ISSN: 2340-3438

Edita: Sociedad Gallega de Otorrinolaringología.

Periodicidad: continuada.

Web: www: sgorl.org/revista

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Acta Otorrinolaringológica Gallega

Caso clínico

SEPTAL NASAL PLEOMORPHIC ADENOMA: CASE REPORT AND LITERATURE REVIEW

ADENOMA PLEOMORFO DE SEPTO NASAL: CASO CLÍNICO Y REVISIÓN DE LA LITERATURA

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Recibido: 25/11/2016 Aceptado: 2/1/2017

Abstract

Background: Pleomorphic adenoma (PA) is a benign mixed tumor and is the most common benign neoplasm of the salivary glands. Although it arises mainly in the major salivary glands, minor salivary gland involvement can be seen in 8% of cases, with the palate being the most common site. PA originated from the minor salivary glands of the nasal cavity is extremely rare.

Case report: A rare case of a PA arising from the nasal septum is presented. A 23-year-old caucasian male complained with a 12-months right nasal obstruction, epistaxis and facial pain and swelling. Physical examination demonstrated a soft tissue mass in the anterior aspect of the right nasal septum. In this patient, an endoscopic approach was used to achieve a wide a *en bloc* resection. Histological and immunohistochemical evaluation revealed the presence of a pleomorphic adenoma.

Discussion: The PA of the nasal cavity commonly arise from the nasal septum, and has a predilection for the female sex. Tumor growth is generally locally and is not known to spread to the neighboring structures. Surgical resection is the treatment of choice.

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Conclusions: Pleomorphic adenomas of the nasal cavity, although extremely rare, are a important differential diagnose to consider in the presence of a slow growth unilateral mass of the nasal cavity. Long -term follow-up, both endoscopic and radiologic, to rule out persistent disease ou malignancy transformation of PA is mandatory.

Keywords: Nose, Nasal tumor, Pleomorphic adenoma, Diagnosis, Histopathology

Resumen

Introducción: El adenoma pleomorfo (AP) es un tumor mixto benigno y es la neoplasia benigna más frecuente de las glándulas salivares. La mayoría de ellos se origina de las glándulas salivares *major*, en las glândulas salivares *minor* ocurre en solamente 8% de los casos. El AP de la cavidad nasal de las glándulas salivares *minor* es extremadamente raro.

Caso Clínico: Se presenta un caso de AP del tabique nasal. Hombre de raza de 23 años de edad que recurre al servicio de urgencias por obstrucción nasal derecha con 12 meses de evolución y epistaxis. A la exploración física se verifica una masa multilobulada en la cavidad nasal derecha con origen en el tabique nasal derecho. Se somete a cirurgia endoscópica de la nariz con resección *en bloc*. La histología y la imunohistoquímica han demonstrado la presencia de un adenoma pleomorfo.

Discusión: El AP de la cavidad nasal se origina en la mayoría de las veces del tabique nasal, tiene predilección sobre el sexo feminino, su crecimento es local y no tiene tendencia a invadir las estructuras vecinas. La resección qirúrgica es el tratamiento de elección.

Conclusión: El AP de la cavidad nasal, aunque extremadamente raro, es un importante diagnóstico diferencial de las neoplasias que se desarrollan en la nariz y senos paranasales. El seguimiento a largo plazo, ya sea endoscópico o radiológico, es obligatorio para excluir enfermedad persistente o la trnaformación maligna.

Palabras clave: Nariz, Tumor nasal, Adenoma pleomorfo, Diagnóstico, Histopatología

Introduction

Salivary gland tumors constitute about 3% of all head and neck neoplasms[1]. Pleomorphic adenoma (PA), also known as benign mixed tumor of the salivary glands, due to the morphologic diversity with both epithelial and mesenchymal components, arise mainly in the *major* salivary glands, specially in the parotid gland (70%), and, less frequently, in submandibular and sublingual salivary glands (15–25 %)[2]. Only 8 to 10% of PA originate from the minor salivary glands. Few cases have been reported in the soft and hard palate, lacrimal gland, lip and external auditory canal[3,4].

PA is extremely rare in the respiratory tract and the incidence is even lower in sinonasal area[5]. In the literature most references found are case reports on nasal PA. The largest published series are those of of Compagno[6] with 40 cases, 25 of which had tumors derived from the mucosa of the nasal septum, and

Suzuki[7], a national study carried out in Japan with 41 cases of PA of the nasal cavity with 90.2% of cases arising from the nasal septum.

Recently, Vento published a national study in Finland with 10 cases of intranasal PA, 60% of them arise from the nasal septum. Intranasal PA generally arise from the nasal septal mucosa even though the seromucosal glands are mainly located within the lateral nasal wall, in particular in the turbinates[8].

Despite being rare in this location intranasal PA is an important differential diagnostic entity. Symptoms are mainly nasal obstruction and epistaxis which are not characteristic.

For the histopathological diagnosis of the mixes tumor it is required to have an epithelial associated with a mesenchymal component[2,9]. The treatment of choice is surgical resection.

CASE REPORT

A 23-year-old male, non-smoker, presented at our emergency room reporting epistaxis from the right nasal cavity associated with right nasal obstruction since the last 12 months. There was no history of visual defect, atopy or nose trauma. On inspection, the lateral wall of the nose was splayed laterally by a right nasal cavity mass although the skin over the the nasal swelling appeared normal. Epistaxis ceased after application of topical vasoconstrictors. Anterior rhinoscopy showed a smooth, pink-pale lobulated mass arising from the nasal septum, at the level of Cottles´ area II. There was a deviated nasal septum to the left nasal cavity. The rest of the ear, nose, and throat examination was normal and thre was no evidence of cervical lymphadenopathy. Computed Tomography (CT) scan revealed a well defined lobular soft tissue mass in the right nasal cavity, not involving the paranasal sinuses, displacing nasal septum to the left and increasing the pyriform aperture on the right. The smooth surface and the preservation of the mucosal lining were consistent with a benign neoplasm (Fig. 1). An endoscopic resection was performed, under general anesthesia. The tumor was completely excised with a segment of mucoperichondral and mucoperiosteal margin. (Fig.2) Histopathological analysis of the tumor demonstrated a mixed epithelial with a mixochondroid componente (Figs. 3 and 4). Immuno-histochemical stainings for p63 (Fig. 5) highlighted the presence of an abundant myoepithelial component. The histopathological and immunophenotypical features observed were consistent with the diagnosis of pleomorphic adenoma.

After one year follow-up, there is no endoscopic evidence of recurrence.

Figure 1: Coronal CT scan of the paranasal sinus showing soft density mass (arrow) between right nasal septum and right nasal process of maxillary bone. Notice the thiness of the right nasal process of the maxillary bone (arrowhead) compared to the left one.

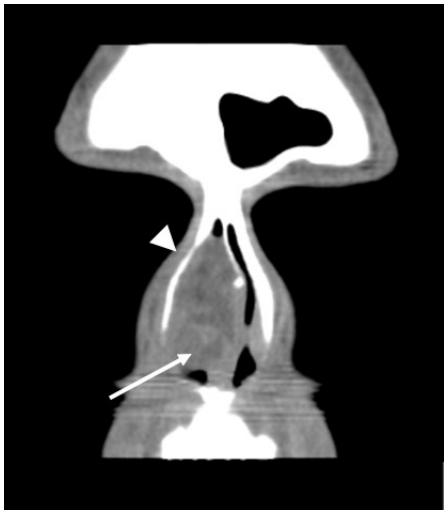
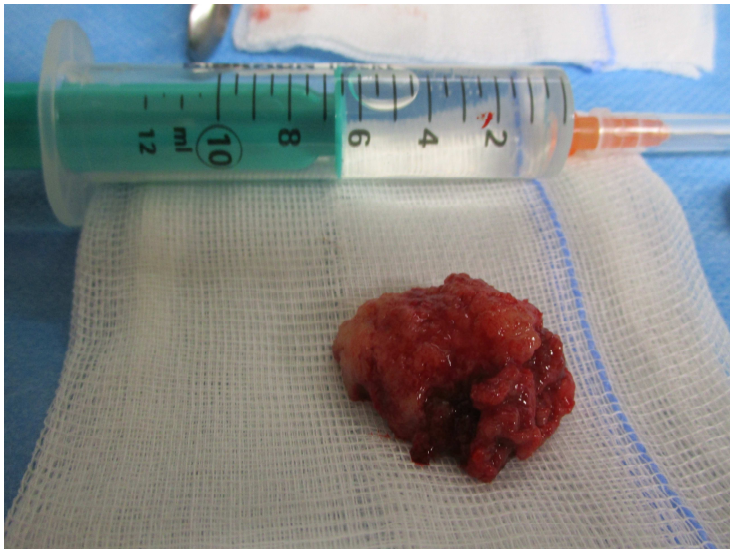


Figure 2: Tumor specimen. Multilobulated tumoral mass, non encapsulated with 35 x 45 x 15 mm.



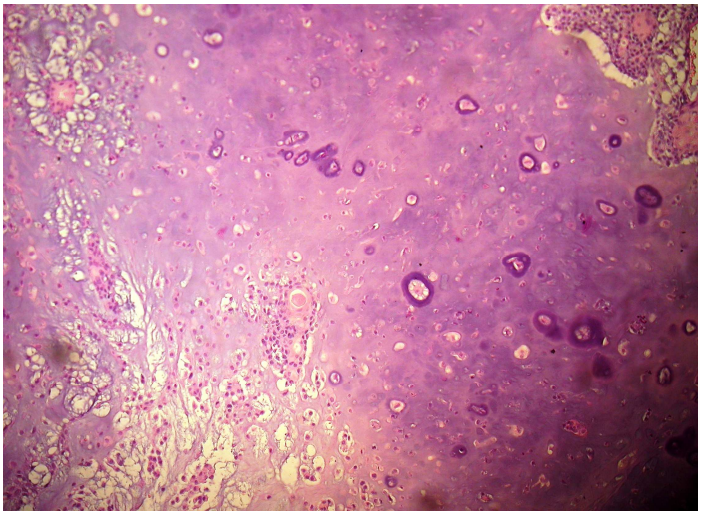


Figure 3: PA with mesenchymatous component: chondroid and myxoid (H&E x40).

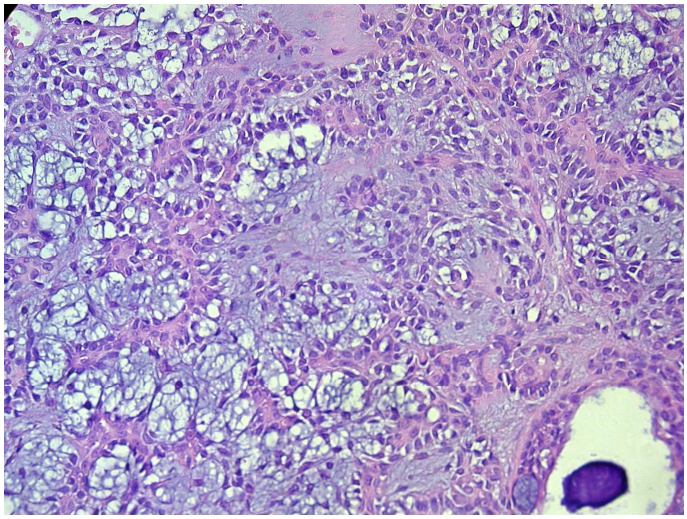
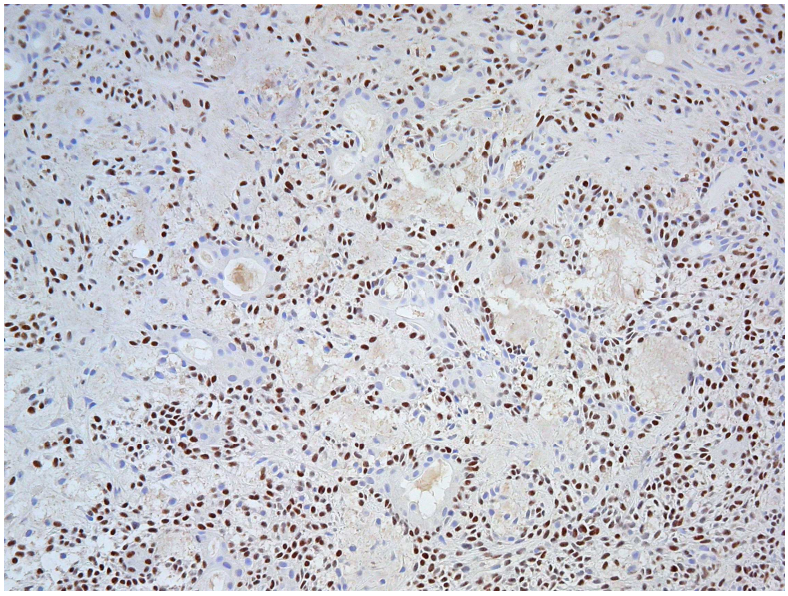


Figure 4: Benign ducts in the fibromyxoid stromal tissue, surrounded by myoepithelial cells (H&E x400)

Figure 5: Immuno-histochemical stainings: positive immunostaining for p63 in myoepithelial cell of PA (brown color) and epithelial ductal cells, in blue, not staining with p63.



Discussion

Salivary gland tumors constitute about 3% of all head and neck neoplasms[2]. PA arise mainly in the *major* salivary glands (MSG), and only 8 to10% of them arise from the *minor* salivary glands (mSG), from in the upper aerodigestive tract including the nasal cavity, pharynx, larynx, trachea, external ear canal and lacrimal glands[3,4]. Despite being the commonest benign neoplasm in the mSG, only 15% of the formations of these glands are benign, mSG are characterized by holding a high rate (85%) of malignant neoplasms[2].

Intranasal PA is so uncommon that there are only two reports statistically sizable series. In 1977 Campagno and Wong[6] reviewed 40 cases of intranasal mixed tumors between 1949 and 1974. Twenty-three patients were females and 17 were males. Most of the tumors (25 out of 40) emerged from the nasal septum mucosa. Also, unlike tumors of the major salivary glands, which are said to be more common in female, intranasal PA showed no significant predilection for either sex. They were able to obtain follow-up data from 85 % of the cases and they found out a recurrence rate of 10% (3 out of 34). None of the patients had a malignant transformation of their lesion. Later, in 1990, Suzuki[7] described a case of intranasal PA and reported a Japanese national study with 41 patients, although not statistically significant there was a female predominance (1:1.18). Only four case were originated in the lateral wall of nasal cavity and all of the other cases, 90%, were in the nasal septum. One case recurred (2.4%) and another case had a malignant transformation (2.4%). In 2016, Vento[8] published a national Finish study with 10 cases and their findings were similar to the previous ones: majority of pleomorphic adenomas (60 %) originated from the septum, female predominance, no recurrence or malignant transformation, however was less than one year in six cases.

Several theories have been proposed to explain the unique origin of nasal septal mucosa PA even though the seromucosal glands are mainly located in the lateral nasal wall.

According to Stevenson[10] PA of the nasal septum originate from remnants of the vomero-nasal organ, an epithelium-lined duct in the cartilaginous nasal septum that degenerates in early fetal life. Later Matthew *et al*[11] pointed out that septal PA resulted from misplaced embryonic epithelial cells, derived from ectoderm and carried via the nasal pits into the septal region. Contrarily, Evans and Cruickshank[12] advocate that PA are of epithelial origin and that they arise in fully developed salivary gland tissue rather than in embryonic remnants.

Viral involvement has been discussed in the pathogenesis of PA regarding the role of Epstein–Barr virus (EBV), human herpes virus 8 (HHV-8), human papiloma vírus (HPV) and human cytomegalovirus (CMV). In 1998 Atula[13] demonstrated EBV DNA positivity, from a pleomorphic adenoma arising in the nasal cavity and HPV, HHV-8 and CMV DNA were not detected. Malinvaud et al.[14] reported three cases of pleomorphic adenomas of the nasal septum with EBV-related blood antibodies in all of them and positive EBV-DNA detection in the tumor in one case. Regarding the environmental exposure of carcinogens, Zheng[15] published an report with 41 cases of salivary gland neoplasms (SGN), without further specification on sub-type, and 414 controls and found that silica dust exposure was linked to a 2.5-fold increased risk of cancer of the salivary gland and Horn-Ross[16] analyzed 199 cases SGN who where related to rubber workers exposed to nitrosamines.

Regarding the clinical features of the intranasal PA, they usually present as a painless slow growing mass ou painless nasal swelling, therefore clinical symptoms only appear after a long silent period. The most common symptoms are gradual worsening of unilateral nasal obstruction and epistaxis. Less commonly, when the tumoral mass reach a relatively large size, an external swelling of the nasal pyramid as well as pain may be present. On examination, it appears as smooth, pink-pale lobulated mass and soft consistency. The absence of ulceration and lack of invasion of surrounding structures suggest a benign nature of the mass. Differential diagnosis includes both benign and malignant tumous such as nasal polyps, papillomas, angiofibromas, osteomas, squamous cell carcinoma, adenocarcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, melanoma and olfactory esthesioneuroblastoma. Computed tomography demonstrate the extension as the invasion, or not, into surrounding, as well as, in many cases is able to evidence the site of tumors' origin.

The treatment is surgical excision with a surrounding cuff of normal tissue to prevent recurrence, especially when the capsule is interrupted and a direct contact with the surrounding normal tissue is present[2,4].

Recurrent pleomorphic adenoma is an unusual but challenging problem as frequently multiple foci of recurrence appear. Malignant transformation is rare and occurs most frequently in patients with long-standing tumors. The risk of malignant transformation in pleomorphic adenoma is 1.5% within the first 5 years of diagnosis, but this increases to 10% if observed for more than 15 years. Cases of benign pleomorphic adenoma metastasizing to cervical lymph nodes have been reported[2].

Pleomorphic adenoma display morphological architectural diversity. Macroscopically, PA tend to form well-defined, ovoid or lobulated tumors. M*ajor* salivary glands PA are encapsulated although it varies in thickness and completeness, whereas *minor* salivary glands PA usually have a poorly developed or absent capsule. On histologic examination, PA consists of an epithelial, myoepithelial and mesenchymal/ stromal component. The epithelial component shows a wide variety of cell types and the epithelium forms sheets or duct-like structures. Myoepithelial cells may form a fine reticular pattern or sheets of spindle-shaped cells. The mesenchymal/stromal component is mucoid/myxoid, cartilaginous or hyalinised. Sometimes the stromal component dominates the main bulk of the tumour[17].

Immunohistochemistry using a monoclonal anti-p63 antibody is considered a highly sensitive and specific marker of myoepithelial cells´ of the normal glandular parenchyma and in PA.[18,19] Immunostaining for p63 is restricted to the nuclei of myoepithelial cells (Figure 5) and confirms the diagnosis.

In conclusion, minor salivary gland pleomorphic adenomas account for a small portion of all pleomorphic adenomas of head and neck. They usually present as focal mass lesions and are found most commonly in the palate. Pleomorphic adenomas of the nasal cavity, although extremely rare, are a important differential diagnose to consider in the presence of a slow growth unilateral mass of the nasal cavity. A complete excision should be performed with control of the margins in order to reduce local and distant spread of neoplastic cells. Long-term follow-up, both endoscopic and radiologic, to rule out persistent disease ou malignancy transformation of PA is mandatory.

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