CASE REPORT

Polymorphous Adenocarcinoma at Rare Locations: A Series of Two Cases

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ABSTRACT

Polymorphous adenocarcinoma (PAC) is a slowly growing malignant minor salivary gland tumor with a very low risk of recurrence and distant metastases. PAC is characterized by cytologic uniformity and architectural diversity. Various morphologic patterns include papillary, tubular, reticular, solid, cribriform, and single-file patterns. A very less percentage of cases have been reported in the nasal cavity and parotid. On cytology, smears are cellular with tumor cells are uniform and arranged in the form of clusters, papillae and singly scattered. We present here two cases, one case in the parotid reported on cytology and later confirmed on histopathology and the other case in the nasal cavity reported on biopsy, of which we later also received the resection specimen. Polymorphous adenocarcinoma is a slow-growing malignancy with an excellent prognosis. Though, it rarely occurs in the nasal cavity and parotid gland but it should be kept among differential diagnoses. Histopathology is the gold standard to diagnose salivary gland tumors but Immunohistochemistry is a useful aid in ruling out close differentials. Surgical excision is the main modality of treatment with excellent disease-specific survival.

Keywords: Polymorphous adenocarcinoma, parotid, nasal cavity, adenoid cystic carcinoma, palate.

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INTRODUCTION

Polymorphous adenocarcinoma (PAC) earlier known as polymorphous low-grade adenocarcinoma is a slow-growing malignant tumor of minor salivary glands, though 5.2% and 4.8% of cases have been reported in Parotid, Nasal cavity and paranasal sinuses respectively[1]. The annual incidence rate is 0.051 cases per 100,000 persons[2]. It is the second most common malignant tumor of the minor salivary glands, particularly in the hard and soft palate after mucoepidermoid carcinoma. The term "Polymorphous Low-Grade Adenocarcinoma" was first proposed by Evans and Batsakis in 1984[3]. Recently, in 2017, in the WHO head and neck tumors classification, the term "low-grade" was deleted considering a subset of these tumors behaving aggressively[4]. We present here two cases, one case in the parotid reported on cytology and later confirmed on histopathology and the other case in the nasal cavity reported on biopsy, of which we later also received the resection specimen.

CASE REPORT

Case 1: A 31-year-old male presented with a complaint of painless swelling below the left ear for 5 months which was gradually increasing in size. On examination, the swelling was non-tender, fixed and hard with well-defined borders. The overlying skin was unremarkable. The patient was a chronic smoker, non-diabetic and non-hypertensive. No positive family history and no other significant medical history were present.

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Fine needle aspiration (FNAC) yielded cellular smears showing tumor cells arranged in the form of papillae, clusters, and few singly scattered **(Fig 1).** Individual tumor cells were monomorphic with moderate amount of cytoplasm, round nucleus and indistinct nucleoli. No hyaline globules or acellular basement membrane material were seen. No nuclear crowding was seen.

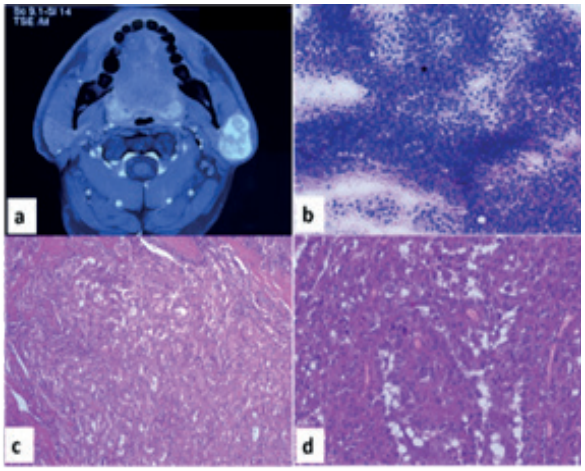

Fig 1. a) CEMRI axial section shows well-circumscribed soft tissue mass in the parotid region. b) PAP-stained smear shows numerous papillae lined by bland-appearing uniform tumor cells with a scant to moderate amount of cytoplasm and round to oval nuclei. (100X) c) Haematoxylin & Eosin-stained section shows an infiltrative tumor with a predominant microcystic pattern in this focus. (100X) d) Section shows the papillary configuration with a central vascular core lined by cuboidal to low columnar cells with round to oval nuclei. (400X)

A diagnosis suggestive of Polymorphous adenocarcinoma, category V according to the Milan System for Reporting Salivary Gland Cytopathology was given. Following FNAC diagnosis, contrast-enhanced magnetic resonance imaging (CEMRI) neck was performed. The study revealed 23×28×30 mm mass involving the superficial lobe of the left parotid gland without evidence of adjacent deep lobe infiltration. The lesion appeared hypointense on T1 and iso to hyperintense on T2/Short tau inversion recovery (STIR) images with evidence of diffusion restriction on Diffusion-weighted imaging/ Apparent diffusion coefficient and heterogenous moderate post-contrast enhancement, suggestive of neoplastic etiology.

A total conservative parotidectomy with selective neck dissection was done. The gross specimen measured 7×5×5cm. On cut a circumscribed unencapsulated grey white area with ill-defined margins was identified measuring 3×3cm which was 1.2cm, 1.7cm, 0.2cm and 1.8cm from anterior, inferior, medial, and lateral margins. On histopathological examination, the Haematoxylin & Eosin-stained sections showed an infiltrative tumor exhibiting multiple architectural patterns including papillary, cribriform, solid, tubular, and reticular. Individual tumor cells were medium-sized uniform cells having bland-appearing oval nuclei, a few of them showed indistinct nucleoli. Frequent perineural invasion was noted. All the resected margins and lymph nodes were free of tumor. Immunohistochemistry was performed with a panel including S100, CK7, p63, p40, GATA3, SMA and Vimentin. S100, CK7, and Vimentin were diffuse and strongly positive. p63 showed focal patchy positivity. p40 and GATA3 were negative. p40 and SMA negativity ruled out Adenoid cystic carcinoma. Negative GATA3 and focal positive p63 ruled out secretory carcinoma. Based on immunohistochemical features, a final diagnosis of Polymorphous Adenocarcinoma, intermediate grade, $pT_2N_0M_X$ was given. The patient received radiotherapy for 30 days postoperatively. Presently patient is doing fine.

Case 2. A 48-year-old male presented with complaints of right-sided nasal obstruction and a bulge present over the right side of the nose for 8 months. The swelling was painless and non-tender. The patient was non-diabetic and non-hypertensive. No significant family history was noted. An incisional biopsy was performed measuring 0.8×0.5×0.4cm Histopathology examination showed predominantly reticular and solid sheets admixed with myxoid stroma. Individual tumor cells were uniform in appearance having round nuclei and pale chromatin. No pleomorphic nuclei, nuclear crowding, hyaline globules or basement membrane material, necrosis, and hemorrhage were seen. We considered the possibility of polymorphous adenocarcinoma, Adenoid cystic carcinoma, and Secretory carcinoma. An immunohistochemistry panel of CK7, p40, p63, GATA3, S100 and SMA was performed. CK7 and p63 were strongly positive, rest of the markers were negative. Considering histopathology and immunohistochemistry a final diagnosis of Polymorphous adenocarcinoma was given.

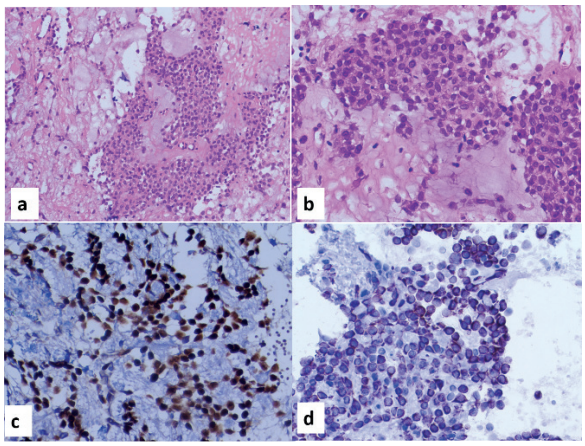

Fig 2. a) Section shows tumour cells arranged in the form of reticular and solid sheets (Haematoxylin & Eosin stain, 100X) b) Tumor cells are monomorphic, small to medium-sized with bland nuclei. c) Diffuse and strong nuclear positivity of p63 (400X) d) Diffuse and strong cytoplasmic granular positivity of S100.

Lateral rhinotomy with excision of the nasal mass was performed and the resection specimen (Fig 2) was sent to us for histopathology examination. We received a single grey-white to grey-brown polypoidal soft tissue mass measuring 5X3X2 cm. On cut, H&E-stained sections showed tumor cells arranged in the form of reticular, solid sheets, trabecular and single file patterns. Cells showed similar morphology as seen in the biopsy. All the resected margins and Nasal bone were free of tumor. No lymph nodes were submitted with the resected specimen. A final diagnosis of PAC Low grade, $pT_2N_0M_X$ was made. No chemo or radiotherapy was given to the patient. Presently patient is doing well.

DISCUSSION

Polymorphous adenocarcinoma was first described in the literature as "Polymorphous low-grade adenocarcinoma" in 1984 by Evans and Batsakis [5]. They published a study of 14 cases and described a clinicopathologic entity characterized by cytologic uniformity with histologic diversity, and various growth patterns while the individual cells are small to medium in size, lacking nuclear atypia and mitotic figures. The term Low-grade was deleted in the 4th WHO classification of salivary gland tumors considering the potential of high-grade transformation and distant metastases.

PAC is slow slow-growing malignant salivary gland tumor with a low risk of recurrence and minimal risk of distant metastases. PAC shows a female predilection with a female-to-male ratio of 2:1 [6].The average age of diagnosis is the 5th-6th decade of life. Though one of our patients developed the disease at the younger age at 31 years. Both our cases were male patient.

49-87% of the cases occur in the hard palate [1,7]. Other sites of involvement are the buccal mucosa, lip, cheek, retromolar trigone, lateral tongue, upper airway, oropharynx, nasopharynx, nasal cavity and paranasal sinuses. Very few cases have been reported in the literature to arise de novo from the parotid gland and nasal cavity [1]. Both our cases were interesting and present at these unusual sites.

The usual presentation is an asymptomatic slow-growing painless may be associated with pain, ulceration, or bleeding. The reported duration of the clinical presentation varies from a few days to several years [8]. Both of our cases presented with a painless mass, firm to hard consistency for a long duration of 5 months and 8 months in the parotid and nasal cavity respectively.

Salivary gland cytology is a well-established minimally invasive diagnostic tool. Jiménez-Heffernan et al in their study of 11 cases published in 2020 described the cytological features of PAC [9]. FNAC smears are usually cellular showing tumor cells arranged in the form of irregular groups few of them with pseudopapillary branching patterns. Also seen are monolayered small clusters and acinar structures. Individual tumor cells are monomorphic, small with scant to moderate cytoplasm with round to oval nucleoli. In addition, small-sized stromal globules are present in many cases. These cytological features are not specific to PAC, other differentials are Adenoid cystic carcinoma (AdCC), Basal Cell Adenoma, and Cellular Pleomorphic Adenoma. Stromal globules of PAC are uniform and small, similar to pleomorphic adenoma and basal cell adenoma. In contrast, stromal globules of adenoid cystic carcinoma are large and variable-sized with overlying tumor cells. Cells of AdCC have minimal cytoplasm with hyperchromatic nuclei. In our case, cytology smears were cellular with uniform tumor cells arranged in the form of papillae with fibrovascular cores, small clusters, and scattered singly. There were no stromal globules in the smears examined.

PAC as the name indicates shows numerous morphological patterns of different proportions

like Papillary, Tubular, Trabecular, Cribriform, Reticular, Single filing, and Solid. Infrequent histologic patterns include Oncocytic change, microcalcification, mucocytes, and high-grade transformation [7]. A few of these morphological patterns in histology also predict disease-free survival. These patterns include cribriform, reticular, solid architecture, necrosis, and lymphovascular invasion [8]. Tumor comprises one cell type only showing none to minimal pleomorphism with round to oval nuclei and opened-up chromatin. PACs show frequent perineural invasion seen in 60-75% of the cases[1]. In our cases, we also found frequent perineural invasion.

Immunohistochemistry (IHC) especially when used in a panel is a helpful tool to reach a diagnosis in salivary gland tumors with morphologic overlap. We put a panel of IHC markers (Table 1) including p40, p63, CK7, GATA3, S100 and SMA on both cases. p63 comes exclusively positive in PAC in almost 100% of cases while p40 is consistently negative. PAC is also positive for CK7 and S100. AdCC is positive for p40, p63 and CK7 [10]. SC shows positivity for CK7, S100 and GATA3 [4, 11]. Our both of cases were positive for CK7, S100 and p63. Both cases were negative for p40, SMA and GATA3.

Surgical resection with or without lymph node dissection and clear margins is the primary treatment. Postoperative radiation or chemotherapy depends on the margin status of the surgical resection, perineural invasion, distant metastasis, or inoperable tumors [2]. Overall prognosis is excellent with 94-99% of cases showing 10-year disease-specific survival. Poor survival is reported with tumor size larger than 2 cm, presence of nodal or distant metastasis, bone invasion, tumor necrosis, invasion of large nerve and advanced-stage disease [1, 2].

CONCLUSION

Polymorphous adenocarcinoma is a slow-growing malignancy with an excellent prognosis. Though, it rarely occurs in the nasal cavity and parotid gland but it should be kept among differential diagnoses. **Histopathology is the gold standard to diagnose salivary gland tumors but** Immunohistochemistry is a useful aid in ruling out close differentials. Surgical excision is the main modality of treatment with excellent disease-specific survival.

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