

Inflammatory Pseudotumor of the Hypopharynx: Clinical Diagnosis, Immunohistochemical Findings and Treatment of this Rare Disease

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Abstract. *Inflammatory pseudotumor (IPT) is a rare benign lesion, often imitating a malignant disease. An IPT was found in the sinus piriformis of a 40-year-old male who suffered from dysphagia, globus feeling and a weight loss of 5 kilograms in six months. Neither common infections previously described in combination with IPT such as human herpes virus (HHV) 8, human immunodeficiency virus (HIV) or acute Epstein Barr virus (EBV), nor evidence of manifestation of a systemic mastocytosis or a malignant disease were found. The primary therapy for IPT in locations other than the orbita is complete resection, if this is not applicable or recurrence occurs then cyclosporine, chlorambucil, indometacin or radiation have been used as alternative treatments. A transoral laser-assisted resection was performed in the case described here, resulting in a complete and lasting cure.*

Inflammatory pseudotumor (IPT) is a benign lesion which often clinically imitates a malignant disease. First described in children's lungs by Brunn (1), it was named by Umiker *et al.* (2). IPT is particularly rare in the head, neck and throat. Histopathological findings vary widely so that many pseudonyms exist depending on the predominant cellular elements and include inflammatory myofibroblastic tumor, plasma cell granuloma and pseudosarcomatous myofibroblastic lesion (3).

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Here a case of an IPT located in the right sinus piriformis of the hypopharynx is reported. The details of its histopathological structure, clinical and histological differential diagnosis, treatment and diagnostic procedures are presented.

Case Report

A 40-year-old male presented with progressive dysphagia and globus sensation. Additionally, a weight loss of 5 kilograms in six months was reported. There was no odynophagia, regurgitation, dyspnea or generalized symptoms such as fever and fatigue. The patient reported a nicotine consumption of ten cigarettes per day and a negative alcohol history. Further diseases, infections, allergy or immune deficiency symptoms were excluded by interrogation. The globus sensation in projection to the larynx level increased when moving the head forward and left. Transoral endoscopy revealed a spheroidal and plain tumor located in the right hypopharynx, arising from the medial aspect of the sinus piriformis and affecting the aryepiglottic fold (Figure 1). The apical part of the tumor showed a tubercular structure with aspects suspicious of a malignant process. On flexible and rigid endoscopy, the findings for the larynx were normal.

Due to the weight loss a malignant process was presumed and computed tomography (CT) scanning and ultrasound imaging of the neck and larynx were performed as well as videofluoroscopic swallowing examinations. The CT scan (with a high-resolution scan of the larynx) revealed a 1.5×1.5 cm tumor of the right piriform sinus located prevertebrally with a central inhomogeneous perfusion of contrast dye (Figure 2). Lymphadenosis was found neither in the CT scan nor by ultrasound. A magnetic resonance imaging (MRI) scan completed the diagnostic efforts, with no further evidence of malignancy (not shown). ALA (aminolevulinic acid) fluorescence-assisted endoscopy revealed the fluorescence pattern of a benign lesion, and the vocal cords showed normal movement. Thus, in accordance with the radiological findings, an infiltration of the larynx was not suspected. To gain additional information about the process and to obtain a biopsy for histopathological investigation a panendoscopy was performed. Histopathology revealed the diagnosis of an inflammatory pseudotumor with high numbers of infiltrating loosely scattered mature mast cells. With no laryngeal



Figure 1. Endoscopic view of the inflammatory pseudotumor in the right sinus piriformis with spheroidal appearance and a tubular appendix.

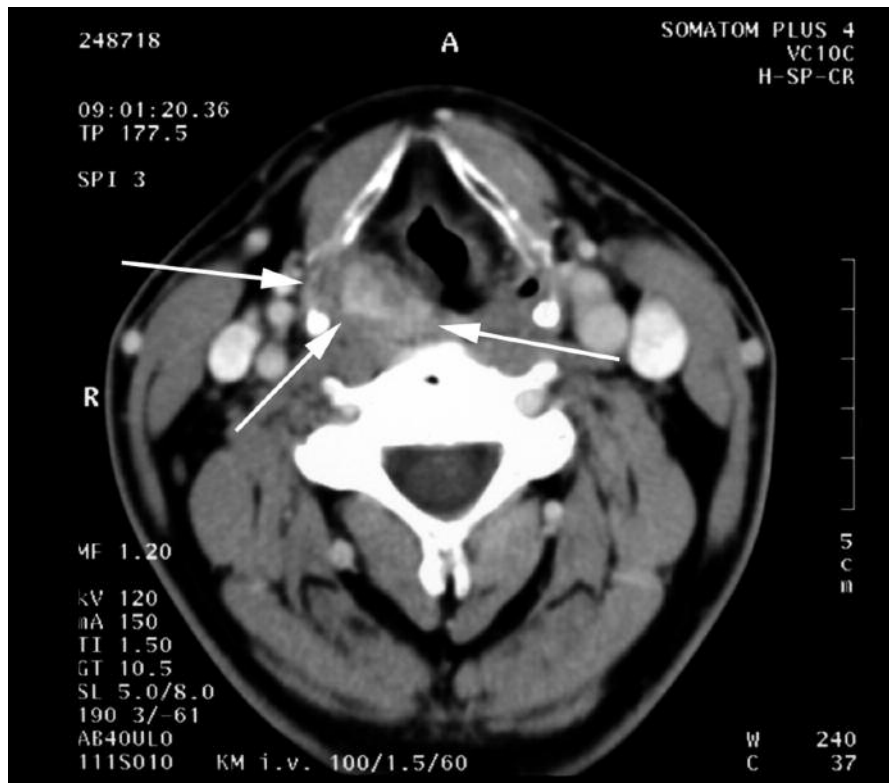


Figure 2. CT scan of the neck using contrast dye revealed a tumor 1.5 cm in diameter, affecting the right sinus piriformis (marked by arrows).

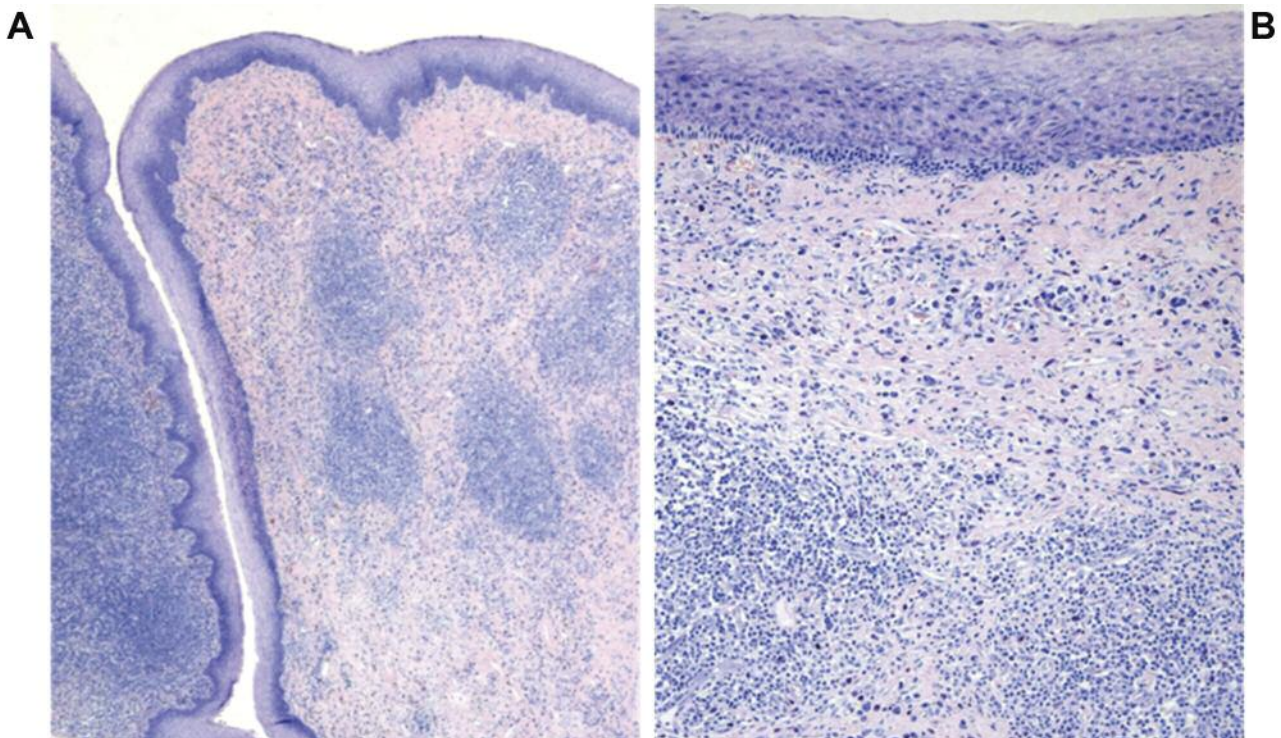


Figure 3. A: Inflammatory pseudotumor of hypopharynx with regular squamous epithelium. Note the disseminated lymph follicles in a granulation tissue, as well as the high number of mast cells. GIEMSA $\times 25$. B: Area from Figure 3A with a regular surface of squamous epithelia and granulation tissue particularly rich in fibroblasts, containing partly roundish, partly spindle-shaped mast cells with strong metachromasia (dark violet). GIEMSA $\times 100$.

infiltration, the best therapeutic option for the removal of the enlargement was a laser resection. Accordingly, the tumor, with margins of 3.5 \times 2.0 \times 2.0 cm overall size, was completely removed transorally, using a scanner-assisted (AcuBlade™, Lumenis GmbH, Dreieich, Germany) carbon dioxide laser. For further investigation, several additional tests were performed: human immunodeficiency virus (HIV)-1/-2 ELISA showed negative results, Epstein Barr virus (EBV)-IgM was negative and EBV-IgG was at 140 U/ml, indicating a past infection with EBV. Prick testing of standard allergens showed non-allergic reactions. Concerning the high numbers of mast cells in the resected tissue, cutaneous mastocytosis was excluded by a dermatological consultant. Tryptase and complete IgE measured by fluoroimmunoenzymatic (FEIA) method showed normal values. Molecular analysis of the routinely processed tissue showed no D816V point mutation of c-kit kinase domain, so that systemic mastocytosis was excluded. Pathological examination of the resectate revealed grey-white tissue measuring up to 3 cm, with a grey-white tumor, measuring 1.5 \times 1 \times 1 cm, which bulged out the mucous membrane. Histologically, the multilayered squamous cellular surface was regular. Disseminated lymph follicles containing predominantly small T-lymphocytes in a granulation tissue partially rich in fibroblasts were also found. Notably, there was a huge number of partly roundish, partly spindle-shaped mast cells with strong metachromasia; compact mast cell infiltrates were not detected (Figure 3A, B). There was no evidence of malignancy. The EBV infection of the tissue was detected through a positive EBER (EBV-encoded small RNAs) reaction. Positive reaction of

CD25 or human herpes virus 8 (HHV8) as formally described in IPT could not be found. There was no evidence for recurrence in transoral endoscopy during follow-up for three years.

Discussion

Inflammatory pseudotumors have been described in the spleen, liver, urinary bladder, uterus, prostate, thyroid gland, soft tissue, the upper respiratory system, esophagus and larynx and, more rarely, in other locations. Usually these lesions show a fibroblastic component with varying inflammatory infiltrates. Morphologically, the spindle-shaped fibroblasts or myofibroblasts may be reminiscent of a malignant process. Nevertheless, the diagnosis of a benign tumor mostly does not pose a problem. Nuclear atypias are possible, although the nucleus-plasma relationship is normal in most cases. In general, the epithelial surface is not involved, however, sometimes the irregular structure of a malignant disease is imitated. The surrounding mesenchymal tissue is usually inconspicuous. Very large lesions may show areas of fibrosis, hemorrhage and necrosis. The differential diagnoses vary with the location, for the hypopharynx and the left ajar larynx, these might be spindle cell squamous cell carcinoma (SCSCC), inflammatory fibrosarcoma, tumors of

nerve sheaths and nodular fasciitis or unspecific inflammation. In contrast, leiomyosarcoma or rhabdomyosarcoma as a rule show elevated mitotic counts and other aspects of malignancy; infiltrates of inflammatory cells are unusual (4, 5). The incidence of IPT is still unknown. To date, there are 992 papers listed in Pubmed with the key word "inflammatory pseudotumor". Forty-seven of these cases describe the occurrence of IPT in the head and neck (orbita excluded), followed by involvement of the paranasal sinus, trachea and parotis. However, there are only very few papers describing a primary site in the hypopharynx. IPT most commonly involves the orbit, with an incidence of 6% of all orbital lesions, it represents the third most frequent primary orbital tumor (6). In children's lungs it is one of the most frequent benign tumor formations, making up 50% of all benign tumors (7, 8). Additional cases from almost all over the human body have been reported (9, 10). The diverse symptoms include fever, pain, vomiting, chills, jaundice and weight loss, malaise, anemia and hypergammaglobulinemia, plus additional symptoms such as dysphagia depending on the location. Altogether, the symptoms occur with an aspect of a malignant process. In association with the location and the state at detection, IPT may be solitary or multiple.

Adequate therapy for IPT is usually complete resection. Disease recurrences, which have been reported in some cases, presumably are caused by incomplete resection. Resection is not appropriate for IPT of the orbita, where primary therapy therefore is administration of high doses of systemic steroids. If these are neither applicable nor effective, cyclosporine, chlorambucil, indometacin or radiation have been used as alternative treatments. Spontaneous regression or remission has also been reported.

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