

A Case Report and Literature Review on Polymorphous Low-Grade Adenocarcinoma of the Parotid Gland

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Abstract

Polymorphous low-grade adenocarcinoma (PLGA) poses challenges in diagnosis, both clinically and histologically, owing to its subtle clinical manifestations and diverse microscopic patterns. The aggressive nature observed in minor salivary glands, in contrast to major glands, seems to be histologically linked to the prevalence of the papillary pattern. However, the biological behavior of PLGA in major salivary glands remains uncertain, as evidenced by cases exhibiting recurrences and metastases irrespective of the presence of a papillary pattern.

We report a case of a 56-year-old patient, diagnosed with a PLGA, the computed tomography (CT) of the facial mass objectified a 2 x 1.5 cm multicystic tumoral left parotid mass. The patient underwent an excisional biopsy of the mass, followed by histological examination and immunohistochemical testing, which indicated the presence of a polymorphous low-grade adenocarcinoma (PLGA). The treatment consisted of surgery (left parotidectomy) followed by adjuvant radiotherapy.

Keywords: Polymorphous low-grade, Salivary glands, Parotid.

1. Introduction

The polymorphous low-grade adenocarcinoma (PLGA) is a rare malignant tumor of epithelial origin in the oral cavity, with unknown risk factors. The term LGPA was introduced by Evans and Batsakis, one year after it was initially described by Freedman and Lumerman under the terms 'lobular' or 'canalicular' carcinoma. [1, 2]. The PLGA develops almost exclusively in the accessory salivary glands (ASGs), preferentially localized in the hard and soft palate. Its presence in the major salivary glands is extremely rare. PLGA is a low-grade malignancy tumor, often asymptomatic, characterized by slow and progressive growth. It presents as a mucosa with normal appearance and non-ulcerated. Histologically, PLGA is distinguished by architectural polymorphism [3]. The polymorphous low-grade adenocarcinoma (PLGA) generally has a favorable prognosis, although the recurrence rate is between 17% and 24%. Metastases to lymph nodes can occur in roughly 9% of cases, while metastases at distant sites are reported in less than 1% of cases, generally has a favorable prognosis, although the recurrence

rate is between 17% and 24%. Lymph node metastases can occur in approximately 9% of cases, while distant metastases are reported in less than 1% of cases. [4, 5].

2. Case report

This is a 56-year-old woman, with no significant medical history, who has a left parotid mass, gradually increasing in size over a period of 7 months, without any other associated sign. A CT of the facial massif showed a 2 x 1.5 cm multicystic tumoral mass that did not involve the parapharyngeal space.

The patient underwent an excisional biopsy of the mass. The pathological analysis indicated the existence of a polymorphous low-grade adenocarcinoma (PLGA). Immunohistochemical testing demonstrated strong positivity for cytokeratin. Actin and S-100 protein showed focal positivity, whereas glial fibrillary acidic protein was consistently negative in the neoplastic cells.

The patient underwent total left parotidectomy with left lymph node dissection (levels II, III). The pathological examination revealed the presence of a well-defined nodule measuring 1.5*1 cm, suggestive of polymorphous low-grade adenocarcinoma (PLGA)

Under the microscope, the lesion displayed uniform round to oval cells with mildly hyperchromatic oval nuclei, occasional nucleoli, and minimal mitotic activity. These cells formed various patterns, primarily lobular and papillary, with infiltration into adjacent adipose and subcutaneous tissues. Cystic spaces were lined by squamous epithelium, sometimes producing keratin, while other areas showed scattered cells within hyalinized material resembling basal lamina. No evidence of perineural invasion or vascular permeation was observed in the analyzed sections. Surgical margins were clear, with no lymph node involvement detected. The patient received radiotherapy using the VMAT technique, with Simultaneous-integrated boost on the tumor bed at a dose of 60 Gy (2Gy/fraction), and the ipsilateral lymph node areas at a dose of 54 Gy (1.8Gy/fraction). The treatment was daily in five fractions per week. The treatment passed without incidence with good tolerance.

After a follow-up of 4 years, the clinical examination did not reveal any signs of recurrence in the local or regional areas, nor did it indicate the presence of distant metastases.

3. Discussion

The polymorphous low-grade adenocarcinoma (PLGA) is a rare malignant tumor, representing approximately 7 to 11% of all malignant and benign tumors, and comprising between 19 and 26% of malignant tumors of the accessory salivary glands [6].

A study conducted by Gonzalez Laguna et al. further reinforced this rarity by demonstrating that no cases of PLGA had been identified among 59 malignant tumors of the salivary glands studied [7].

The polymorphous low-grade adenocarcinoma (PLGA) develops almost exclusively in the accessory salivary glands (ASGs). The palate is the most common location, accounting for 65% of cases, primarily involving the hard palate. The lips are affected in 13% of cases, followed by the oral mucosa in 10% of cases, and less commonly, the retromolar region, oral floor, and tongue. The major salivary glands are rarely affected by PLGA, as are the nasal cavities and nasopharynx (0.5 to 1% of cases) [8, 9].

The polymorphous low-grade adenocarcinoma (PLGA) typically presents in adults, with an average age of 59 years, and shows a clear female predominance (sex ratio = 2/1) [10-12].

The polymorphous low-grade adenocarcinoma (PLGA) typically presents as a mass or nodule, ranging in size from 0.5 to 4 cm. It is characterized by its lack of pain, slow growth, and is covered by a mucosa with normal, intact, and non-ulcerated appearance. In some cases, it may adhere to the underlying tissue.

The risk of ulceration remains extremely rare and may result from trauma, such as biting, or be iatrogenic, occurring after a biopsy, for example [12]. At inspection and palpation, the description of the lesion reported in our clinical observation does not differ from what is described in the literature. Medical imaging, whether it be computed tomography (CT) or magnetic resonance imaging (MRI), is essential to specify the locoregional extension, particularly in the maxillary sinuses, nasal cavity, and palatal bone, although the latter is rarely involved [13].

The histological diagnosis of PLGA is based on three main criteria: architectural polymorphism, monomorphic appearance of tumor cells, and infiltrative growth pattern. Architectural polymorphism is manifested by an arrangement of tumor cells in lobules, microcysts containing papillae, cribriform areas, as well as trabecular or tubular structures[10]. It is a delicate diagnosis that poses a real challenge, especially on small biopsies. This complexity is particularly encountered with pleomorphic adenoma (PA) and adenoid cystic carcinoma (ACC), especially for lesions with a large number of cells, a small matrix, and lacking a fibrous capsule. Unlike PLGA, pleomorphic adenoma is not always well circumscribed and is characterized by epithelial, myoepithelial proliferation, as well as a predominantly chondromyxoid stroma [3, 14].

The distinction between the polymorphous low-grade adenocarcinoma (PLGA) and adenoid cystic carcinoma (ACC) is mainly based on cytological appearance. ACC presents with basaloid cells that are not observed in PLGA. A publication by Schwarz et al. emphasizes a great similarity in the clinical-pathological parameters between PLGA and ACC, with a treatment plan that remains practically identical [15].

In some situations, definitive diagnosis can only be established by utilizing immunohistochemistry. The polymorphous low-grade adenocarcinoma shows positivity to immunohistochemical markers such as S-100, cytokeratin CAM 5.2, and vimentin [6, 16]. As for our specimen, the diagnosis was made without resorting to immunohistochemistry. The polymorphous low-grade adenocarcinoma (PLGA) generally has a relatively favorable prognosis, which depends on various factors, including the timing of consultation and the quality of surgical excision. The quality of surgical excision remains a treatment-related prognostic factor, highlighting the importance of early detection and surgical expertise. Salivary gland cancers located in the oral cavity tend to have a better prognosis than those originating in the paranasal sinuses, due to their easier surgical accessibility. However, accessory salivary glands are generally not encapsulated and are often intertwined with muscle or adipose tissue, making it difficult to assess invasiveness. PLGA located outside the palate is described as more aggressive [17].

The most appropriate treatment for low-grade polymorphic adenocarcinoma (LGPA) remains complete surgical resection, with significant safety margins. Lymph node dissection is only recommended if cervical lymphadenopathy is present on clinical examination or imaging and is never performed systematically.

Chemotherapy has little interest as its effectiveness has not been demonstrated in patients with salivary gland cancer, regardless of their stage. As for postoperative radiotherapy, there is no established benefit, although this approach has been practiced by many authors, except for certain limited cases such as lymph node metastases, incomplete resections, and inoperable patients. [18].

Uemaetomari et al. deemed postoperative radiotherapy necessary, but a large retrospective study conducted by Castle et al. showed that 97% of patients did not experience recurrence approximately a decade after their surgery. They recommend a conservative approach and note that adjuvant treatments such as radiotherapy and chemotherapy have no significant impact on improving prognosis [12, 19].

The follow-up for the polymorphous low-grade adenocarcinoma (PLGA) includes quarterly clinical examinations for the first two years, followed by semi-annual follow-up during the third and fourth years, and then annual follow-up for 10 years. Radiological and complementary examinations will be prescribed based on the initial localization and difficulties of clinical surveillance. In the specific case of your patient, who has been undergoing regular follow-up for one year, no recurrence has been detected. Although PLGA may recur in approximately 17% to 24% of cases over an average of 15 years, recurrences often demonstrate greater aggressiveness. Metastases to regional lymph nodes can occur in 9% of cases, and distant metastases are reported in less than 1% of cases. The need for regular follow-up is justified by the high aggressiveness of LGPA in case of recurrence or metastasis, associated with an exceptional risk of transformation into a high-grade neoplasm [20, 21].

4. Conclusion

The polymorphous low-grade adenocarcinoma (PLGA) represents an uncommon malignant neoplasm, relatively recently discovered, primarily developing in the accessory salivary glands. It behaves similarly to benign tumors, characterized by a low degree of malignancy, limited tendency for recurrence and metastasis, as well as mild symptoms, making diagnosis difficult and often delayed. In conclusion, the dentist plays an essential role in screening for oral cavity cancers

5. References

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