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Case Report

Intraosseous polymorphous adenocarcinoma of mandible

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ABSTRACT

Polymorphous Adenocarcinoma (PAC) is a type of salivary gland tumor commonly arising in the minor salivary glands with palate being the most frequent site of origin. PACs harbor recurrent PRKD1 E710D hotspot mutations in >70% of cases. It has propensity of malignant transformation along with locoregional or distant metastasis. However, the latter is very rare entity. Often challenging for both the pathologist and surgeon is the histologic difference between other conditions like pleomorphic adenoma, adenoid cystic carcinomas and adenocarcinoma not otherwise specified. Interestingly, very rare sites of occurrence may herald the rarity, therefore the intraosseous origin in the maxilla and the mandible are seldom encountered. One such very rare case of PAC of the mandible with extensive destruction of hemimandible and the areas in the vicinity of the tumour with nodal and distant bony metastasis described here.

Keywords: Salivary glands, Malignant disease, Mandible

INTRODUCTION

The original terminology of polymorphous low-grade adenocarcinoma (PLGA) attributed to Evans and Batsakis in 1984, has witnessed change in nomenclature due to varied histomorphology and noted malignant transformation.[1] Currently the term polymorphous adenocarcinoma (PAC) is mostly used for this. The traditional belief of it originating in the minor salivary glands exclusively has been challenged by clinical reports and now been reported in the breast, paranasal sinuses, orbit, lungs, the pelvic structures and skin as well.[2-6] The rarity of an uneventful malignant transformation predisposes the condition for loco regional perineurial and perivascular invasion potential. Distant nodal metastasis is very rare.[7] Mandibular polymorphous adenocarcinoma is very rare. There were only one case of maxillary and three cases of mandibular polymorphous adenocarcinoma reported in English literature.[8-11] It is reported as the second most common malignancy of the minor salivary gland following mucoepidermoid carcinoma.[12] As per the retrospective study by Bradley, the incidence for benign tumours alone ranged from 6.2 to 7.2, and for malignant neoplasms it ranged from 0.83 to 1.38/ lakh population.[13] The diagnostic dilemma of polymorphous adenocarcinoma is further met with a challenge of mandatory immunohistochemistry analysis in an effort to distinguish it from pleomorphic adenoma and adenocystic carcinoma. Often challenging for the surgeon is the mapping of initial lesion, the provision of biopsy as well as excision from such sites in the face keep in consideration the aesthetic reconstruction. These perspectives are brought about in this presentation.

CASE REPORT

A 59-year-old male presented with a diffuse, ill-defined swelling at the right angle of jaw for 6 months. Mouth

opening was less than 3 finger breadths. Intraoral examination showed missing right lower second and third molar and bilateral 2nd molar in the upper jaw, with normal alveolar socket area. There was a diffuse mucosal swelling in the region of right retro molar region and associated bone of the angle of mandible, signifying an intra-osseous lesion. Orthopantamograph (Figure1) reveals radiolucent lesion with ill-defined sclerotic borders extending from ramus till the coronoid process of right hemimandible.

Figure 1: Radiolucent lesion with ill-defined sclerotic borders extending from ramus till the coronoid process of right hemimandible.

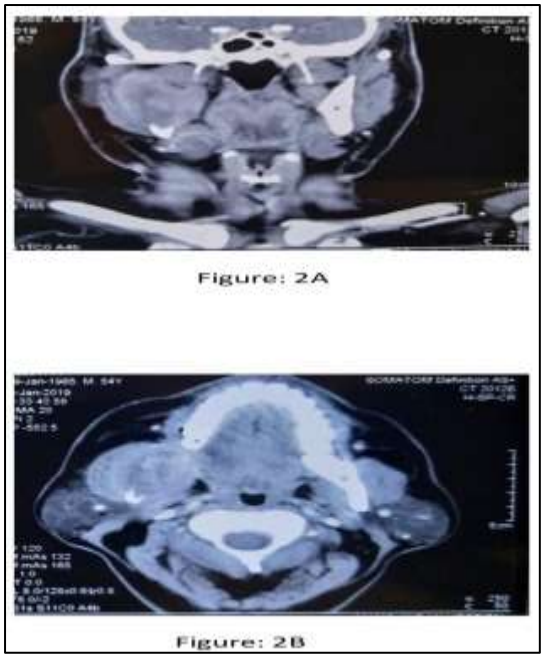

Figure 2: (A, B) CECT oral cavity and neck revealed mass lesion centred on the right ramus of mandible of size around 5.5×3.5×4.5 cm with associated bony destruction. Partial destruction of the right coronoid process was also seen.

CECT oral cavity and neck (Figure 2A, 2B) revealed mass lesion centred on the right ramus of mandible of size around 5.5×3.5×4.5 cm with associated bony destruction. Partial destruction of the right coronoid process was also seen. Right massetter and medial pterygoid muscle were bulky. Incisional biopsy revealed isomorphic cuboidal epithelial cells with scanty cytoplasm, ovoid or round, vesicular hyperchromatic nuclei arranged in solid, ductal, tubular, papillary and cribriform patterns suggestive of pleomorphism.

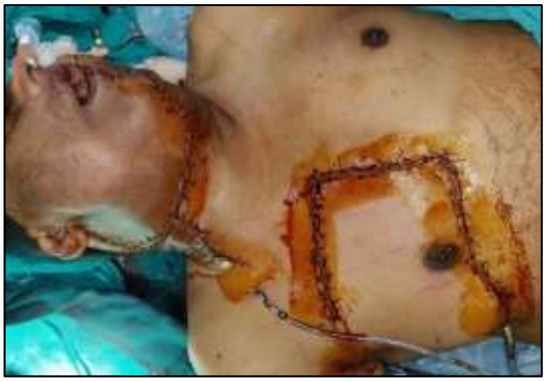

Figure 3: Intraoperative image showing reconstruction using PMMC flap.

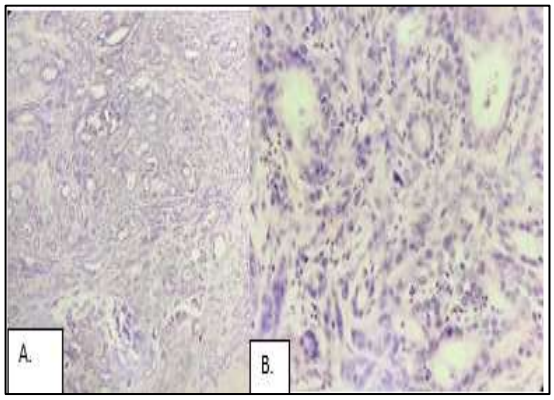

Figure 4: (A) Tumor composed of monotonous looking cells arranged in trabeculae, tubular and reticular pattern. The nucleus is pale with clearing of chromatin. (B) High magnification view of Fig 3A (HE x 200).

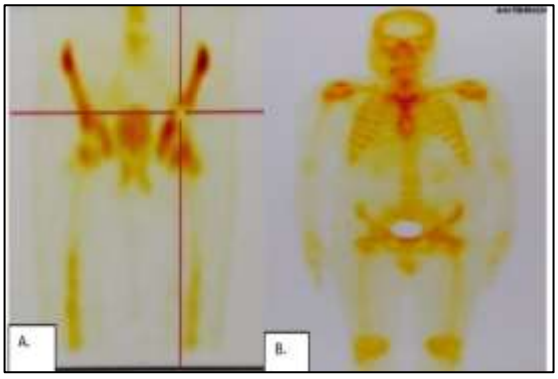

Figure 5: Bone scan showing metastatic deposits in left acetabulum, neck of both femora and photon deficient areas suggestive of lytic lesion involving sternum, L2 vertebra and left iliac bone.

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 PAC. Subsequently, patient underwent right hemimandibulectomy with right parotidectomy and right modified radical neck dissection) followed by pectoralis major myocutaneous flap (PMMC) repair (Figure 3).

Grossly specimen showed a soft tissue mass measuring 6×6×3cm present along the angle of mandible and infiltrating through the underlying bone. Histopathology of gross specimen showed features of perineural invasion with few areas of mitosis and focal areas of necrosis were noted. Specimen of sternocleidomastoid, parotid, superficial and deep lobe, submandibular gland was free of tumor. Tumor deposit was found in one of the level 2 lymph nodes dissected. Immunohistochemical markers showed positivity for EMA (Epithelial membrane antigen) and negative for S 100 and CD 68. The diagnosis of PAC was confirmed. At the tumor periphery, cells were arranged in a linear, single-cell arrangement resembling "Indian file" or "Beads on a string" pattern of infiltration (Figure 4A, 4B). Post-surgery patient was doing well but after two weeks he complained of backache and bilateral lower limb pain. On full body bone scan there was metastatic deposits in left acetabulum, neck of both femora and photon deficient areas suggestive of lytic lesion involving sternum, L2 vertebra and left iliac bone most likely metastasis (Figure 5A, 5B). Confirmation of bony metastasis was performed by bone biopsy and subsequent chemo-radiotherapy was started.

Investigations

Orthopantamograph (Figure1) reveals radiolucent lesion with ill-defined sclerotic borders extending from ramus till the coronoid process of right hemimandible. CECT oral cavity and neck (Figure 2A, 2B) revealed mass lesion centred on the right ramus of mandible of size around 5.5×3.5×4.5 cm with associated bony destruction. Partial destruction of the right coronoid process was also seen. Right massetter and medial pterygoid muscle were bulky. Incisional biopsy revealed isomorphic cuboidal epithelial cells with scanty cytoplasm, ovoid or round, vesicular hyperchromatic nuclei arranged in solid, ductal, tubular, papillary and cribriform patterns suggestive of pleomorphism. 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 PAC. Subsequently, patient underwent right hemimandibulectomy with right parotidectomy and right modified radical neck dissection) followed by pectoralis major myocutaneous flap (PMMC) repair.

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Treatment

Patient underwent right hemimandibulectomy with right parotidectomy and right modified radical neck dissection) followed by pectoralis major myocutaneous flap (PMMC) repair.

Outcome and follow up

Post-surgery patient was doing well but after two weeks he complained of backache and bilateral lower limb pain. On full body bone scan there was metastatic deposits in left acetabulum, neck of both femora and photon deficient areas suggestive of lytic lesion involving sternum, L2 vertebra and left iliac bone most likely metastasis (Figure 4A, 4B, 4C). Confirmation of bony metastasis was performed by bone biopsy and subsequent chemo-radiotherapy was started.

DISCUSSION

PAC is a rare entity, especially when it presents within the bone. The proposed common sites are palate (58.5%) followed by buccal mucosa (14%), lip (13%), retromolar area (1.5%) and posterior trigone region (0.5%). Intraosseous PAC is rare and only one case involving maxilla and 3 cases in mandible were reported. This is the fourth case in the mandible and third case in the posterior region of the mandible to be reported as per available literature. 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 submandibular gland or more convincingly from neoplastic transformation of mucous cells constituting the epithelial lining of dentigerous cyst or odontogenic epithelium.[14] The previous series of PAC cases indicates there was 9-33% of local recurrence with regional lymph node metastasis in 6-35% cases. Metastasis to the para-oesophageal lymph nodes, lungs, orbit and skin have been reported but overall distant metastasis develops in less than 1% of cases.[4,6] The present case manifested with nodal deposits and metastasis to bones of sternum, lower vertebra, iliac bones and femur. Histological diagnosis of PAC is very challenging and exhibits a 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. Necrosis is a rare event but most tumor 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. The papillary variant is more likely to recur, metastasizes to regional and distant sites. According to Evans and Luna, the presence of more than focal extent of papillary growth pattern is associated with an increased risk of cervical lymph node metastases, but not with local recurrence or distant metastases.[15] Owing to the possibility of local and regional recurrence, an adequate follow up period of at least 5 years is vital after initial surgical management. The morphological features of PAC are generally distinctive, but diagnostic difficulties can arise with some other primary salivary neoplasms, in particular adenoid cystic carcinoma, salivary duct adenocarcinoma and epithelial-myoepithelial carcinoma. As per Arau´jo et al in PAC, the majority of the tumor cells were positive for vimentin and CK7. CKs 8 and 18 were positive in almost all lobular PAC.[16] Although, other studies have shown positivity to CEA, S-100 protein, BCL-2 and anti-GFAP, vimentin and CK 7 in all the tumor cells is enough to support the diagnosis of PAC. WHO in 2017 classified PAC into "classical variant" and "Cribriform adenocarcinoma of minor salivary glands", the differences amongst the two are in the site distribution, higher regional aggressiveness and partly different genetic alterations. PAC is defined as "a malignant epithelial tumour characterized by cytological uniformity, morphological diversity, and an infiltrative growth pattern.[17]

However, as per study by Sebastiao et al PKRD 1 mutation present in more than 70% of PAC.[18] Creane et al suggested that therapeutic neck dissection should 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.[19] The rate of conversion of PAC to high grade variant is very rare. The insidious growth and asymptomatic state of the disease made the patient underestimate the potential fatality that may be associated with the tumor in the long run. The principal concern of the patient at presentation was an aesthetic and functional limitation imposed on the lower lip by the tumor. Although known to have a good prognosis, when adequately followed, the incidence of local recurrence with PLGA may be as high as 33% and distant metastasis of 7.5%.[19]

CONCLUSION

Intraosseous Polymorphous low-grade adenocarcinoma (PLGA) is a very rare tumor with minimal chance of nodal metastasis. Distance metastasis to bone is not reported anywhere in the literature. Treatment modality of choice is surgical excision followed by radiochemotherapy. Distant metastasis particularly to long bone should be looked for before going to any definitive treatment.

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