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Case Report

Polymorphous low-grade adenocarcinoma: a report of two cases

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ABSTRACT

Polymorphous low-grade adenocarcinoma (PLGA) is an infrequent type of malignant epithelial tumor that occurs almost exclusively in minor salivary glands. It commonly presents in women between the sixth and eighth decade of life, usually as an asymptomatic mass of long evolution and slow growth in the oral cavity but can erode and infiltrate adjacent bone. We present 2 case reports and review the literature on the subject. One case presented with a growing mass that developed over the course of 12 years, incorrectly diagnosed in the first incisional biopsy as a benign tumor. The second case presented as a recurring PLGA 19 years after the first, which appeared at an unusually young age. Both cases were managed with the treatment of choice: surgery with wide excision margins. Although prophylactic neck dissection is not the rule, it was part of the postoperative treatment in both cases, along with life-long follow-ups to find recurrences at early stages. A high level of suspicion and knowledge regarding its presentation are essential for correct diagnosis and management.

Keywords: Polymorphous low-grade adenocarcinoma, Salivary glands tumors, Palate

INTRODUCTION

Salivary gland tumors make up to 3% of head and neck tumors, of which less than 20% correspond to malignant epithelial tumors. Within this group, polymorphous low-grade adenocarcinoma (PLGA) is infrequent and occurs almost exclusively in minor salivary glands.[1,2]

Although PLGA is a slow-growing tumor, it can erode and infiltrate adjacent bone.[3] Given its low frequency, we will now present 2 clinical cases and a literature review on the subject.

CASE REPORT

Description of 2 clinical cases from the head and neck surgery unit at Hospital Clínico Universidad de Chile (HCUCH), with review of the literature.

Case 1

60-year-old male patient, with a history of non-insulin-requiring type-2 diabetes, arterial hypertension, active smoking with pack-year index of 17, and deep vein thrombosis 2 years ago.

He consults for enlargement of the left hard palate present since 2009. An incisional biopsy was performed originally compatible with monomorphic adenoma of the buccal mucosa. During 2020, there was progressive growth of the mass associated with pain, slight weight loss, bleeding, and ulceration. Due to persistent bleeding and pain, in a dental check-up in 2021 he was referred to HCUCH for another check-up, where a new incisional biopsy was performed, which diagnosed a PLGA.

Positron emission tomography (PET/CT 18F-FDG) was performed and showed a left hypermetabolic vascularized

mass with involvement of the ipsilateral hard and soft palate, measuring 30×20×20 mm, extending to the floor of the ipsilateral nasal cavity, with nonspecific bilateral submandibular lymph nodes, with no evidence of distant dissemination (Figure 1).

In physical examination of the oral cavity, there was a 3 cm, slightly painful, non-friable lesion in the left paramedian of the hard palate with mucosal involvement. Left nostril was permeable, without evidence of increased volume in nasal floor. There were no palpable adenopathies in neck examination.

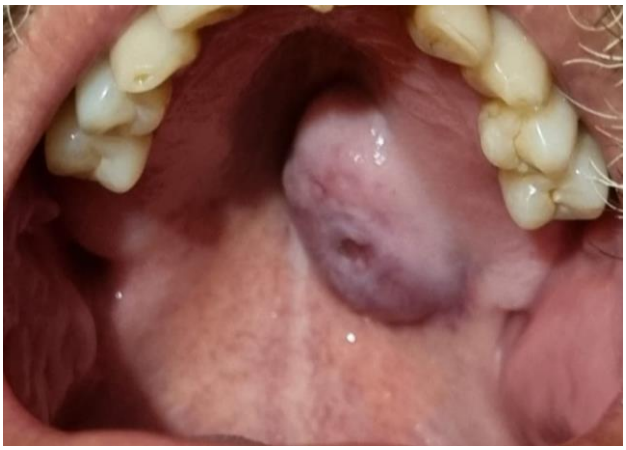

Figure 1: 3 cm palpable left paramedian hard palate lesion.

Computed tomography (CT) showed a solid expansive process of 23×26×16 mm in the left hard palatine with bone remodeling of the medial wall of the ipsilateral maxillary sinus and permeation and partial destruction of the floor of the left nasal cavity. Inflammatory changes in ethmoidal cells and mucosal retention cyst in the right maxillary sinus were also shown, without cervical lymphadenopathies (Figures 2a and b).

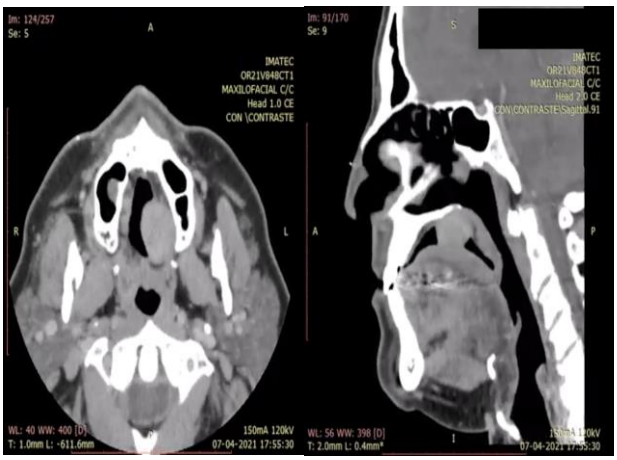

Figure 2: (a) and (b) CT of left palatal tumor with bone remodeling of the medial wall of the ipsilateral maxillary sinus with partial destruction of the left nasal cavity floor.

The patient was admitted to HCUCH for surgical resolution of PLGA, where left maxillectomy was performed with left cervical dissection of levels Ib, II, III and IV, along with a left radial free-flap and placement of 2 osseointegrated implants, first to zygoma and second to piece 11. The procedure was performed without incidents.

The anatomopathological report of the intraoperative biopsy reported development of a poorly delimited epithelial neoplasm with infiltrative borders, arranged in multiple architectural patterns, with the diagnosis of a PLGA measuring 26×22×14 mm with perineural permeation but no vascular permeation. Both superior and posterior margins resulted positive; thus, more tissue was resected, resulting in subsequent negative margins.

During the postoperative period, the patient presented flap congestion, being therefore re-admitted to the ward for re-exploration along with heparinization and permeabilization of the flap. The flap eventually had to be removed due to necrosis, with posterior installation of an obturator plate programmed by the rehabilitation team, achieving adequate phonation and swallowing. The patient evolved with acute urine retention and bilateral pulmonary thromboembolism without hemodynamic compromise, managed with the installation of a foley catheter and anticoagulants, respectively. Patient was discharged 16 days after surgery.

By decision of the oncology committee, adjuvant radiotherapy (RT) was indicated by means of 32 continuous daily sessions of 37 Gray (Gy), initiated in September 2021. Gastrostomy was performed prior to RT. During the course of therapy, he developed radiodermatitis and grade-4 mucositis.

10 months post-RT, the patient is in good general conditions, without recurrence evidence in control PET/CT 18F-FDG. Currently, he is in speech therapy with satisfactory progress in phonation and swallowing, and implementation of new obturator plate due to irritative cough after leakage of food content into the nasal leakage of food content into nasal cavity" ADD: "with satisfactory results. In addition, patient refers pain on cervical mobilization and left omalgia in current kinesiological treatment.

Case 2

44-year-old female patient with a history of hard-palate cancer type PLGA resected in 2001, without bone resection, and closure by second intention. She evolved in good conditions. After 19 years, during 2020, the patient reported an increase of volume in the left hard palate detected in dental control, with expectant management. During February 2021, in the next dental check-up, there was evidence of accelerated growth of the involved region, with local pain, without ulceration. Thus, the patient was referred for histological study of the lesion, consulting in

HCUCH with results that reported the lesion as recurrent PLGA.

Among previous reports, the patient had a definitive biopsy from 2001 which informed a salivary gland tumor morphologically consistent with PLGA, with negative surgical margins. Left jugulodigastric lymph node was also resected, without neoplastic involvement.

A CT scan of the brain, neck and thorax was performed for staging, detailing a mass of 25×43×28 mm in the left hard palate with osteolysis of the left anterior half of the hard palate, extending to the retromolar trigone of the upper jaw and to the base of the ipsilateral pterygoid process. The lesion pushes towards the left maxillary sinus floor, thinning the bone (Figures 3a and b). Nonspecific bilateral cervical lymph nodes are observed, mainly in groups I and II, without categorical malignant characteristics.

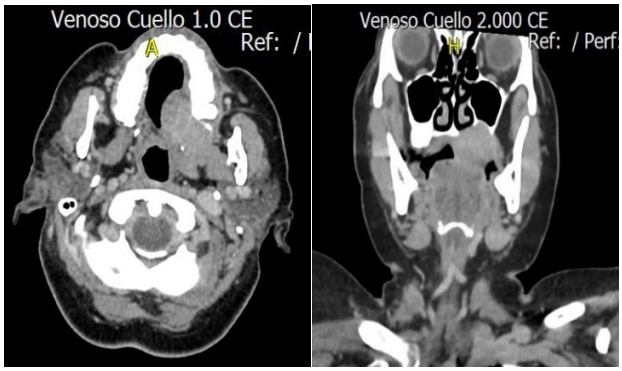

Figure 3: (a) and (b) Left hard palate mass extending to the retromolar trigone of the upper jaw and to the base of the ipsilateral pterygoid process.

Patient was admitted to HCUCH for surgical resolution. Partial maxillectomy was performed with left cervical dissection of levels Ib, II, III, and IV. The palate was reconstructed with a free radial flap of the left forearm. The procedure was performed without incidents.

The anatomopathological report of the initial intraoperative biopsy showed a posterolateral positive margin, thus, an extension of the margins was performed with a subsequent intraoperative biopsy that was reported lesion-free.

During the postoperative period, nasoenteral feeding tube was indicated with poor initial tolerance, presenting episodes of nausea, vomiting, and self-limited diarrhea, resulting in hypokalemia which was investigated and satisfactorily corrected. Given the tolerance improvement, the patient progressed to oral feeding with adequate evolution during the course of the days.

After 8 days of postoperative period, the patient presented dehiscence of the flap and nasal reflux of food content. Flap-plasty was performed, reinforcing the area with sutures with satisfactory results and adequate tolerance to oral feeding, being optimal at discharge, on postoperative day 23.

The patient was presented to the oncologic committee, which indicated 30 fractions of adjuvant RT of 54 Gy in the intervened tissues and 60 Gy in the tumor bed, which was completed developing grade-2 mucositis.

Posterior pathology report showed hard palate mucosa infiltrated by adenocarcinoma, with small ovoid hyperchromatic cells with stromal reaction of desmoplastic aspect. Left partial maxillectomy of 70×50×25 mm showed polymorphous adenocarcinoma of 35×30×20 mm, mild pleomorphic, slightly hyperchromatic ovoid nuclei, with few mitoses and cytoplasm, desmoplastic stroma, positive perineural and intraneural infiltration with negative vascular permeation. Initially posterolateral surgical margins were positive for neoplasia, with posterior extension of margins resulting lesion free. In addition, 24 lymph nodes groups Ib, II, III, and IV were dissected without tumor involvement.

DISCUSSION

Salivary gland tumors make up to 3% of head and neck tumors, of which less than 20% correspond to malignant epithelial tumors. Among these, PLGA is infrequent and occurs almost exclusively in minor salivary glands. It commonly presents in women with a ratio of 2-3:1, between the sixth and eighth decade of life, usually as an asymptomatic mass of long evolution and slow growth in the oral cavity, reaching up to 4 cm.[1,2,4] It is mostly located in the palate (57%), being extremely rare in extraoral location.[5] Given its typical location and indolent clinical manifestations, the main differential diagnoses to consider are pleomorphic adenoma and adenoid cystic carcinoma.[6]

Both reported cases had characteristic clinical presentation: growth of mass. However, the early presentation is striking in case 2, which presented for the first time at 24 years of age, and then recurred 20 years later with accelerated mass growth and pain, which, as mentioned, is not the classic evolution of PLGA.

To date, no risk factors for PLGA have been described. In terms of genes, activating mutations of PRKD1 were recently identified in PLGA which probably constitute oncogenic drivers. This mutation was identified in 72.9% of PLGA and not in other salivary gland tumors.[7]

Its histology is characterized by varied morphology, invasive growth, and uniformity of the nucleus. It typically shows an infiltrative growth pattern with characteristic neurotropism, evidenced in 30% of the cases.[6] The diagnosis is histologic, requiring a sample of the entire lesion. It is recommended, especially in smaller lesions, the use of excisional over incisional biopsy, since the latter may not be representative of the complete lesion and lead to an incorrect diagnosis by showing only a single pattern of the whole lesion.[2,6] For example, in case report 1, the initial incisional biopsy showed a benign tumor.

Immunohistochemical analysis has recently been proposed to distinguish PLGA from other malignant neoplasms, but controversy persists concerning its real utility.[8]

Wide-excision margin surgery is the treatment of choice, exact margins unspecified in literature, commonly including resection of the underlying bone. Prophylactic cervical dissection is not indicated as a rule, although in our reported cases we chose to perform dissection of groups IB, II, III, and IV.[4] In the first case, this was mainly because of the accelerated mass growth in the last year, raising doubts about tumor histology and its aggressiveness. In case 2, prophylactic dissection was also performed due to the presence of somewhat prominent cervical lymph nodes on the ultrasound, mainly in groups I and II, along with the history of tumor recurrence.

The indication of adjuvant radiotherapy is controversial; being a low-grade tumor, its utility could be low. Therefore, its use is reserved for patients with positive or unclear margins, extensive primary tumors, perivascular invasion, or other high-risk characteristics.[9] Perineural invasion is not a significant poor-prognostic factor in PLGA, hence not a sufficient argument on its own in favor of administering radiotherapy if there are negative margins.[4]

In both cases presented, adjuvant radiotherapy was indicated. This was partly due to the atypical presentation of progressive and accelerated growth. In the second case, in addition, there was a history of tumor recurrence and a negative but small margin, given its proximity to the internal carotid artery.

There is currently no evidence available to support the use of chemotherapy or immunotherapy in the treatment of PLGA.[9]

Annual follow-up is recommended[2] for life, some even recommend a stricter follow-up during the first years, because although PLGA usually has a good prognosis and a low probability of distant metastasis, local recurrences are frequent.[8,9]

In case 2, local recurrence of PLGA can be evidenced 19 years after the first surgery, showing the great importance of strict and lifelong follow-up of these patients. PLGA is usually a neoplasm with a good prognosis and slow growth, although it can erode and infiltrate the adjacent bone. Local recurrences are frequent, with low risk of distant metastases, ranging in literature from 0.6% to 7.5%.[8,10]

24% present local recurrences and 6% present cervical metastases, and so far, only one case of death has been reported.[5]

CONCLUSION

PLGA is a rare kind of neoplasm, with slow growth and good prognosis. Its treatment of choice is oncologic surgery with wide excision margins, with the possibility of adding adjuvant radiotherapy in select cases. It should be followed up in the long term to detect eventual recurrences at an early stage.

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