Hybrid salivary gland tumour: interpreting conflicting morphologies in final needle aspiration cytology

Solange De Noon
Gayani Pitiyage

Abstract

Cytological assessment of salivary gland tumours can be a challenging endeavour that requires careful assessment and interpretation of cytomorphological features. We present a case of a hybrid salivary gland tumour with both elements detectable on fine needle aspiration cytology and consider the relevant differential diagnoses when faced with multiple contrasting morphologies on salivary gland sampling. We also discuss the proposed pathogenesis, relevant nomenclature and key clinical considerations for this rare neoplasm.

Keywords cytology; differential diagnosis; hybrid tumour; neoplasm; salivary gland

Case report

An 80-year-old female presented with a six-month history of a left neck swelling. Ultrasound demonstrated a left parotid mass of indeterminate nature, and a fine needle aspiration was performed. Direct smear preparations revealed a cellular sample groups comprising crowded sheets of ovoid to spindled cells with moderate cytonuclear atypia and prominent nucleoli (Figure 1a, b). Also present were separate groups of cells with papillaroid architecture and evidence of pseudostratification (Figure 1c). Although the exact nature of this tumour could not be ascertained on cytological preparations alone, this was recognized as a malignant neoplasm and a total left parotidectomy was performed.

Histology showed a single mass with two distinct and contrasting appearances. There was a glandular component composed of cribriform and cystically dilated glands lined by crowded mucinous epithelium (Figure 1d). Papillary and micropapillary structures were also present. These areas were juxtaposed to solid regions formed of plump spindled cells arranged in sheets, fascicles, and anastomosing cords (Figure 1e, f). Geographic tumour necrosis was present in the solid areas, with mitoses ranging from 9 per 10 high power fields (HPF) in the glandular epithelium to 25 per 10 HPF in the spindled areas. Immunohistochemical studies also revealed two distinct patterns of expression, with the glandular and cystic areas showing strong positivity for epithelial and glandular markers CAM5.2, EMA, CEA and BER-EP4, CK7 and GATA3. Staining for myoepithelial markers in these areas was restricted to the basal layer surrounding glands. Conversely, diffuse expression of CK5, SOX10 and SMA was seen in the solid spindled regions of the tumour, which showed only weak CK7 and GATA3 expression.

Overall, these findings confirmed the diagnosis of a hybrid salivary gland malignancy, in this instance composed of a low grade papillary cystadenocarcinoma and a high grade myoepithelial carcinoma. The tumour showed extra glandular extension but no perineural or lymphovascular spread.

Discussion

Hybrid tumours are generally defined as a single tumour mass formed of two or more defined tumour entities, which arise in the same topographical area but can be histologically distinguished from each other.[1,2] This contrasts with collision tumours, which are the result of the meeting of two entities which originally arise independently in different locations. These tumours should also be distinguished from other more common scenarios including carcinomas with highly variable appearances as a result of clonal diversity, benign tumours showing malignant transformation, and finally synchronous salivary gland tumours. By this definition true hybrid tumours of the salivary glands are rare occurrences, with less than 20 reported in the English literature,[1–3] predominantly occurring in the parotid gland. Published cases reveal great variety in tumour compositions, although to our knowledge this represents the first published case of a hybrid tumour comprising both low grade papillary cystadenocarcinoma and high grade myoepithelial carcinoma elements.

Making the diagnosis of a hybrid tumour on fine needle aspiration can be particularly challenging. In this case, features supportive of an adenocarcinoma including papillaroid and glandular structures are present. However, the finding of microbiopsies composed solely of spindle cells should raise the suspicion of a secondary component. A biphasic appearance on fine needle aspiration raises several differential diagnoses which should be excluded before making the diagnosis of a hybrid tumour. These include carcinoma ex-pleomorphic adenoma, synchronous salivary gland tumours, carcinomas with a

Solange De Noon *MD Histopathology Specialty Trainee, Royal National Orthopaedic Hospital NHS Trust, Stanmore and Clinical Research Fellow, UCL Cancer Institute, London, UK. Conflicts of interest: none declared.*

Gayani Pitiyage *FRCPath PhD Consultant Pathologist, St. George's University Hospital NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

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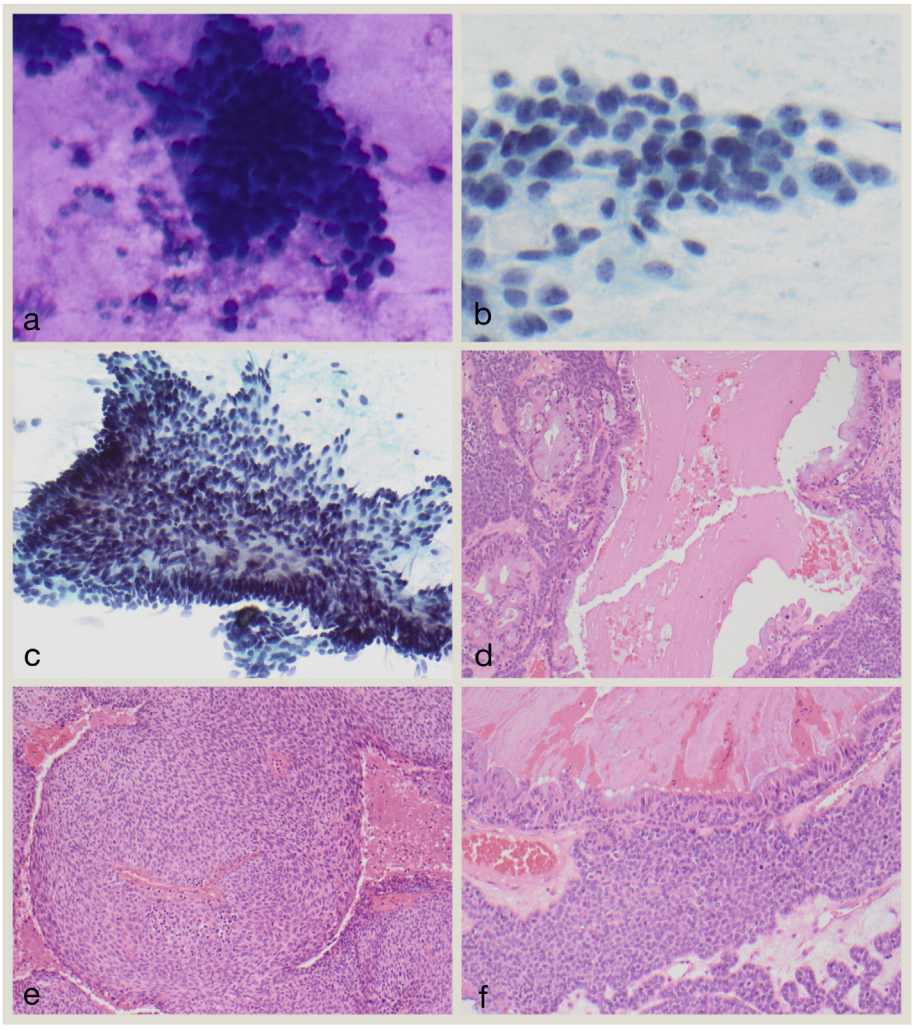

Figure 1 (**a**) Direct MGG smear preparation featuring a three dimensional cluster of myoepithelial cells. (**b**) Pap stain showing myoepithelial cells with nuclear pleomorphism and prominent nucleoli. (**c**) Pap stain demonstrating a gland forming epithelial component with the impression of papillary growth and pseudostratification. (**d**) Histology of the resected mass revealed areas formed of papillary and cystic structures lined by tall mucinous cells with thick mucinous luminal contents. (**e**) Within the same lesion, separate regions showed solid sheets of malignant spindled cell proliferations with geographic areas of necrosis. (**f**) Juxtaposition of cystadenocarcinoma and myoepithelial carcinoma elements.

sarcomatoid component, and collision/hybrid tumours. Unlike tumours showing high grade differentiation or sarcomatoid tumours, hybrid tumours rarely show areas of morphological transition from one entity to the other, and often these distinct areas can be clearly demarcated from each other. Immunohistochemistry is particularly useful to demonstrate a clear demarcation between tumour morphologies within these lesions. From a management perspective, the recognition of at least one of these components as malignant on cytology is sufficient to guide surgical management, with the final diagnosis being made on the resection histology.

The pathogenesis of these tumours remains unclear due to their rarity. Genetic analysis of hybrid salivary gland tumours is further limited, but evidence to date supports the theory that the distinct tumour elements in a given tumour arise from independent events rather than a single event with subsequent divergence.[3,4] Case series have demonstrated that prognosis is determined by the higher-grade and histologically aggressive component— even if this represents the minority of the lesion.[1,3]

Conclusion

Hybrid salivary gland tumours highlight the importance of careful assessment and interpretation of all material in cytological preparations, and consideration of dual pathologies in the face of contrasting morphological appearances. ◆

REFERENCES

1 Seifert G, Donath K. Multiple tumours of the salivary glands—terminology and nomenclature. *Eur J Cancer B Oral Oncol* 1996; **32:** 3–7.

2 Hellquist H, Skalova A, Azadeh B. Salivary gland hybrid tumour revisited: could they represent high-grade transformation in a low-grade neoplasm? *Virchows Arch* 2016; **469:** 643–50.

3 Nagao T, Sugano I, Ishida Y, et al. Hybrid carcinomas of the salivary glands: report of nine cases with a clinicopathologic, immunohistochemical, and p53 gene alteration analysis. *Mod Pathol* 2002; **15:** 724–33.
4 Zhou Y, Martinez Duarte E, Eleff DJ, Tafe LJ, Leibowitz JM, Kerr DA. An unusual hybrid salivary gland tumor: molecular analysis informs the potential pathogenesis of this rare neoplasm. *Case Rep Pathol* 2019; **2019:** 2713234.

Practice points

- Hybrid salivary gland tumours are single lesions composed of two or more recognized morphological entities arising within the same topographical area, but which can be demarcated from each other.
- Biphasic appearances on salivary gland fine needle aspirates are not uncommon, and several differential diagnoses should be considered before making the diagnosis of a hybrid tumour, particularly tumours with high grade transformation.
- Clinical outcomes for hybrid tumours are determined by the most aggressive component of the tumour regardless of the proportion of the tumour mass this occupies.

Self-assessment questions

1. Which of the following is an example of a hybrid salivary gland tumour?

a) Pleomorphic adenoma with focal area of salivary duct carcinoma
b) Submandibular mass containing mucoepidermoid carcinoma and areas of basal cell adenoma
c) Malignant mixed tumours
d) Parotid gland containing a Warthin's tumour and an adenoid cystic carcinoma

Correct answer: b) Submandibular mass containing mucoepidermoid carcinoma and areas of basal cell adenoma

2. What is the most common site of hybrid salivary gland tumours?

a) Submandibular gland
b) Minor salivary glands
c) Parotid gland

Correct answer: c) Parotid gland

3. Which cytological feature MOST raises the differential of a hybrid tumour?

a) Presence of epithelial and myoepithelial elements within a single group
b) Papillaroid clusters
c) Significant cytological atypia
d) Separate cell groups with distinct morphological appearances

Correct answer: d) Separate cell groups with distinct morphological appearances