■ CASE STUDIES

Carcinoma on Pleomorphic Adenoma in Cervical Salivary Heteropia. Handling of One Case and Literature Review

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The presence of salivary tissue outside of the salivary glands, a term called "salivary heterotopia," is not very common. The co-existence of carcinoma expleomorphic adenoma in a salivary heterotopia in the upper third of the neck can be considered unusual.
We present an infrequent and clinically unsuspected case of carcinoma expleomorphic adenoma in the upper third of the neck and independent of the salivary glands. The tumour developed within heterotopic salivary tissue, with the histopathological study of the surgical extract being decisive for its diagnosis. The cervical salivary embryogenesis of heterotopias and their oncogenesis is analyzed. Their clinical signs are reviewed to indicate the difficulty in distinguishing the different types of diagnosis from other primary or metastatic tumours so as to assist in choosing the therapy to follow.

Key words: Neoplasia of salivary gland. Salivary carcinoma expleomorphic adenoma. Heterotopic salivary tissue.

Carcinoma sobre adenoma pleomorfo en heterotopia salival cervical. Manejo de un caso y revisión de la literatura

La presencia de tejido salival fuera de las glándulas salivales, denominada "heterotopia salival", es poco frecuente y es insólito que concurra un carcinoma ex adenoma pleomorfo en una heterotopia salival en el tercio superior del cuello.
Presentamos un caso raro y clínicamente insospechado de carcinoma sobre adenoma pleomorfo en la región superior del cuello e independiente de las glándulas salivales. El tumor se desarrolló dentro de un tejido salival heterotópico, y fue decisivo el estudio histopatológico de la pieza quirúrgica para su diagnóstico. Se analiza la embriogénesis de las heterotopias salivales cervicales y su oncogénesis. Se revisan sus manifestaciones clínicas y se señala la dificultad en el diagnóstico diferencial con otros tumores primarios o metastásicos que nos harían vacilar sobre qué terapia aplicar.

Palabras claves: Neoplasia de glándula salival. Carcinoma ex adenoma pleomorfo. Heterotopia salival.

INTRODUCTION

Salivary heterotopia (SH), also known as aberrant salivary gland tissue, choristoma, or hamartoma, is the presence of salivary tissue anywhere other than in the salivary glands[1]; although numerous authors identify it with the concept of ectopic salivary gland tissue[2-5], this disorder differs in that normal salivary tissue has been displaced into a different location.

SH has been found in several parts of the body, but it is infrequent in the upper neck region. Neoformation of this tissue is unusual, albeit greater in the upper third of the neck than in the lower third[4]. The appearance of a carcinoma on a pleomorphic adenoma or a carcinoma ex pleomorphic adenoma on a heterotopia is exceptional.

We have felt it is of interest to report this case due to its rarity and because it is useful to analyze the embryogenesis of cervical SHs and their oncogenesis, as well as to review their clinical manifestations and highlight the diagnostic difficulty vis-à-vis primary or metastatic cervical tumours that might cast doubt on which treatment to apply.

CASE STUDY

Male, 51 years of age, whose only personal history of note is smoking-related chronic laryngitis. He came to the

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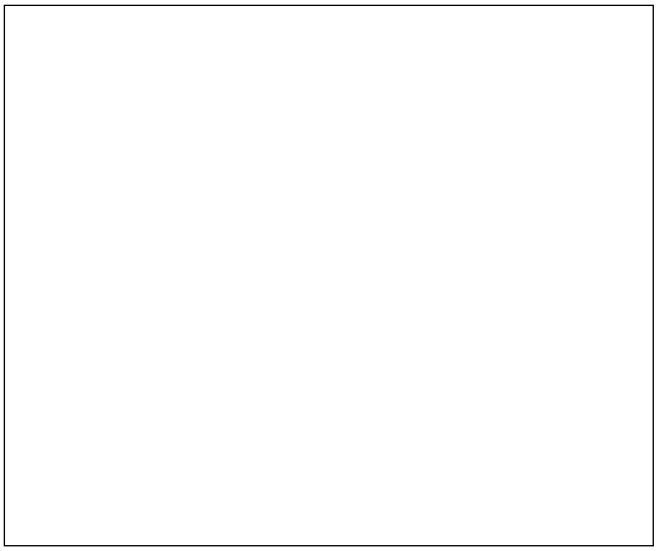

Figure 1. Right cervical ultrasound scan. The rectangles indicate the 33×23 mm loop attached to the internal jugular, partially thrombosed.

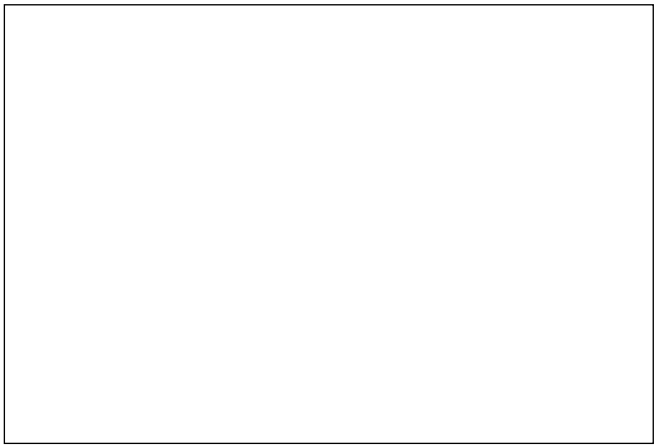

Figure 2. Computerized tomography of the neck. A 2.8×2.5×3 cm mass (*) can be seen with thrombosis of the internal jugular vein.

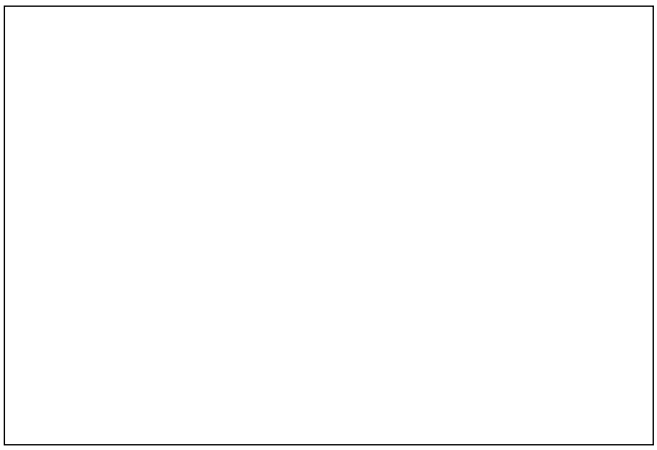

Figure 3. Microscopic study of the lesion: the tumoral proliferation is multinodular, infiltrating and forms large masses separated by fibrous tracts with small vessels and lymphoid accumulation (HE 10×).

otorhinolaryngological out-patient clinic one month after the onset of a hard tumoration in the right cervical region, not painful and adhering to the planes. The rest of the general and otorhinolaryngological examination was normal, except for a leucoplastic lesion mainly on the right side of the larynx.

The cervical ultrasound scan was reported as an increase in the thyroid gland at the expense of several nodes. In the upper right cervical region, a mass of 33×23 mm was seen to be adhering to the internal jugular, compatible with an adenopathy and, underlying this, an intraluminal image partly obstructing the lumen of the jugular vein due to possible thrombosis (Figure 1). The computerized tomography (CT) of the neck detected a solid mass of 2.8×2.5×3 cm with thrombosis of the right internal jugular vein. The remaining cervical structures are normal (Figure 2). The abdominal ultrasound scan and the chest x-ray did not reveal significant alterations.

The biopsy of the cervical mass by means of fine-needle puncture-aspiration (FNPA) was reported to be cytologically compatible with pleomorphic adenoma and the FNPA of the thyroid revealed no malignant cytology.

In view of the results of these studies and the characteristics of the tumour (hard and adhered), surgical treatment was decided. Endoscopy was performed on the upper aerodigestive tracts with biopsies taken from the right vocal cord and the mucosa of the rhinopharynx. In addition, the right cervical area was excised, including the internal jugular vein (due to thrombosis and tumour infiltration), the right submaxillary gland (although it seemed healthy, it was adhered to the tumour) and the right hemithyroid.

The pathology study reported signs of inflammation on the right vocal cord and the rhinopharynx, a normal right salivary gland and a node measuring 2×1.5 mm in the right thyroid lobe. In the 8×6 cm cervical tumoration, a solid, 4×4 cm neoplastic node was identified, with infiltrating limits and invasion of a venous vessel. Under the microscope (Figure 3), the tumoral proliferation was multinodular, infiltrating, forming large masses separated by fibrous tracts with small vessels and lymphoid accumulations. The solid, papillary tumoral pattern is made up of spindly or polygonal cells with atypical nuclei and frequent mitoses. It had massively infiltrated the adjacent adipose tissue and the jugular vein where there was a large bypassed thrombus. Peripheral remains of pleomorphic adenoma were visible, without distinguishing any normal salivary gland.

The pathologist's diagnosis was carcinoma on pleomorphic adenoma (carcinoma ex pleomorphic adenoma) with invasion of soft tissue and the internal jugular vein. Radiotherapy was thus prescribed and he received 50 Gy at 200 cGy/5 times a week.

DISCUSSION

The case reported here is exceptional: we have only found 1 published case of an adenocarcinoma on pleomorphic adenoma with salivary heterotopia[2] and 1 adenocarcinoma with salivary heterotopia[6] in the upper third of the neck.

Since Hunczovsky indicated the existence of SHs back in 1789, these have been found in numerous parts of the body. In the neck, there seems to be a predilection for the lower area, along the anterior edge of the sternocleidomastoid (SCM) muscle; it is found less frequently in the upper third[4] and is exceptional in the middle third of the neck[7].

The onset of this disorder has to do with embryonic development and differs depending on the anatomical site. In 1968, Willis put forward three general hypotheses: *a)* abnormal persistence and development of vestigial structures; *b)* the abnormal differentiation of local tissues (heteroplasias); and *c)* the dislocation of a portion of a definitive rudimentary organ during its movement and development. In the upper third of the neck, it would be due to the entrapment of salivary tissue in the periparotid ganglia during embryonic development, in the same was there is ganglionar tissue trapped in the parotid gland. In the lower third, SH would be secondary to heteroplasias developed from and within embryonic remains of the pre-cervical sinus of His.

Cervical SHs are manifested as a mass, cyst or fistula[8], generally in adulthood. The definitive diagnosis is provided by a histological study while clinical presentation and imaging findings are indicative. Treatment must be surgical and without major delay in order to avoid its becoming malignant[9].

SH may be the seat for any salivary neoformative disease; benign forms are more frequent, located in the upper third of the neck and mainly observed in adults[4].

More serious is the development of a malignant tumour, as in the case reported here. The oncogenic mechanism has not yet been clarified in SH, perhaps because the intraganglionar salivary tissue is more immature and has greater potential for differentiation and growth than normal salivary tissue[10].

Carcinomas ex pleomorphic adenoma is a tumour with the signs of malignancy corresponding to a carcinoma between residual areas of a mixed benign tumour or a mixed tumour with development of a second malignant neoplasia. It is diagnosed between the fifth and seventh decades of life[11]. Our patient is within this age range.

Pathogeny is controversial and two theories have been propounded. The first is that the tumour would primarily be malignant (it is initially found in up to 60% of cases without any history of a pre-existing tumour; in addition, among young people without age differences between these tumours and mixed tumours). The second theory supports the carcinomatous transformation of the pleomorphic adenoma, backed by technical engineering fact that most of them have a history of a mass over many years and this suddenly increases in size with other accompanying symptoms[12].

In our patient, the pathogeny would conform to the first theory in terms of the sudden onset of the lesion (less than 1 month) and his relatively young age (51 years).

Diagnosis was confirmed by the histopathological study, supported by the simultaneous presence of remnants of pleomorphic adenoma and the carcinomatous contingent. The FNPA biopsy may lead us to the diagnosis, although this is difficult if the carcinomatous component is not seen, as happened in our case. The tumours are poorly defined or even broadly infiltrating, with malignant findings among adenoma areas. Neural and/or vascular invasion is frequent. The difficulty in reaching the histological diagnosis lies in finding adenoma areas, especially if these are very small, and multiple slices are required.

The differential diagnosis may also be arduous. The confusion would lie in whether or not the mass is a metastasis of a primary salivary gland tumour or a neoplasia in an SH or secondary to the implantation of a tumour following surgical treatment, or even a primary ganglionar tumour. The extirpation of the ganglia in the neck is sometimes required in order to come to a diagnosis, in view of a suspected metastasis of a tumour of unknown origin.

In our patient, the diagnosis was reached through the histopathological study of the lesion excised. It was initially thought that it might be a metastasis of a pharyngolaryngeal tumour caused by smoking, the laryngeal lesion present and the imaging study. Furthermore, the cytology did not pin down the diagnosis as the report indicated pleomorphic adenoma.

The natural history and prognosis of these tumours is more severe than when they are carcinomas *ex novo* and up to 50% of them develop recurrences, in which case the ganglionar metastases increase. The factors darkening the prognosis include a size greater than 4×4 cm, the high degree of malignancy, the high percentage of adenocarcinomatous findings and the invasion of adjoining tissues[12].

Treatment is no different than for other carcinomas: first choice is radical exeresis with prophylactic ganglionar surgery and adjuvant radiotherapy. There is a question mark against chemotherapy to control the high percentage of remote metastases[9].

CONCLUSIONS

When faced with any cervical tumoration, we have to suspect that there might be an SH providing shelter for a salivary involvement, either benign or malignant.

The appearance of cervical SHs is related to embryonic development and the number of cases published is on the rise, probably due to better performance of diagnostic methods.

A carcinoma in a pleomorphic adenoma may arise *ex novo* or through carcinomatous transformation of the pleomorphic adenoma. Its diagnosis in an SH is complicated by the need to discard the possibility of metastasis of a primary salivary tumour or an implantation of a tumour following surgical treatment or that it is a primary tumour of the ganglia. This situation requires close co-operation with the pathologist, a careful search for a primary tumour and confirmation of the normality of the salivary glands and the absence of hidden carcinomas, as there are no clear criteria to differentiate a primary salivary tumour in a cervical SH from a metastasis secondary to a salivary tumour.

The management of these tumours entails, first of all, the prevention of their appearance by the prompt elimination

of any benign tumour, and the most appropriate treatment is surgical exeresis and subsequent radiotherapy.

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