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Synchronous palatal polymorphous adenocarcinoma and canalicular adenoma: A rare case presentation and literature review

Salivary gland tumors are extremely heterogenous group of lesions with overlapping clinical and histomorphological features, oftentimes leading to diagnostic hardship particularly in the absence of auxillary techniques. Histological type (identical or different), topographic distribution (unilateral or bilateral) of unrelated tumors in a chronological fashion (synchronous or metachronous), popularly designated as multiple salivary gland tumors (MSGTs), adds to the difficulties [1]. Noteworthy, MSGTs can occur in three main combinations: 1) two distinctive benign tumors, 2) two exclusively malignant tumors and 3) a benign and a malignant tumor; the first being the most common presentation [1,2]. MSGTs are rare and affect mainly the major salivary glands [2]. A case of synchronous polymorphous adenocarcinoma (low grade) and canalicular adenoma of the palate is described here with emphasis on various diagnostic difficulties and probabilities aided by immunohistochemistry and literature.

A 61 years old Dravid Indian male (linguistically Tamil) reported with a chief complaint of recent pain and ulceration of his palatal swelling, of otherwise eight years duration. The patient had noted the swelling around eight years back which slowly grew to the present size of 1.9X1.5x1.3 cm. The patient is a past smoker, diabetic (under medication) and has history of multiple teeth extraction in both arches with uneventful healing. On clinical examination, a well-circuscribed nodular and sessile growth was noted on the posterior hard palate, centered slightly towards the left side (Fig. 1). The central area appeared ulcerated. The lesion was soft in consistency and tender on palpation. MRI showed a well defined lobulated enhancing mass with central ulceration. CBCT showed no bony involvement. Based on the appearance, and imaging findings, malignant salivary gland neoplasm was considered, and an incisional biopsy was performed; however, a note was made to the deceptive indolent course of the disease. The specimen was received in 10% buffered formalin for histopathological examination in multiple small pieces.

H&E stained sections from incisional biopsy showed a neoplasm of glandular origin with cuboidal to columnar tumor cells showing moderate amount of amphophilic cytoplasm and monomorphic bashophilic nuclei arranged in anastomosing branching cords and tubules, which appeared to float in the edematous and vascular stroma (Fig. 2). Hyperplastic overlying oral epithelium was noted at areas. The tumor cells were diffusely positive for pan-CK, CK7, S100 and c-kit (moderate intensity). SMA, p63 and p40 were negative (Fig. 3). The proliferation index as assesed by Ki-67 was <1%. A diagnosis of canalicular adenoma (CA) was made and the tumor was excised in toto (Fig. 4).

The excised specimen showed another type of sub-epithelial tumor along with areas similar to features mentioned above. The predominent tumor consisted of uniformly sized cells with open face nuclei arranged in a variegated morphologies ranging from tubules, microcystic, 'single file', swirls/'eddy-like' and strands (Fig. 5 a-f). The tumor appeared to be circumscribed at few areas while showed infiltrative tumor margins. The tumor cells, at areas, appeared to arise from the adjacent minor mucous salivay gland. There was unifocal perineural invasion and the involved nerve measured <1 mm (Fig. 5 g). No lympho-vascular emboli were noted in the multiple sections studied. The resected margins and base were free of tumor. The canalicular adenoma like areas (Fig. 5 h) showed similar immunoprofile as in incisional biopsy while, other areas suggestive of polymorphous adenocarcinoma (PAC) additionally showed p63 positivity (p40 negative), both of which remained negative in CA like areas (Fig. 6). The Ki-67 proliferation index was <5 %. A final diagnosis of low grade PAC with synchronous CA was made (pT_1). The postoperative healing was uneventful and the patient is on regular clinical follow-up.

Literature revealed one previously reported similar case in a 61-year-old female patient who had focal area of PAC and multiple CAs on her upper lip [3]. Their case showed pan CK, CK7 and S100 positivity in both tumor types. PAC specifically showed S100, SMA and p63 depicting myoepithelial (ME) differentiation. Vimentin was positive in PAC, in contrast CA was immunonegative for it. The proliferation index was low in both tumors. In the present case, the diagnosis on incisional biopsy was consistent with CA as SMA and p63, makers for ME differentiation were negative and the tumor cells showed exclusively luminal differentiation as highlighted by pan CK, CK7 and c-kit. Consistent with the diagnosis of CA, S100 showed strong positivity. However, the excision specimen showed co-existent CA and PAC. Unlike CA, tumor cells in PAC were reactive for ME markers. As previously described PAC areas in our case showed discordant p63+/p40-profile [4,5]. Thus, p63 could be regarded as a better marker than vimentin for distinction of closely resembling salivary gland tumors, in conjunction with p40. This holds true particularly for PAC, adenoid cystic carcinoma and cellular pleomorphic adenoma.

PAC is rare and is the second most common intraoral malignancy of salivary gland origin [6]. Cribriform adenocarcinoma of minor salivary glands (CAMSG), a histomorphological variant of PAC, is considered to show a more aggressive behavior [6]. With advanced molecular techniques, it has been demonstrated that classical PAC often shows PRKD1 gene point mutation unlike CAMSG, which shows PRKD1/2/3 translocations [7–9]. These point mutations and gene translocations are further helpful in differentiation of PAC from CA and sometimes rarer malignancies such as secretory carcinoma. The association of PRKD gene with the prognosis and outcome of PAC is being explored. In general, the

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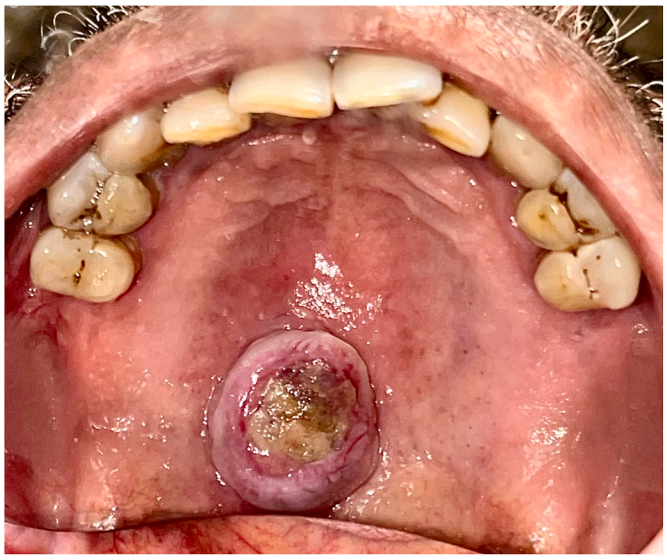

Fig. 1. Intraoral picture showing a sessile growth of the palate with surface ulceration.

cases with gene mutation show better disease free survival and lower incidence of regional metastasis than those without translocations.

We believe that the present case showed actual co-existent PAC with CA rather than malignisation of CA which theoretically is less acceptable owing to the histogenesis of these tumors. Canalicular adenoma is a benign neoplasm composed primarily of luminal/acinar cells in contrary to polymorphous adenocarcinoma which is differentiated from luminal and modified ME cells and histologically lack obvious proteoglycans and basal lamina production. Thus, it may be prudent to believe that in our case, CA could be the primary tumor which over a period of time would

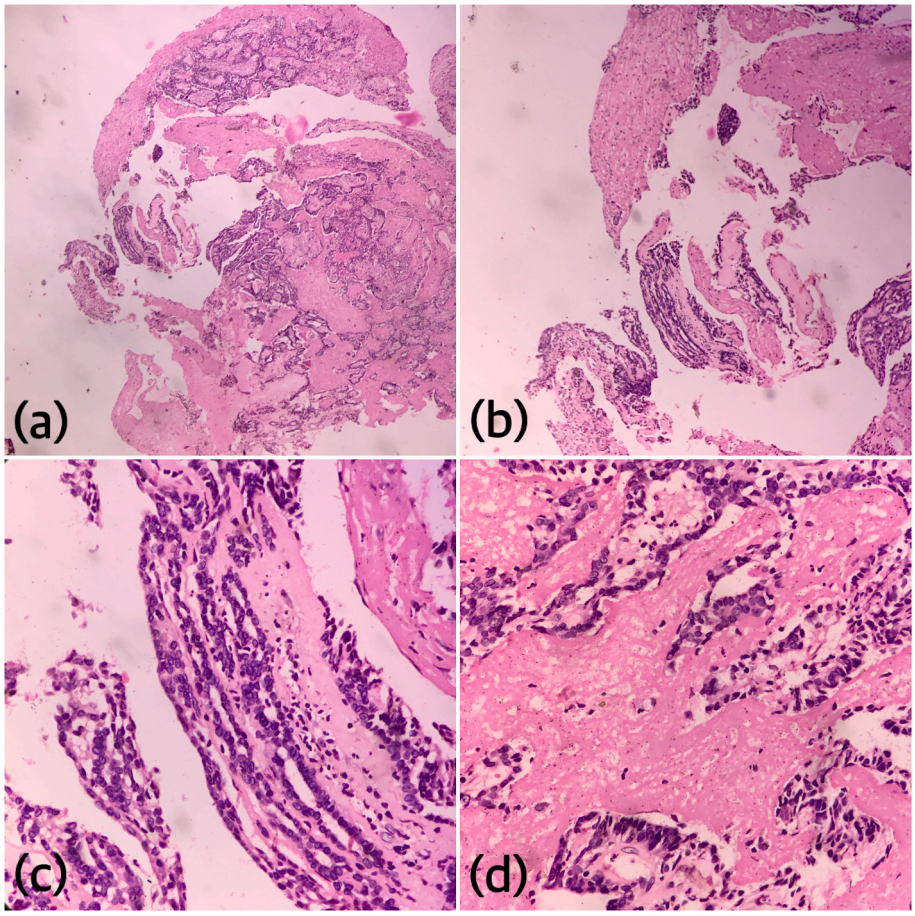

Fig. 2. Photomicrographs of the H&E stained sections from incisional biopsy showing tubular and beaded appearance of tumor cells (a–b: 4X; c: 40X) which appear to float in a loose stroma (d:40X).

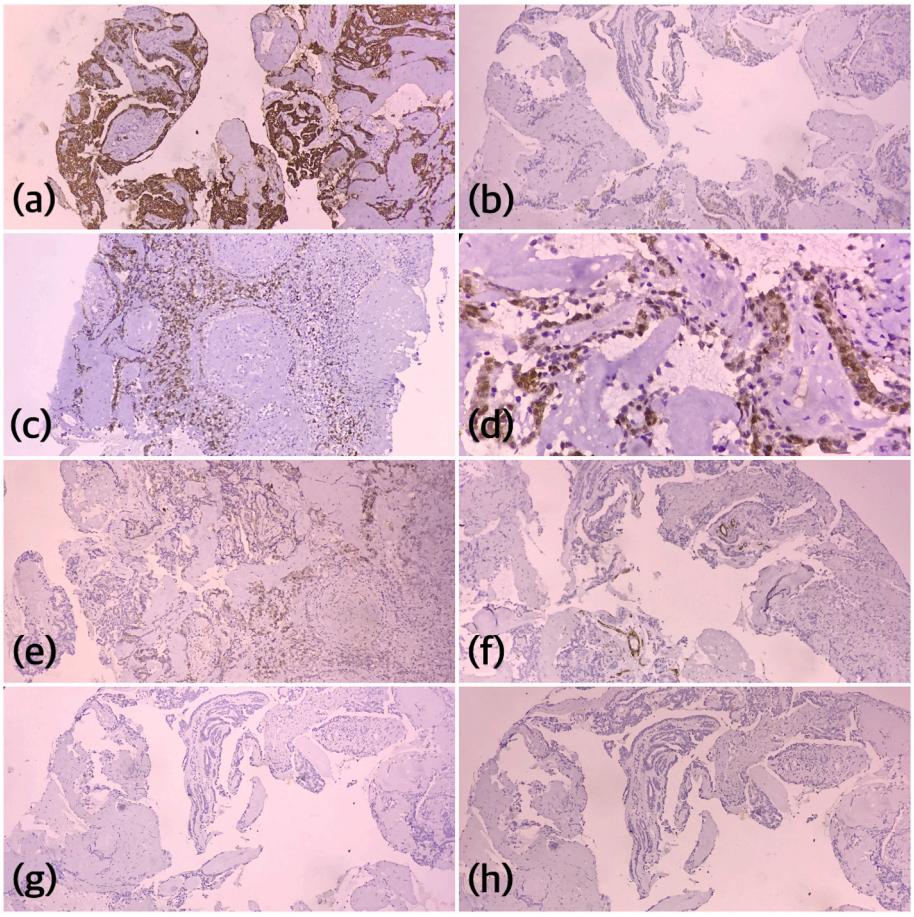

Fig. 3. Photomicrographs of the IHC sections from incisional biopsy showing strong pan-CK positivity (a), moderate and focal CK7 positivity (b), strong S100 positivity (c–d), moderate c-kit positivity (e), and negative SMA (f), p63 (g) & p40 (h).

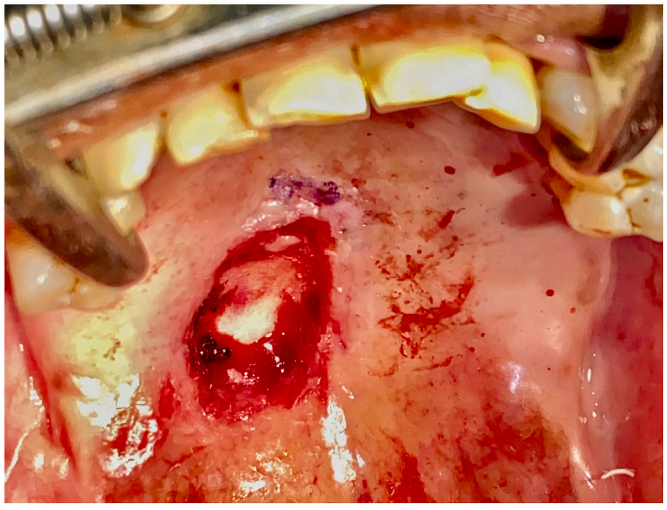

Fig. 4. Intraoperative picture after excion of the lesion.

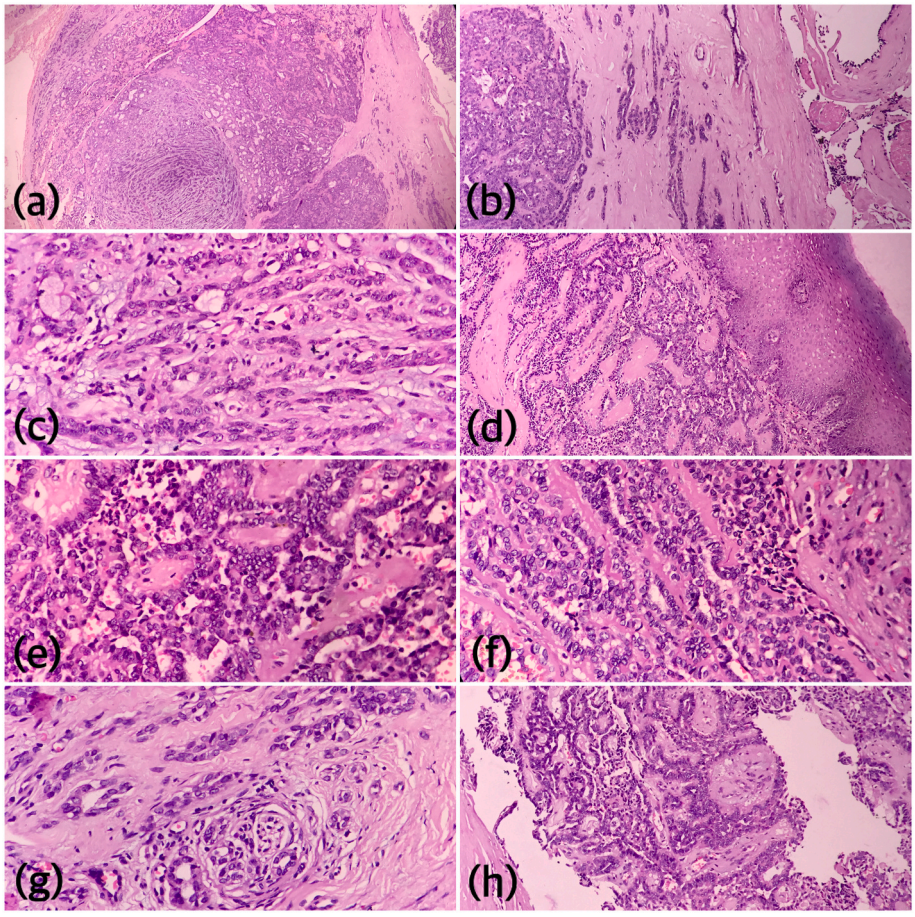

Fig. 5. Photomicrographs of the H&E stained sections from excision specimen showing variegated apprearance of polymorphous adenocarcinoma (a:4X), single file arrangement of tumor cells (b: 10X), tubular and ductal arrangement (c: 40X), subepithelial tumor cells which appear to merge with the oral epithelium (d: 10X), tumor cells with open faced 'orphan Annie eye' nuclei which were arranged in clusters at areas (e–f: 40X), unifocal perineural invasion (g: 40X) and canalicular adenoma like areas (h: 10X).

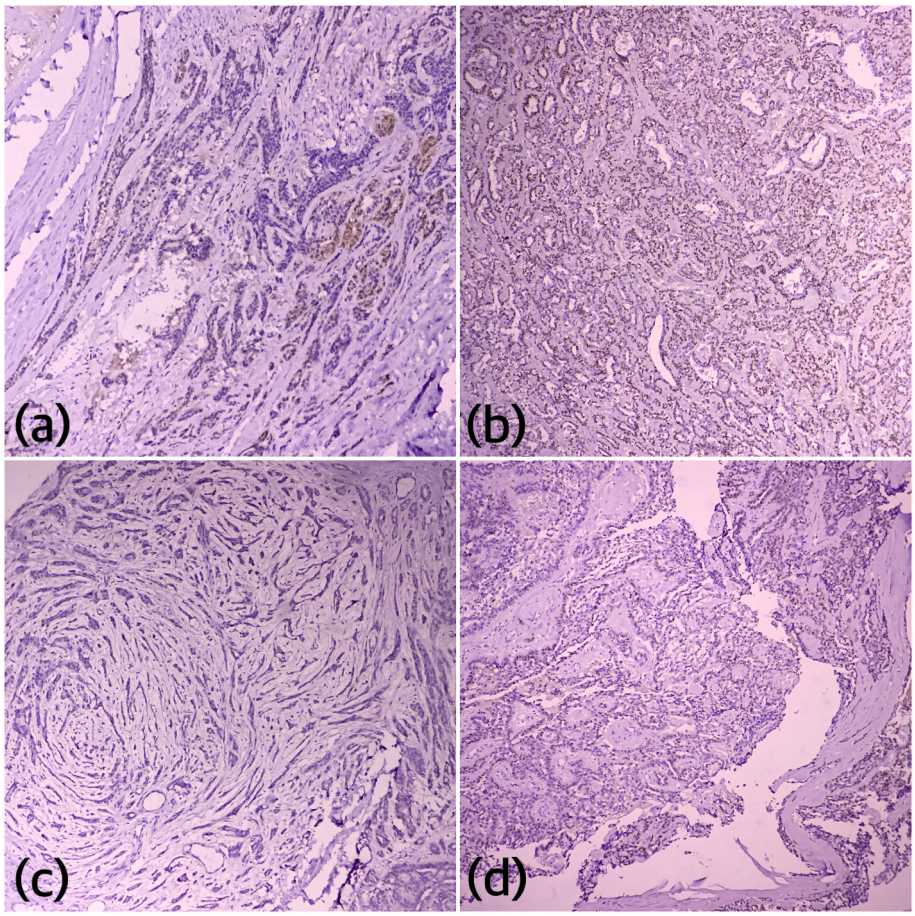

Fig. 6. Photomicrographs of the IHC sections from excision specimen showing patchy patchy S100 positivity (a), p63 positivity (b) and p40 negativity (c) in PAC areas and (d) p63 negativity in CA like areas.

have been replaced and overtook by excessive proliferation of modified ME cells in addition to the luminal cells, analogous to the concept of 'irrevocable proxy'. This case further highlights that the malignant salivary gland tumors particularly, low grade tumors, may also show an indolent course, any sudden increase in size accompanied by pain and ulceration should be considered as an alarming clinical sign and managed accordingly.

CRediT authorship contribution statement

Deepak Pandiar: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft. **Neha Kannan:** Conceptualization, Methodology, Writing – review & editing. **Reshma Poothakulath Krishnan:** Supervision, Writing – review & editing. **Karthikeyan Ramalingam:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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