post-contrast(C) T1-weighted MPRAGE image show enhancement of the 7th and 8th cranial nerves within the internal auditory canals bilaterally. (arrows).

Ethambutol and Azithromycin but he died 6 weeks after discharge from presumed disseminated MAC.

Discussion

MAC are non-tuberculous mycobacteria that are ubiquitous in nature, with the heaviest concentrations in soil and water sources, and can cause chronic lung infection. The mere presence of these in pulmonary specimens does not establish active infection but rather needs supportive radiographic and clinical findings to establish the diagnosis. Official Statement of the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) for Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases (2007) MAC can occur in the context of lung disease caused by, for example, bronchiectasis, chronic obstructive pulmonary disease (COPD) or cystic fibrosis (CF), and also in people with apparently normal lungs. The incidence of nontuberculous mycobacterial (NTM) pulmonary disease caused by Mycobacterium avium complex (MAC) in apparently immune-competent people is increasing worldwide Though most cases are in immunocompromised patients, commonly in AIDS, MAC infections have also been reported in people without predisposing conditions. To et al. (2020), Prince et al. (1989), Flor et al. (1996) Dissemination can occur with immunosuppression as in HIV positive individuals, thus requiring these patients to be on prophylaxis when CD4 counts fall below 50 cells/ul. Kaplan et al. (2002 Jun 14) MAC can be difficult to completely eliminate as their hydrophobic wall provides antibiotic resistance and recurrent infection or relapse is not uncommon.

Involvement of the CNS in MAC is extremely rare and literature on this is limited. The overall incidence of CNS involvement is unclear, but can range from 3 to 10% and is often associated with an immunocompromised state like AIDS, lymphoma, leukemia, transplant recipients or immunosuppressant use. Ballesteros and Garino (Apr 2016) Prior literature has described intracranial abscess with MAC, meningo-encephalitis as well as inflammation secondary to immune reconstitution syndrome especially in HIV positive patients. Fortin and Rouleau (2005), Kwon and Kim (2018) Our case of MAC is unique as he mainly presented with multiple cranial neuropathies in the setting of disseminated MAC infection causing meningitis. It also highlights the devastating complication of this disease in an immunocompetent patient and need for early empiric therapy in suspected cases even before confirmatory test results are available. Diel et all in their systematic review report five-year all-cause mortality exceeding 25% in MAC pulmonary disease, indicating poor prognosis. They identified male sex, advanced age and presence of co-morbidities as predictors of worse outcome (Diel et al., 2018).

To the best of our knowledge this presentation of intracranial MAC with multiple cranial neuropathies has not been previously reported.

Diagnosis in these cases is challenging but the presence of meningitis with suggestive pulmonary lesions could raise clinical suspicion. Gold standard is diagnostic biopsy with demonstration of the bacteria. Treatment is initiated when a patient meets diagnostic criteria and fibro-

cavitary disease is seen. If treatment is not initiated, disseminated MAC can be life threatening and has a mortality rate of 35–70%. The recommendation is to start Clarithromycin 1000 mg/day or Azithromycin 250 mg/day as a first line, Ethambutol 15 mg/kg/day as a second line with or without Rifabutin or Rifampin and with Amikacin and Moxifloxacin as a third line drug with total duration of treatment for at least 1 year. When there is pulmonary disease, treatment should be continued until sputum cultures become consecutively negative for at least one year. Initiation of steroids can be detrimental and worsen the disease with dissemination as was seen in our case. As confirmatory tests take time to result, a high index of suspicion and early empiric treatment could lead to better outcomes.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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