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CASE REPORT

Myocbacterium-Avium Intracellulare Associated Inflammatory Pseudotumor of the Anterior Nasal Cavity

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Abstract In this case report, we describe an unusual case of mycobacterial associated inflammatory pseudotumor that occurred in a patient with a previous history of cocaine abuse. We discuss inflammatory pseudotumor (IPT) in general and emphasize the rare entity where an associated mycobacterial infection is seen. The histogenesis is not yet completely understood. The lesion can pose challenges for practicing pathologists and a misdiagnosis of malignancy can occur at multiple facets. A discussion about the differential diagnosis and clues to make the distinction is presented. In addition to spindle cell proliferation, the presence of a background of mixed inflammatory cell infiltrate and foamy macrophages are clues to make the diagnosis. In the case of mycobacteria associated IPT, Acid Fast Bacilli (AFB) stains will easily highlight the organisms confirming the diagnosis.

Keywords Inflammatory Pseudotumor · Mycobacteria

Introduction

Inflammatory pseudotumor (IPT) is a broad descriptive term that embraces a heterogeneous spectrum of reactive, infective and neoplastic entities. These lesions are characterized by a clinical mass which is mostly identified either grossly or as an enhancing lesion on computed tomography (CT) scan. More than often, these masses pose features suggestive of malignancy, including ulceration and infiltration of adjacent structures [1–3]. Histologically, they reveal a dense chronic inflammatory infiltrate in a fibrous background and an abundance of plasma cells and/or histiocytes. While the pathogenesis is not entirely known, many features of IPT can be related to production of inflammatory cytokines that sometimes can occur following surgery or even minor trauma [4–8]. Their occurrence is well-documented in the presence of another malignancy or secondary to multiple infectious agents [1,5, 7, 9].

We present a rare case of *Mycobacterium avium* complex (MAC) associated inflammatory pseudotumor of the nasal cavity in a patient with a history of intranasal cocaine abuse. To our knowledge and after thorough review of the English literature, we found only one documented case of IPT in a patient with a history of cocaine abuse where the lesion affected the parapharyngeal space [10].

The pathogenesis of MAC in IPT is not clearly understood. Many cases have been reported demonstrating their presence in various other body sites associated with IPT [11–14].

Regardless of the cause, these lesions have the propensity to appear deceptively malignant at all interfaces, whether clinical, radiological or even at the histological level. We are presenting this case to call attention to its existence and to avoid making an erroneous diagnosis of malignancy [1–3, 9, 15, 16].

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Report of a Case

A 63-year-old man presented with right nasal obstruction and several months history of blood tinged discharge from the right nostril. He had no prior history of nasal or sinus symptoms. No pain or discomfort was reported. He denied any fever, coughing, night sweats or recent weight loss. He had no history of wood-working or furniture building, and had not been exposed to dust or construction places. Personal history was significant for intranasal cocaine use and moderate alcohol consumption. He smoked intermittently for 25 years, but quit 5 years prior to his current presentation.

He had a history of diffuse large B-cell lymphoma involving the cervical and the supraclavicular lymph nodes for which he received six cycles of R-CHOP chemotherapy. He completed his last chemotherapy regimen 6 years prior to this presentation. He had a regular annual follow up by imaging studies, laboratory tests and physical examinations for 5 years after his initial lymphoma diagnosis. The lymphoma surveillance period continued for 5 years, after which he was considered cured with no evidence of recurrence or clinical immunosuppression. On one of his imaging studies, an abnormal uptake on the thyroid gland was discovered, where papillary carcinoma was diagnosed. He was treated by total thyroidectomy and post operative radio-iodine therapy. He has been on thyroid hormone replacement therapy since then.

On fiberoptic rhinoscopy, a bloody, friable, irregular polypoid mass was seen. A CT-scan revealed a 1 cm soft tissue density in the anterior right nasal cavity, raising the possibility of a mass lesion that is consistent with the clinically appreciated lesion (Fig. 1).

There were no additional neck masses or lymphadenopathy seen. The patient recalled removal of a polyp/mass from the right nasal cavity 20 years prior, stating that it was not a cancer, but could not remember the discussion of an unusual infection.

During surgery, the mass was adherent to the superior portion of the septum. With the use of a biting cup forceps, the mass was removed. The base of the mass on the septum was cauterized with suction cautery device. The pathology laboratory received a pink-tan irregular firm mass measuring 1.5 cm in greatest dimension that was totally submitted for histological examination.

Histological sections at low power view showed fibrous stroma with abundant spindle cell proliferation in a vaguely storiform pattern (Fig. 2). A fibrohistiocytic proliferation of mildly atypical spindle cells was seen with elongated and slightly rounded nuclei. However, there was no significant cellular or nuclear atypia. Also seen was a mixed predominantly chronic inflammatory cell infiltrate of neutrophils, lymphocytes, histiocytes and plasma cells (Fig. 3).

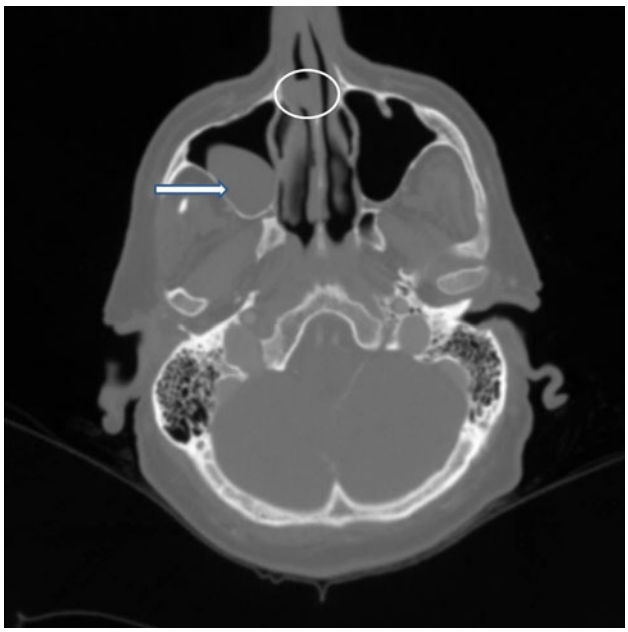

Fig. 1 An anterior-posterior view of a CT scan showing an approximate 1.0 cm soft tissue density in the anterior right nasal cavity representing the clinically appreciated abnormality (*circle*). The density appears homogenous and the radiological impression was of a mass of unknown nature. Note the presence of a mucous retention cyst in the right maxillary sinus (arrow)

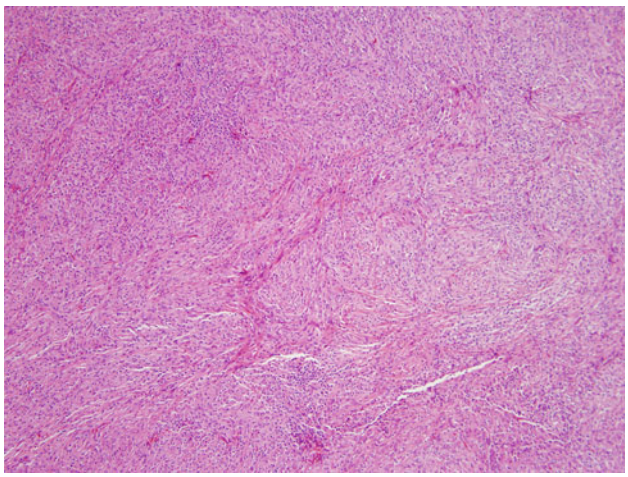

Fig. 2 Low power view showing fibrous stroma with abundant spindle cell proliferation in a vaguely storiform pattern (Hematoxylin and Eosin, ×100)

There were other areas, where abundant foamy macrophages were seen, a few single and some in clusters (Fig. 4). The presence of these foamy macrophages prompted us to perform a Ziehl-Neelsen stain looking for intracytopalsmic mycobacterial bacilli. The stain showed numerous intracytoplasmic acid-fast bacilli (AFB) with a thin, wavy non-beaded appearance morphologically consistent with MAC (Fig. 5). Well-controlled immunohistochemical stains were

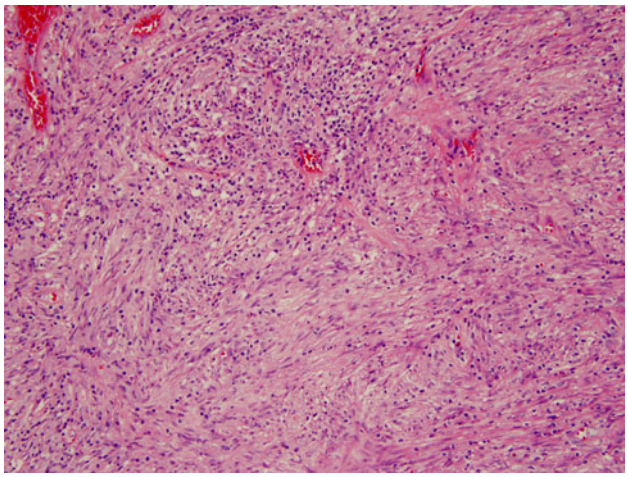

Fig. 3 Fibrohistiocytic proliferation of spindle cells with elongated and slightly rounded nuclei with mild cellular and nuclear atypia. Also seen is a mixed predominantly chronic inflammatory cell infiltrate of lymphocytes, histiocytes and plasma cells (Hematoxylin and Eosin, ×200)

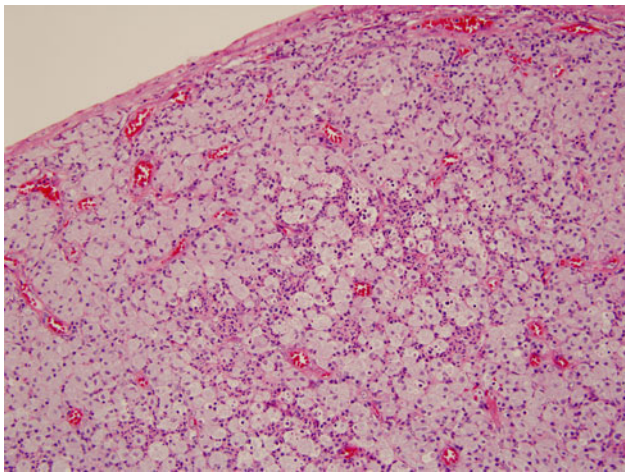

Fig. 4 Abundant foamy macrophages are seen in other areas, a clue that organisms may be present, which triggered ordering special stains (Hematoxylin and Eosin, ×100)

performed where these macrophages were positive for CD 68 (Fig. 6) and were negative for CD 34, S 100, Cam 5.2, P 63 and Smooth Muscle Actin.

The diagnosis of MAC associated IPT was made. A concurrent nasal mucosal swab was also taken and sent for mycobacterial culture. The direct acid fast stain was positive, and the culture was positive for *Mycobacterium avium* complex. No other organisms were found. The Human Immunodeficiency Virus status was tested on his recent admission and was negative. A repeated CT-scan of the sinuses 2 months post procedure showed normally patent ostiomeatal complexes with no evidence of recurrence (Fig. 7). The patient is well 1 year after therapy with no evidence of recurrence.

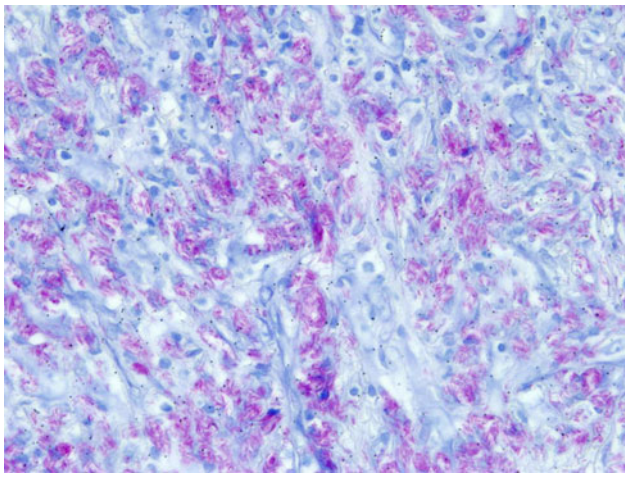

Fig. 5 Numerous intracytoplasmic Acid-Fast Bacilli are seen (Ziehl-Neelsen stain, ×400)

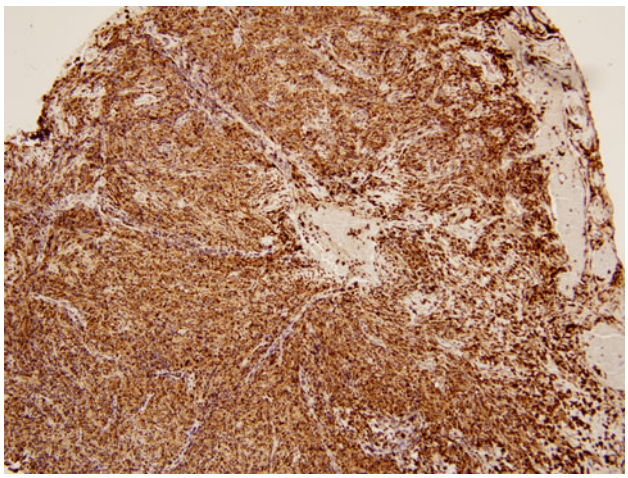

Fig. 6 The macrophages are positive for CD68 (×100)

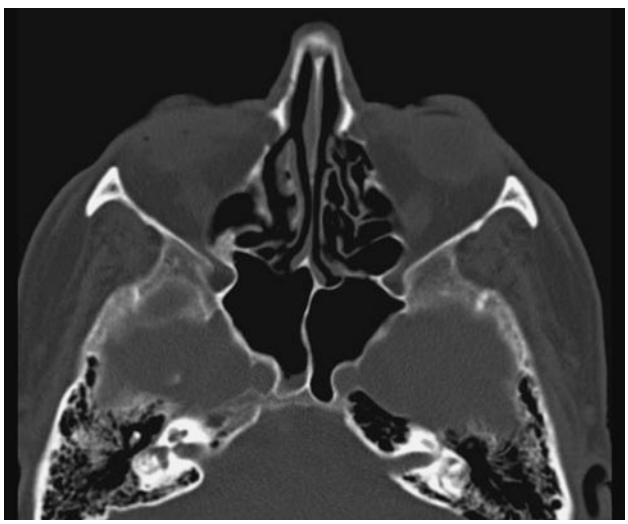

Fig. 7 Cut of a CT-scan showing complete resolution of the previously seen mass in the right anterior nasal cavity. Ostiomeatal complexes are unremarkable

Comment

IPT is an uncommon, benign, idiopathic lesion that has been described in various viscera and deep soft tissues. Clinical presentation can vary from slow growth with minimal mass effect, to bony destruction that can mimic malignancy. This entity was first described in the orbit by Birch-Hirschfield in 1905 [4]. Over the decades, IPT has been reported in multiple body sites and in varying clinical backdrops, mostly affecting immunocompromised patients, but at times also in immunocompetent individuals. While the pathogenesis is not entirely known, their occurrence has been shown following events such as trauma, surgery, chronic irritation and multiple infectious agents [1, 4, 5–9]. Organisms found in association with IPT are mycobacteria (both typical and atypical), Epstein-Barr virus, *Actinomycetes* and *Nocardia* species, *Corynebacterium Equi*, *Pseudomonas* species and *Coxiella Burnetii* [1, 5, 7, 9, 15, 17].

Mycobacterium avium complex comprises two closely related organisms: *Mycobacterium avium* and *Mycobacterium intracellulare.* These organisms are aerobic, non-spore-forming, nonmotile atypical mycobacterial bacilli. They grow slowly (10–21 days on solid media) and produce thin-translucent or domed-opaque colonies. Colonies are usually light tan in color, although some MAC strains produce a yellow pigment that increases with light exposure. MAC isolates can be identified as *M.avium* or *M. intracellulare* by DNA probes or polymerase chain reaction analysis [18]. They are widespread in the environment and they have been isolated from water, soil, food, house dust and several animals. However, the specific sources responsible for human infection are not known [19]. Three major disease syndromes are produced by MAC in humans: pulmonary disease, usually in adults whose systemic immunity is intact; disseminated disease, usually in patients with advanced human immunodeficiency virus (HIV) infection; and cervical lymphadenitis. *Nocardia* species were not detected on the smears nor cultures of our patient. These typically appear as delicate filamentous beaded gram-positive branching rods, with fine right-angled branching filaments that are usually weakly acid fast and therefore they are better visualized on another modified form of acid fast stain, the Fite stain.

Other infectious considerations in such presentation include rhinoscleroma, lepromatous leprosy and syphilis as they commonly present with thickening of the nasal mucosa and many deformities.

Rhinoscleroma is a chronic granulomatous bacterial disease of the nose that can sometimes infect the upper respiratory tract. It is caused by *Klebsiella rhinoscleromatis*, a gram-negative, encapsulated, nonmotile, rod-shaped bacillus, member of the Enterobacteriaceae family. Cultures are only positive in 50–60% of cases. Diagnostic characteristics are most commonly found in the granulomatous stage and include chronic inflammatory cells, Russell bodies, and pseudoepitheliomatous hyperplasia, and groups of large vacuolated histiocytes containing *Klebsiella rhinoscleromatis* which are called Mikulicz cells [20]. These features were not present in our case and the strong AFB stain practically ruled it out. Another potential differential diagnosis is lepromatous leprosy. However, in these cases, the AFB will involve nerves and will be seen inside the cytoplasm of endothelial cells which was not the case in our patient [21]. As for syphilis, no single microscopic feature is pathognomonic; however, the diagnosis should be considered when there are unusual epithelial hyperplasia, granulomatous or plasma cell-predominant chronic inflammation, endarteritis and neuritis [22]. Certainly, the AFB stain will be negative and the treponemal stain will be positive.

Interestingly, our patient had a history of intranasal cocaine abuse. Whether there is any relationship between this history and the development of IPT is not certain and we can only speculate; however it raises the possibility of an association. We only found one well-documented case of IPT with history of cocaine use. However, in that case, Hytiroglou et al. reported it in the parapharyngeal space [10].

Cocaine is derived from the leaf of erythroxylon coca plant and is available as a hydrochloride salt of intravenous and intranasal administration. Cocaine abuse can cause severe ischemia secondary to sympathetic mediated vasoconstrictive effects. The effects of chronic cocaine abuse have been widely described in the literature. Common complications include nasal septal perforation, saddle-nose deformity, and palatal perforation [23]. It can also be associated with a wide spectrum of rheumatic manifestations such as pseudovasculitis causing aggressive nasal destruction and various skin lesions and thus has been confused with Wegener granulomatosis or leukocytoclastic vasculitis [24]. Skin biopsy can establish the diagnosis of pseudovasculitis [25]. A case of necrotizing granulomatous vasculitis associated with nasal destruction and an oronasal fistula in a chronic cocaine user has been reported [26]. In another patient, erosion of the external structures of the face including multiple oronasal fistulas in the anterior gingival sulcus was also observed [23].

Cocaine associated midline facial destruction is among the benign reactive infiltrates that are considered as angiocentric lesions of the head and neck. This includes angiocentric eosinophilic fibrosis, Wegener's granulomatosis, and microscopic polyangiitis [27]. Microscopically, a pauci-cellular necrosis of the nasal mucosa with associated vasculitis is usually seen. None of these characteristic features was seen in our patient.

Collectively IPT may present as a mass lesion and the clinical features vary depending on the size and the

anatomic location. When in the orbit or sinonasal cavity, they can induce bony changes such as erosion, remodeling and sclerosis [5].

In the lung and gastrointestinal tract they may present with cough, dyspnea, hemoptysis, abdominal pain and iron deficiency anemia [5].

The histopathology is the most interesting aspect of IPT where, at first glance, it can raise the suspicion of a malignant spindle cell neoplasm with a mild degree of cytological and nuclear atypia [7]. However, careful histological examination will help avoid misdiagnosis and resolve both the clinical and radiological findings. These important features include the presence of mixed type inflammatory cells infiltrate admixed with spindle cells, lack of significant cytological and nuclear atypia and rarity of mitoses with absence of atypical ones[7]. In addition, particularly in cases of bacterial IPT, abundance of foamy macrophages is another clue [7].

Immunohistochemistry may play a helpful role, where the spindle cells show smooth muscle differentiation and are smooth muscle actin (SMA) positive. It has also been reported that in some cases, these cells may express certain cytokeratins, such as cytokeratin 8 and 18 [28]. Macrophages light up in the background with CD68 immunoreactivity (Fig. 6). The lymphocytes are mostly reactive polyclonal T cells as well as the plasma cells. In our case, performing Ziehl-Neelsen staining easily highlighted the intracytoplasmic acid-fast bacilli with a characteristic thin wavy non-beaded appearance, consistent with MAC. Differential diagnoses include malignant entities such as inflammatory fibrosarcoma, follicular dendritic cell sarcoma and malignant fibrous histiocytoma. Both light microscopic findings and immunohistochemistry can help rule out these lesions. Inflammatory fibrosarcomas tend to be more cellular with closely packed spindle shaped fibroblasts in interlacing fascicles or a distinctive herringbone pattern. In addition, the sarcoma will contain frequent mitosis and occasional atypical ones.

Follicular dendritic cell sarcomas would show sheets of more plump spindle cells with an infiltrative growth pattern. The spindle cells in this case will be smooth muscle actin negative and CD21 positive. Since these features were not present in our case and the AFB stain was strongly positive, CD 21 stain was not performed. Hemangiopericytoma can present in the neck region, but characteristically these cases will exhibit branching blood vessels in a staghorn appearance and the surrounding neoplastic cells would be CD 34 positive. In our case, the CD 34 was only positive in the endothelial cells of the tumor nutrient blood vessels. Malignant fibrous histiocytomas can be differentiated by the presence of numerous mitoses, bizarre giant cells, high cellularity, poor circumscription and necrosis.

The biologic behavior of IPT is highly variable, but generally they have an innocuous course. Complete surgical resection, if possible, is the treatment of choice with the exception of orbital lesions [5]. Recurrence can occur and has been reported in approximately 25% of the cases and is usually treated by repeated surgical excisions [15]. In few cases spontaneous regression may also occur [15].

Radiation therapy has been tried in unresectable cases. Steroids have been used with variable success and are the recommended first line intervention in cases of orbital tumors [5].

In summary, we present an unusual case of a MAC associated inflammatory pseudotumor in the nasal cavity in a patient with a history of cocaine abuse. IPT is benign and may histologically demonstrate mild atypia in the spindle cell population. However, it is emphasized that thorough histological evaluation of mixed inflammatory cell infiltrate coupled with the presence of numerous foamy macrophages should be a clue to its benign nature. Utilizing acid fast bacilli stain will confirm the diagnosis.

Conflict of interest The authors claim no conflict of interests

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