CASE REPORT

Mycobacterium avium Infection of Nasal Septum in a Diabetic Adult: A Case Report

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Abstract *Mycobacterium avium complex* (MAC) is primarily a pulmonary pathogen that affects individuals who are immune deficient or immunocompromised. In this report, we describe a very rare case of MAC infection clinically presenting as a nasal polyp in a patient with type 2 diabetes mellitus. This case illustrates an atypical anatomic location for MAC, the anterior nasal septum in nasal cavity, as well as often overlooked cause of immune compromise, diabetes mellitus. We present the laboratory findings that lead to the diagnosis as well as a brief review of MAC infections.

Keywords Nasal cavity · Mycobacteria · Type 2 diabetes medulla · Infection

Introduction

Nontuberculous mycobacteria (NTM) plays an increasingly significant pathogenic role in patients who are HIV-positive, with chronic lung disease or other chronic conditions, and the elderly. MAC organisms are the most frequent isolates among NTM [1]. In non-HIV patients, MAC pulmonary infections are well documented, but there are not many case reports in the literature to describe isolated MAC infections with primary sites other than lung. These reported cases of extra-pulmonary MAC infections include pleuritis [2], nasal cavities [3], lymph nodes, skin and soft tissue [4–7]. There are very few reported MAC associated

inflammatory pseudotumors of anterior nasal cavity cases. These reported inflammatory pseudotumors are caused by *Mycobacterium avium-intracellulare* and occurred in patients with immunosuppressed disease including HIV or post chemotherapy in a DLBC lymphoma [3]. To our knowledge, there is no previous reported *Mycobacterium avium* associated inflammatory polyp of nasal septum in patient with T2DM.

Case Report

The patient is a 69-year-old male with T2DM who was admitted with a 2 months history of left lateral frontal headache. The pain was fluctuating and partially relieved by pain medications. He also complained of mild cough, but chest X-ray was unremarkable. There was no evidence of disseminated infection either clinically or radiologically. He had no prior medical history of nasal or sinus symptoms. CT scan shows a large mucus retention cyst along the floor of the left maxillary sinus, filling half the antrum with the remainder of the sinuses unremarkable. It was also noticed that the nasopharyngeal mucosal space was greatly thickened, narrowing the nasopharyngeal airway, which is common for the patient's age. Intranasal exam and CT scan revealed a sessile polypoid lesion (1.5 cm in diameter) on the right anterior nasal septum (Fig. 1). Bilateral turbinates showed atrophic changes. His past medical history included normally controlled type 2 diabetes mellitus. His hemoglobin A1c was between 5.9 and 6.4 % (with a reference range of 4.5–6.7 %). The Human Immunodeficiency Virus status was tested and was negative. No history of malignant tumor or travel outside the United State. An excisional nasal biopsy was performed. The gross examination revealed tan-yellow polypoid soft tissue fragments.

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Fig. 1 Sessile polypoid lesion on right anterior nasal septum (CT scan)

Microscopic examination showed stratified squamous epithelium overlying numerous foamy histiocytes with admixed inflammatory cells including lymphocyte, neutrophils, eosinophils and plasma cells. There was no multinucleated giant cell (Langhans giant cell) or caseation necrosis identified in this lesion (Fig. 2). Acid fast stain and PAS stain highlighted numerous short, uniformly staining coccobacilli within the foamy histiocytes (Figs. 3, 4). The sheet of foamy histiocytes are strongly positive for CD68 (Fig. 5), but they are negative for S100 (Fig. 6) and CD1a. There were no fungal elements identified by Gomori Methenamine Silver (GMS) and Periodic acid-Schiff (PAS) stains. No intracellular bacteria were identified by Gram's stain. CD3 and CD20 immunohistochemical stains were also performed and they highlighted scattered T cells and B cells respectively. The patient underwent a second biopsy at the same location and biopsy tissue was sent for

Fig. 2 Sheet of foamy histiocytes with admixed inflammatory cells without features of caseating granulomas or necrosis (H&E stain)

Fig. 3 Numerous intracytoplasmic Acid-Fast Bacilli present inside the histiocytes (Ziehl-Neelsen stain)

Fig. 4 Numerous intracytoplasmic Bacilli present inside the histiocytes (PAS stain)

Fig. 5 Foamy histiocytes are positive for CD68

Fig. 6 Formyl histiocytes are negative for S100

culture. The cultures show smooth, colorless colonies and it was later confirmed as *Mycobacterium avium* by genome sequences analysis. No other organisms were found. As there was no evidence of systemic infection and the patient's incision had healed well, no antibiotics were initiated. The patient was followed up at 6 months with intranasal examination showing a scar with no evidences of a mass or other abnormalities.

Conclusion

MAC comprises two closely related organisms, *Mycobacterium avium* and *Mycobacterium intracellulare*, which are the most common isolates among the nontuberculous mycobacteria (NTM) found in specimens. Unlike *Mycobacterium tuberculosis*, for which humans are the definitive host, NTM is believed to be acquired from the environment. Human disease due to NTM is assumed to be acquired from environmental sources either directly by inhaling organisms in aerosols or indirectly by ingesting contaminated food or water. Recent research suggests that municipal water sources may be an important source of *Mycobacterium avium* lung infections [8–10]. MAC most commonly occurs in the setting of advanced human immunodeficiency virus (HIV) disease, especially in patients with CD4 T lymphocyte (CD4) cell counts <50 cells/mm³. In non-HIV patients, MAC infections are commonly seen in older people with underlying lung disease, or in other chronic conditions, but it is rarely reported in type 2 diabetes mellitus (T2DM) patients. Some researchers have claimed there is no association between T2DM and MAC infection [11], but there are a few case reports claiming MAC infections can occur in type II diabetes patients [12]. Patients with T2DM are immunocompromised and have an increased incidence of infections mainly in the bone and skin, as well as

in the respiratory, enteric and urinary tracts [13, 14]. It is believed that the mechanism of immunodeficiency in T2DM patients is impaired phagocytic activity [15].

While the pathogenesis is not entirely known, MAC infections sometimes can occur following surgeries or even minor traumas. Middleton et al. [16] showed exposing extracellular matrix by epithelial damage and poor mucus clearance will predispose to MAC airway infection. Previously reported cases of nasal and sinobronchial infections of MAC included history of cocaine use and long term aerosol inhalation cine-scintigraphy usage, which suggested that an impairment of the local defense mechanisms may play role in the pathogenesis of MAC infection [3, 17]. Solyar et al. reported thirty-seven Atypical mycobacterium (AM) associated chronic refractory rhinosinusitis (CRS) cases, which accounts for 5.3 % of out-patients and 2.6 % of OR patients with CRS. Among these 37 cases, 10 had one or more risk factors for AM including foreign body, non-HIV immune dysfunction, and previous chemoradiation. Majority of the cases occurred in the absence of above risk factors or overtly altered innate/adaptive immunity. The most frequently identified AM species were *Mycobacterium abscessus* (57.1 %), followed by *Mycobacterium avium-intracellulare* complex (14.3 %) and *Mycobacterium chelonae* (14.3 %) [18].

Isolated infection of MAC in the absence of disseminated infection, in particular in isolated nasal cavity localization is uncommon. In such cases, the diagnosis of MAC infection is a challenge for both clinicians and pathologist. A biopsy is needed to establish a definite diagnosis of mycobacterial infection in an isolated intranasal localization. The pathogen should be cultured or identified in tissue sample or by highly specific molecular techniques. Obviously, the precise identification of typical or atypical mycobacterial infection is relevant in starting proper pharmacological treatment [19]. Treatment also requires expert management with the ability to cure such infections related to the host's underlying immunosuppressive status [20]. In addition, it is very important to exclude MAC pulmonary infection which requires at least 3 effective drugs for a minimum of 12 months after sputum conversion to negative cultures [21]. After excluding pulmonary and systemic infections, similar to other inflammatory pseudotumors, complete surgical resection is the treatment of choice for AMC associated local inflammation with the exception of orbital lesions [21, 22]. In our case, the patient was treated with focal resection, and neither 6-month or 1-year follow-up showed any recurrence.

In addition to MAC infection, the differential diagnosis of a histiocytic proliferative disorder in nasal cavity should include Rhinoscleroma, Extranodal sinus histiocytosis with massive lymphadenopathy, eosinophilic granuloma (Langerhans cell histiocytosis), plasmacytoma, and fungal

infection. Rhinoscleroma (RS) is a chronic, progressive, granulomatous infectious disease of the upper respiratory tract that is typically caused by the gram-negative bacillus *K. rhinoscleromatis*. It is endemic to regions of Guatemala, El Salvador, Mexico, Colombia, and Egypt [23]. RS are rare in the United States, but recent reports suggest an increase in cases because of migration from endemic areas [24]. Histopathological examination reveals foamy macrophages with intracytoplasmic bacilli. In our case, the patient had never been outside the United States. The Gram's stain of biopsy tissue did not show Gram negative bacilli and the culture was negative for gram negative bacilli which made RS unlikely in this case. Extranodal sinus histiocytosis with massive lymphadenopathy (ESHML, also referred to as Rosai-dorfman disease) is another very rare benign indolent disorder that can occur in the nasal cavity. Compared to MAC infection, ESHML has similar morphologic features with infiltrating granular or vacuolated foamy histiocytes, but the histiocytes are strongly reactive with antibodies against S100 and CD68. In our case, the immunohistochemical stains for histiocytes are negative for S100, which excluded the diagnosis of ESHML. Langerhans cell histiocytosis (LCH) is a rare clonal neoplastic proliferation of Langerhans-type cells that can occur in nasal cavities. LCH can be differentiated from other disorders with the presence of smaller and notched nucleus and CD1a and S100 positivity. In this case, both S100 and CD1a were negative, which made LCH very unlikely. Fungal infection was excluded based on the negative culture result and absent of fungal elements on GMS and PAS stains. The CD3 and CD20 immunohistochemical stains highlighted the scattered T and B cells, which made an extranodal lymphoma unlikely.

In summary, insolated MAC associated inflammation can occur in non-HIV patients without systemic infection. Patients with T2DM are in an immunosuppressive status and more vulnerable to infections including MAC infection. During histologic evaluation, mixed chronic inflammation with prominent foamy histiocytes should prompt consideration of MAC, especially in patients with any immunosuppressive condition including diabetes mellitus. Acid-fast stains, polymerase chain reaction (PCR), and tissue culture can be used to confirm the diagnosis of *Mycobacterium avium* infection.

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