CASE REPORT

Papillary cystadenocarcinoma of the hard palate

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SUMMARY

Papillary cystadenocarcinoma (PCC) is an uncommon malignant tumour of the salivary gland, sometimes involving the minor salivary gland. Previously this entity was classified as an atypical type of adenocarcinoma, malignant papillary cystadenoma, low-grade papillary adenocarcinoma or mucus producing adenopapillary carcinoma. PCC is a glandular tumour with an indolent biological behaviour characterised by cysts and papillary endophytic projections. We report two cases of PCC involving the minor salivary gland of the hard palate. Both the patients presented with a swelling in the palate with difficulty in chewing. MRI revealed an extensively destructive lesion involving hard palate, alveolar ridge and maxillary antrum. Clinical and radiological features suggested the malignant nature of the lesion. Histopathology of incisional biopsy revealed tumour proliferation in a multicystic pattern, with extensive papillary proliferation. Diverse and cellular cytomorphology, and cellular and nuclear pleomorphism with few mitotic figures were the prominent features. Both the lesions were confirmed as PCC.

BACKGROUND

Intraoral minor salivary gland tumours constitute an important area in the field of oral pathology. Although uncommon, these tumours are by no means rare. They account for 9–23% of all salivary gland tumours in major series.¹ Papillary cystadenocarcinoma (PCC) of the salivary gland is an extremely rare malignant tumour described by WHO in 1991 (International Classification of Diseases (ICD) code 8440/3 version 10).^{2–3} Until then, this tumour was classified as an atypical type of adenocarcinoma or was also called malignant papillary cystadenoma, low-grade papillary adenocarcinoma or mucus producing adenopapillary carcinoma.^{3–5}

Cystadenocarcinoma of the salivary gland represents a distinct group of epithelial malignancy characterised by diverse cytomorphological features with a predominant cystic and invasive growth pattern. The presence of nuclear pleomorphism, mitosis and an infiltrative growth pattern confirm the malignant nature of the lesion.^{3–4}

The present article reports two cases of PCC (who did not have any family history) involving the hard palate with special emphasis on the histomorphological features and differential diagnosis.

CASE PRESENTATION

Case 1 was a 70-year-old female patient who had a swelling on the right side of the face and upper jaw with difficulty in chewing for 6 months. Extraoral examination revealed a facial asymmetry in the

middle third of the face on the right side without any palpable regional lymphadenopathy. Intraorally, a large, well-circumscribed exophytic lesion of size 6×5 cm was noticed involving the right alveolar ridge, extending to the posterior part of the hard palate, and crossing the midline. The lesion was more extensive on the palatal aspect. Anteroposteriorly it was involving alveolar ridge from 14 region to maxillary tuberosity on the same side. Teeth 16, 17 and 18 were missing and the area was entirely occupied by soft tissue growth, which showed occlusal indentation of mandibular molars. The lesion was almost smooth and convex surfaced on the palatal aspect; while smooth but with an uneven surface buccally. The posterior-most area of the lesion on the alveolar ridge appeared to be ulceroproliferative and tended to bleed on the slightest provocation (figure 1).

The present case 2 was a 38-year-old female patient, who reported with swelling on the left side of the face and upper jaw with difficulty in chewing for 4 months. An extraoral examination revealed mild facial asymmetry on the left side of the middle third of the face. There was no palpable regional lymphadenopathy. Intraoral examination revealed a large, well-circumscribed, exophytic growth of size 5×4 cm. The lesion was more extensive on the palatal aspect than in the vestibular area and was smooth surfaced, convex and slightly lobulated. Anteroposteriorly lesion was involving alveolar ridge from 25 region until maxillary tuberosity on the same side, while mesiodistally it involved the buccal vestibule, alveolar ridge and hard palate until the midline. Teeth 25, 26, 27 and 28 were missing and the area was entirely occupied by soft tissue growth (figure 2). On palpation, the lesion was firm and mildly tender.

Figure 1 Intraoral examination of case 1 revealed an exophytic lesion involving the alveolar ridge and hard palate on the right side.

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Figure 2 Intraoral examination of case 2 revealed a large, firm, exophytic mass involving the buccal vestibule, alveolar ridge and hard palate on the left side.

General, systemic and hard tissue examination of dental structures of both patients was within normal limits.

MRI of case 1 revealed a large soft tissue mass destroying the alveolar ridge and floor of the right maxillary antrum. The medial wall of the maxillary antrum appeared to be intact; however the lateral wall was disrupted. Apical root resorption was noticed with teeth 14 and 15 (figure 3). Water's view of case 2 revealed large radio-opacity obstructing the maxillary

Figure 3 MRI of case 1 revealed a soft tissue mass involving the hard palate, alveolar ridge and extending to the right maxillary antrum destroying the floor and lateral wall.

Figure 4 Water's view of case 2 showing a large radio-opaque lesion involving the left maxillary antrum.

antrum on the left side (figure 4). CT scan and MRI helped us to rule out metastatic foci elsewhere in the body.

Fine needle aspiration cytology (FNAC) from the lesion in both the cases displayed tumour cells with papillary fragments and sheets in the mucoid background. The tumour cells exhibited cellular atypia in the form of cellular and nuclear pleomorphism, altered nuclear and cytoplasmic ratio and few mitotic figures (figure 5). Cytological features suggested the diagnosis of malignant salivary gland lesion.

Gross examination revealed there was a well-encapsulated, lobular soft tissue mass measuring approximately 5×4×3 cm (figure 6A) and the cut section appeared whitish brown, irregular, soft to firm in consistency, approximately 2×2×1.5 cm,

Figure 5 Cytological smear revealed atypical tumour cells in papillary fragments and sheets in a mucoid background (H&E stain, ×720 magnification).

Figure 6 (A) Gross specimen showing well encapsulated, lobular soft tissue. (B) Cut section showing whitish brown, irregular, soft tissue with mixed solid and cystic areas.

partly solid and partly cystic with cystic areas containing a small amount of mucinous fluid (figure 6B).

Histopathological examination of the tissue exhibited tumour proliferation, intermixed with cystic areas of variable sizes. Tumour tissues showed extensive papillary projections extending into the cystic lumen (figure 7). The papillary projections were composed of one or two layers of cuboidal or columnar epithelial cells. Some of the cells were characterised by nuclear atypia, such as hyperchromatism, increased mitotic figures with few prominent nucleoli. The supportive connective tissue stroma displayed variable presentation, which was sparse in places and hyalinised in other areas. Moderate, predominantly mononuclear inflammatory infiltrate was also evident (figure 8). Periodic acid-Schiff (PAS) staining revealed some PAS-positive

Figure 7 Photomicrograph showing papillary projections (P) lined by single or double row of atypical cuboidal to columnar epithelial cells (C) (H&E stain, ×720 magnification).

Figure 8 Photomicrograph showing periodic acid-Schiff stain (PAS) positive mucous staining (×160 magnification).

tumour cells and secretory pools (figure 9). Histopathological features strongly suggested the diagnosis of PCC.

INVESTIGATIONS

The following investigations were performed

- ▶ Orthopantomograph (OPG)
- ▶ Water's view
- ▶ MRI
- ▶ CT scan
- ▶ Routine haemogram
- ▶ FNAC
- ▶ Incisional biopsy

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes cystadenoma, polymorphous low-grade adenocarcinoma (PLGA), papillary-cystic variant of acinic cell carcinoma, salivary duct carcinoma, adenoid cystic carcinoma (ACC) and metastatic carcinoma showing papillary structures.

TREATMENT

Wide surgical excision was carried out. Postoperative radiotherapy was not performed since there was no regional metastasis.

Figure 9 Photomicrograph showing periodic acid-Schiff stain (PAS) positive mucous staining (×160 magnification).

OUTCOME AND FOLLOW-UP

Periodic follow-up initially every 3 months for 1 year revealed prognosis to be excellent with no recurrence. Later on the patient was followed every 6 months for another 1 year, which revealed no recurrence.

DISCUSSION

The WHO in 1991 described PCC as an extremely rare malignant tumour of the salivary gland (ICD code 8440/3 version 10).^{2 6–8} It represents distinct group of epithelial malignancies, characterised by diverse cytomorphological features and a predominant cystic and invasive growth pattern. Malignancy is confirmed by nuclear pleomorphism, mitosis and infiltrative growth pattern.^{4 9}

Salivary gland tumours account for about 3% of all head and neck neoplasms, most of which show an epithelial origin. About 90% of these neoplasms are located in the major salivary glands and 10% in the minor salivary glands.¹⁰ According to the Armed Forces Institute of Pathology, 65% PCCs originated in the major salivary glands and 35% in the minor salivary glands of which only 2% developed in the hard palate.^{7 11} Cystadenocarcinoma of the minor salivary glands involves the lip, buccal mucosa, palate, tongue, retromolar area and floor of the mouth in descending order of frequency.² The present article also describes two cases of PCC of minor salivary gland origin located in the hard palate. To our knowledge very few such cases have been previously reported. The unusual location of the present cases arising from the minor salivary glands of the hard palate makes them more interesting. Furthermore, a few of the more interesting findings noted in the present cases were the large size of the tumours (approximately 6×5 cm and 5×4 cm, respectively), the short progression time of only 4–6 months and the ulceration. To our knowledge these features have been reported by very few previous investigators.

MRI of case 1 and CT scan of case 2 revealed a destructive lesion. Koc *et al*³ suggested that imaging is very important for confirming the presence of a mass, determining its relationship with the salivary gland and adjacent structures, determining its extent of infiltration, and ascertaining whether it is solid, necrotic or cystic. Indeed, a few authors have suggested that many times they may be non-specific (Grunstein *et al*, 2006).¹²

Primary PCC of the thyroid, ovary or prostate are not rare. Distant metastasis although rare can affect the lungs, bone, breast, kidney, prostate, colon, cavernous sinus and brain. Almost 40% of carcinomas of ovary are found to be PCC.^{13 14} Metastasis to the oral cavity is a rare event and accounts for 0.1% of all malignancies of the oral cavity. Primary tumours of the lung, breast, kidney, prostate, oesophagus and colon can metastasise to the gingiva, tongue, lips, buccal and palatal mucosa and mandible, etc.¹⁵ The most common site for metastasis to the oral cavity is the gingiva (55%) followed by the tongue (30%). The gingiva has a rich capillary network. Chronically swollen gums with rich neovascularisation can more easily attract the metastatic cells as compared to other sites and thus are easily affected. Oral metastasis is usually evidence of widespread disease and poor prognosis.¹⁶ The CT scan and MRI in the present case helped us to rule out metastatic foci elsewhere in the body.

FNAC of both cases revealed a highly cellular smear and a mucoid background with mild dysplasia. These findings were very much similar to those of Aloudah *et al*.⁶

Histopathology of the present cases displayed features very similar to those described in the literature, such as cystic spaces,

papillary projections, spaces lined by cuboidal to columnar epithelium either single or bilayered and mixtures of mucous cells.^{2 17} Many investigators divide PCC histologically into low-grade and high-grade malignancy depending on the presence of intense dysplasia.^{4 12} Since these features were subtle in the present cases, we labelled them as low-grade malignancy.

A few investigators also classify PCC based on cellular morphology into small cuboidal cell type, large cuboidal cell type, columnar cell type and a combination of these cell types.^{4 10} Both of the present cases displayed a mixture of cell types, suggestive of fourth type.

The WHO in 1991 classified PCC (ICD code 8440/3 version 10) separately as salivary gland carcinoma,¹⁸ the important differential diagnosis of which included cystadenoma, PLGA, papillary-cystic variant of acinic cell carcinoma, salivary duct carcinomas, ACC and metastatic carcinoma.

Cystadenoma was excluded as it has a bland, regular cytology and low mitotic rate. Also, cystadenoma lacks evidence of infiltration in submucosa and muscle tissues. Moreover, the presence of features such as the pattern of solid growth in focal areas, cellular atypia, mode of invasion, permeation or destruction of glandular parenchyma and breakdown of the glandular lobe architecture helps in the diagnosis of PCC.^{8 19}

It is difficult to differentiate PLGA from PCC. However, lack of extensive papillary projections, a more variable histology and mixed growth pattern, the infrequency of any degree of cyst formation, and the perineural invasion help to differentiate PLGA from PCC.^{2 20}

The papillary cystic variant of acinic cell carcinoma causes the most difficulty in differential diagnosis. Generally this neoplasm lacks the many small cystic spaces noted in PCC, while cystadenocarcinoma lacks the solid to microcystic growth pattern and characteristic mixture of acinar and intercalated duct cells of acinic cell carcinoma.²

Distinguishing these tumours from intraductal papilloma was easy as these are generally benign tumours, unicystic without projections of glandular tissue outside the single cystic structure,^{8 21} whereas inverted ductal papilloma differs from PCC in that squamous cells extend into the surrounding connective tissue.⁸ Since the present cases showed multicystic papillary projections, distinguishing them from ductal papillomas was not difficult.

Differentiation from oncocytoma was not necessary in our cases since no oncocytic cell were discerned. Moreover, differentiation from mucus cystadenoma was also not necessary due to extensive papillary projections in the present cases.⁸

Learning points

- ▶ Variable patterns and arrangements of cells and extracellular material along with overlapping features present a great difficulty in diagnosing salivary gland neoplasms.
- ▶ Any tumour arising from the hard palate should be considered as a possible minor salivary gland tumour as although rare, these tumours do exist.
- ▶ The present case report adds to the few reports of this rare salivary gland carcinoma. The few notes on differential diagnosis should help the decision-making stage, although referral to a multidisciplinary head and neck clinic and the guidance of a pathologist experienced in the field of salivary glands is strongly recommended.

Since chest X-ray, MRI and the CT scan revealed no evidence of primary foci, a diagnosis of metastatic carcinoma was ruled out.

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