Intraosseous polymorphous low-grade adenocarcinoma of mandible: A rare entity

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ABSTRACT

Polymorphous low-grade adenocarcinoma is a rare type of minor salivary gland malignancy. The characteristic features of these tumors are the varied histomorphology and the malignant, albeit indolent behavior. It occurs commonly in the minor salivary glands, with the palate (58.5%) being the most common intra-oral site. Maxillary area (2%), mandibular mucosal area (1.5%) and posterior trigone region (0.5%) are the least affected areas. An occasional case has been reported arising from an intraosseous location i.e. the maxilla, and only two cases have been reported in the English literature originating from the mandible. One such very rare case of polymorphous low-grade adenocarcinoma of the mandible, which radiographically has a soap bubble appearance, is reported here.

Key Words: Adenocarcinoma, adenoid cystic, mandible, salivary gland neoplasms

INTRODUCTION

The term polymorphous low-grade adenocarcinoma (PLGA) was first used in 1984 to describe a series of minor salivary gland tumors with a great diversity of growth patterns in spite of their cytologic uniformity. The salient features of these tumors are the varied histomorphology and the malignant, albeit indolent, behavior. Because of the resemblance to architectural arrangement of lobular carcinoma of breast, these tumors were referred as lobular carcinoma.[1]

PLGA is now a well-recognized tumor in minor salivary glands and, after mucoepidermoid carcinoma this is the second most common type of malignant neoplasm at these sites. Common sites being palate (58.5%) followed by maxillary area (2%), mandibular mucosal area (1.5%), and posterior trigone region (0.5%) being the least affected areas.[2] It represents 11% of all tumors and 26% of malignant tumors. Only three cases of intraosseous PLGA’s are reported in the English literature, one in the maxilla[3] and two in the mandible.[4,5]

PLGA with its morphological diversity and histologic overlap with other salivary glands leads to markedly different treatment regimens and prognosis. Hence, some investigators have advocated complete excisional biopsy of a suspected PLGA to achieve the exact diagnosis.[6] The earlier cases reported have been managed surgically by partial mandibulectomy and surgical resection.[4,5]

This article describes a solitary exceptional case of PLGA that radiographically presented as a soap bubble appearance in the mandible which was treated by hemimandibulectomy with radical neck dissection.

CASE REPORT

A male patient aged 52 years reported with a complaint of swelling in the right lower posterior region of 7 years duration and also complained of difficulty in chewing and speech for 3 months and occasional blood discharge from the mass.
Past dental history revealed that the patient had sustained a fracture of his lower right molar while trying to crack an arecanut, following which a local practitioner extracted the tooth after symptomatic treatment. Subsequently he had noted a swelling in the extracted area, which progressively increased and attained the present size. Patient was habituated to smoking bidi (beedis or biris, is a leaf-rolled cigarette made of coarse, uncured tobacco, tied with a string at one end) for a period of 5 to 6 years, but had discontinued from the past 5 years. Medical history was non-contributory.

Extra oral examination showed a diffuse solitary swelling on the right side of the face with no obvious surface changes [Figure 1]. On palpation, swelling was non-tender, firm in consistency and had well-defined borders. The lesion measured about $6 \times 4$ cm, extended superiorly till zygomatic arch, inferiorty till inferior border of mandible, anteriorly till right commissure, and posteriorly till anterior border of ramus. Right submandibular nodes and level IV nodes were palpable, which were firm and mobile.

Intra oral examination presents a solitary, well-defined swelling of right posterior mandible, extending both buccally and lingually and measuring about 6 cm anteroposteriorly and 4 cm mediolaterally. It extended anteriorly up to 46, posteriorly up to retromolar trigone and anterior pillar of fauces. The growth prevented proper closure of mouth. The surface over the lesion was pink to red in color and showed indentations of upper molars. It was firm in consistency, non-tender, fixed to underlying tissues.

Orthopantamograph exposed a solitary multilocular radiolucency containing coarse and fine trabeculation within, giving a typical ‘soap bubble’ appearance [Figure 2]. It involved the body and ramus of the right side of mandible and extended anteroposteriorly from 45 to ramus with an intact lower border of mandible. Lesion measured approximately $8 \times 10$ cm in size with well-defined borders. 47, 48 were missing and 46 showed resorption of both roots.

Blood examination revealed an increased ESR (58 mm in one hour), and alkaline phosphatase (245 IU/L) levels and a decrease in fasting blood sugar (40 mg) level, which could be due to patient’s poor oral intake as he was unable to open his mouth due to pain.

In view of the above findings, a provisional diagnosis of ameloblastoma or odontogenic myxoma or central giant cell granuloma was made.

An incisional biopsy specimen histopathologically revealed isomorphic cuboidal epithelial cells with scanty cytoplasm, ovoid or round, vesicular hyperchromatic nuclei arranged in solid, ductal, tubular, papillary and cribriform patterns. The stroma showed mucoid/hyaline/fibrovascular areas with scattered blood vessels. Lesional tissue was well separated from the overlying epithelium of varying thickness by a fibrous lamina propria. These features were suggestive of PLGA.

Subsequently, hemimandibulectomy with radical neck dissection was performed. Grossly it showed a smooth lobulated well circumscribed grayish to white colored lesional mass measuring about $6 \times 5$ cm, extending from distal of 46 and involving the entire ramus falling short of coronoid process. The lingual view shows the clear separation of the submandibular salivary gland from the lesion [Figure 3]. On sectioning the gross specimen, considerable destruction of bone was seen. Cut surface revealed

**Figure 1:** Extraoral image showing diffuse solitary swelling on the right side of the face with no obvious surface changes

**Figure 2:** Orthopantamograph showing multilocular radiolucency containing coarse and fine trabeculation within, giving a typical ‘soap bubble’ appearance
brownish black areas intermixed with grayish white firm areas, with frank blood oozing out [Figure 4]. The inferior alveolar nerve was destroyed in that portion. Lymph node from all levels (I to V) dissected from the RND specimen and sections from various aspects of the tumor proper were studied. Histopathologically, the lesional tissue was partly well circumscribed in areas and was in close association with minor salivary glands at the periphery [Figure 5a]. The overall features of cells and stroma were same as that seen in the incisional biopsy specimen with predominantly papillary cystic pattern. The cystic and ductal spaces contained a basophilic fibrillary/homogenous material which appeared mucinous [Figure 5b]. The cells were monomorphic cuboidal/columnar with indiscernible eosinophilic/amphophilic cytoplasm with ovoid or round and vesicular nuclei containing finely dispersed/stippled chromatin [Figure 5c]. Focal areas showed clear cells and periphery showed single file or Indian file patterns. Large areas of hemorrhage, few areas of necrosis and chronic inflammatory cells were also observed along with areas showing perineural invasion by the tumor cells within the stroma [Figure 5d] and had no evidence of tumor infiltration in the nodes submitted from level I to level V. The diagnosis of PLGA was confirmed.

DISCUSSION

The term PLGA refers to a broad spectrum of architectural patterns, characterized by proliferation of uniform type of cells with a female predominance (67%) in the age group between 6th and 8th decade. Patients usually complain of a painless mass or swelling with increase in size that is occasionally associated with bleeding or discomfort.

Though PLGA affects minor salivary glands, rare examples have also been reported in the major glands, either arising de novo or as the malignant component of a carcinoma ex pleomorphic adenoma. Palate is the most common site (58.5%) followed by buccal mucosa (14%), lip (13%), retromolar area (1.5%) and posterior trigone region (0.5%). Intraosseous PLGA'S are rare and only one case involving the maxilla in a 58-year-old female patient where it presented as a cystic lesion has been reported and two cases in the mandible. The first case in the mandible was reported in a 40-year-old female patient where it presented as a cystic lesion has been reported and two cases in the mandible. The second case was a recurrent case in a 50-year-old female wherein the condition had a...
history of 15 years that presented as a small rounded swelling in the anterior region of the mandible which gradually increased in size for which it was excised after few years, but it had recurred again in the same region extending from the left mandibular lateral incisor to the right mandibular second premolar. However, this is only the first intraosseous PLGA in a male patient manifested in the mandible as a multilocular radiolucrency giving a typical soap bubble appearance on OPG. It is the third case in the mandible and second case in the posterior region of the mandible.

The purported origin of intraosseous salivary gland tumors is from ectopic mucous glands of the retromolar area, entrapment within the bone of glandular remnants during the development of the submandibular gland or more convincingly from neoplastic transformation of the mucous cells constituting the epithelial lining of dentigerous cysts or odontogenic epithelium. In our case it could have arisen from the intraoral ectopic minor salivary glands destroying the mandible. This possibility seemed likely since the patient gave a long history of slow and painless growth.

Previous series of PLGA cases indicated 9-33% of local recurrence with regional lymph node metastasis in 6-35%. Metastasis to the paraesophageal lymph nodes, lungs, orbit and skin have been reported but overall distant metastasis develop in less than 1% of cases. The present case did not show any lymph node metastasis.

Histopathologically, this tumor exhibits variety of different growth factors such as tubular, solid, fascicular, cribriform, cystic, ductular, trabecular, papillary, papillary cystic with frequent combinations and transitions from one to another within the same tumor or from tumor to tumor. The cells are characteristically cuboidal to columnar, small to medium sized, eosinophilic, and with a low rate of mitosis and atypia. Cells have a uniform ovoid to spindle shaped nuclei with chromatin varying from vesicular to stippled, but basophilic nuclei can also be seen. Stroma exhibits mucinization and hyalinization. Necrosis is a rare event but most tumors show peripheral infiltration in a single file (Indian file) pattern at the periphery of the tumor. Perineural invasion and a targetoid disposition of the neoplastic cells around nerves are characteristic. The present case was locally aggressive with perineural invasion showing destruction of nerve bundles.

Recently some morphological characteristics have been suggested that may determine those PLGA that may not be low grade and neoplasms with a papillary cystic pattern fall into this category. The papillary variant is more likely to recur, to metastasize to regional and distant sites, and to result in death. According to Evans and Luna, the presence of “more than focal” papillary growth pattern is associated with an increased risk of cervical lymph node metastases, but not with local recurrence or distant metastases. The amount of papillary growth that is associated with this increased risk was not made clear. But McHugh et al. in their reports mention that when 10% or more papillary growth is identified, acknowledging this as an arbitrary cutoff.

A case reported in the palate in a 14-years-old female patient which recurred twice in a span of two years behaved aggressively and ultimately metastasized to cervical lymph nodes. An altered histological picture, with a papillary cystic pattern and necrosis becoming progressively more prominent, accompanied this. The present case, although being predominantly papillary cystic, did not present aggressively.

Despite its bland morphologic appearance, there are also a few reported cases where the tumor has undergone differentiation to a high-grade carcinoma, and often after a considerable period of years since the diagnosis. The morphological features of polymorphous low-grade adenocarcinoma are generally distinctive, but diagnostic difficulties can arise with some other primary salivary neoplasms, in particular adenoid cystic carcinoma. Low-power microscopy shows that both are diffusely invasive, and both may display solid and cribriform patterns. However, fascicular areas and micropapillary structures are confined to polymorphous low-grade adenocarcinoma.

Cells of adenoid cystic carcinoma are generally more angular, basoloid, and lack the eosinophilic cytoplasm and vesicular nuclei a typical of PLGA. Separating these two neoplasms is far from just an interesting academic exercise, as even the most well differentiated adenoid cystic carcinomas (tubulocribriform pattern without solid areas) have only a 39% survival rate at 15 years. In contrast, recurrence, metastasis and death due to tumor are unusual in PLGA.

Other tumors which may be confused with PLGA include pleomorphic adenoma and, perhaps, salivary duct adenocarcinoma and epithelial-myoepithelial carcinoma. Pleomorphic adenoma can show a variety of histological patterns, but it is well circumscribed
and lacks an invasive edge. However, a polymorphous pattern may be seen in a carcinoma arising from a pleomorphic adenoma and, thus, the two tumors may co-exist. Salivary duct adenocarcinoma is also invasive, but it arises exclusively in the major glands and, histologically, it closely resembles ductal carcinoma of the breast with areas of comedo necrosis. Double-layer ducts characterize epithelial-myoepithelial carcinoma, typically with clear cells in the outer layer.[13] It usually arises in the major glands, but has been described intra-orally. Areas of polymorphous low-grade adenocarcinoma can display this growth pattern, but these only represent a minor component in an otherwise variable tumor.[12]

Owing to the possibility of local and regional recurrence, an adequate follow-up period of at least 5 years is vital after initial surgical treatment. Only with no recurrence noted, can final reconstruction with a microvascular free graft and a fixed or detachable prosthetic reconstruction with or without implant placement be contemplated.[16]

Creane et al. (1996) suggests that therapeutic neck dissection be reserved for clinically and radiographically positive cervical lymph nodes and recommends radiotherapy after surgery only when unclear margins or perineural or perivascular invasion is present, with cervical lymph node involvement.[17]

CONCLUSION

Intraosseous presentation of this tumor is very rare. The prognosis of polymorphous low-grade adenocarcinoma is good, with a recurrence rate of approximately 25% and only one case is presented intraosseously in the maxilla and only two cases in the mandible. Thus, our case will be the third reported case of PLGA of mandible and first intraosseous PLGA in a male patient. It is also important to note by the radiologist and oral surgeon that low-grade salivary gland tumors can also present itself as a soap bubble appearance intraosseously which can be misdiagnosed as odontogenic tumor or central giant cell granuloma.

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