

## CASE REPORT

### Endocrine mucin-producing sweat gland carcinoma - newly described skin appendageal tumours

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#### Abstract

**Introduction:** Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a recently described adnexal tumour with a predilection for the face particularly the eye-lids. Considered to be a precursor lesion of mucinous adenocarcinoma, it may represent part of a morphological spectrum. We described a case of this entity, which we believe is the first case to be reported in Malaysia. **Case report:** A 59-year-old Chinese male presented with a slow-growing cystic lesion over the left lower lateral canthal region. The lesion became progressively larger and nodular within the last 6 months. Histologically, the lesion is a well-circumscribed intradermal tumour with pushing borders extending into the subcutaneous tissue. The tumour cells were arranged in lobules of solid, papillary and cribriform architecture. The cells displayed uniform, medium-sized, round to oval nuclei with stippled chromatin pattern and ample eosinophilic granular cytoplasm. Intracellular mucin (as highlighted by mucicarmine stain) was observed in areas with focal extracellular mucin seen. Mitotic figures were not particularly impressive. By immunohistochemistry study, the tumour cells expressed ER, PR, CK7, GCDFP-15, mammaglobin and EMA diffusely. Chromogranin A and synaptophysin highlighted a significant number of tumour cells. **Discussion:** The morphology and immunohistochemical profile similarities between EMPSGC and solid papillary carcinoma of the breast (SPCOTB) makes the former considered as the cutaneous analogue of the latter. In fact, one should rule out the possibility of metastatic SPCOTB before considering the diagnosis of EMPSGC.

**Keywords:** endocrine, mucin-producing, sweat gland carcinoma

#### INTRODUCTION

Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a low-grade neuroendocrine neoplasm and cutaneous analogue of the breast, solid papillary adenocarcinoma. It is a recently described skin adnexal tumour in the current WHO Classification of Skin Tumours, with a predilection for the face particularly the eyelids and periorbital skin.<sup>1,2</sup> The entity is considered to be a precursor lesion of mucinous adenocarcinoma, with at least 50% of EMPSGC had coexisting invasive mucinous adenocarcinoma on histology.<sup>3</sup> It commonly affects the elderly with an age predilection of 70 years old. Females are affected twice as frequently as compared to males. We describe a case of this entity, which we believe is the first case to be reported in Malaysia.

#### CASE REPORT

A 59-year-old Chinese male presented with a slow-growing cystic lesion over the left lower lateral canthal region (Fig. 1A). The lesion became progressively larger and nodular with occasional itchiness within 6 months period. There was no numbness or pain associated. He also denied any constitutional symptoms.

Histologically, the lesion showed a well-circumscribed intradermal based tumour without epidermal connection (Fig. 1B), with pushing borders, extending into the underlying subcutaneous tissue. The tumour cells were arranged in lobules (Fig. 1B) of predominantly solid with occasional cribriform pattern and papillary architecture (Fig. 1C). The latter was associated with delicate fibrovascular cores. The cells displayed fairly uniform, medium-

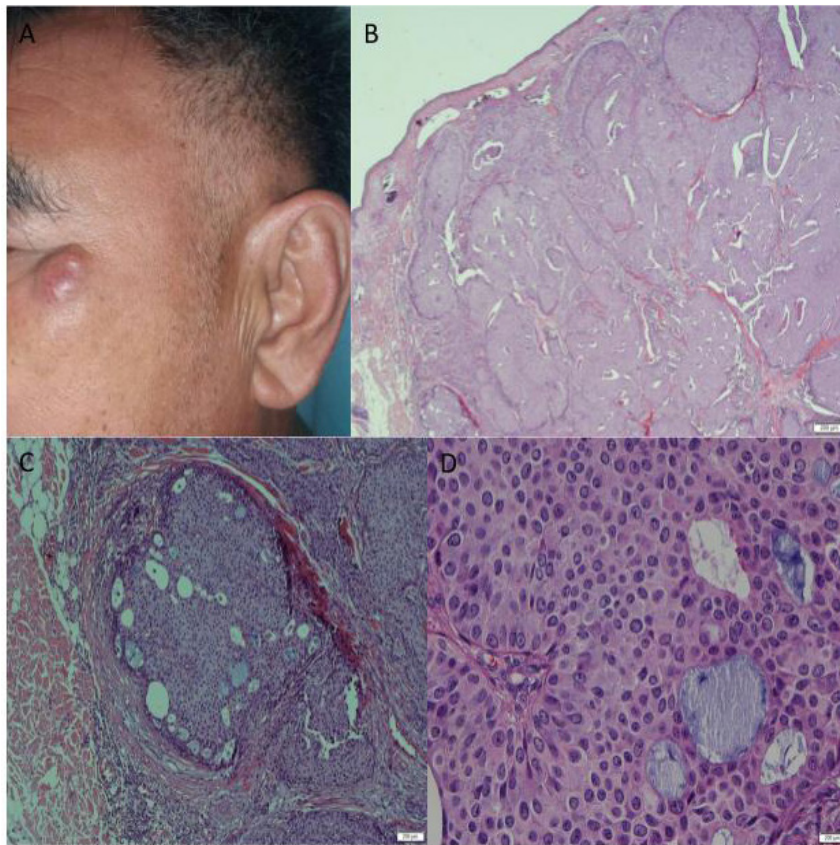


FIG. 1: A nodular lesion over the left lower lateral canthal region (A). Low power view shows tumour lobules with pushing borders and architecture similar to solid papillary carcinoma of the breast (B, H&E, x40). In focal areas, cribriform pattern with luminal formation containing mucin are apparent (C, H&E, x100). The tumour cells display round to oval nuclei with stippled chromatin pattern and ample eosinophilic granular cytoplasm (D, H&E, x400). All magnifications are original microscope magnification (scale bar = 200 $\mu$ m).

sized, round to oval-shaped nuclei with stippled chromatin pattern and ample eosinophilic granular cytoplasm (Fig. 1D). There was no nuclear pleomorphism noted. Myoepithelial cells were preserved in most of the tumour lobules.

Intracellular mucin was observed in areas with focal extracellular mucin seen. This was highlighted by mucicarmine stain (Fig. 2D). Mitotic figures were not particularly impressive. The proliferative index as estimated by Ki-67 was low at 5%. Tumour necrosis was not seen. There was no lymphovascular or perineural invasion identified. The tumour was seen in the deep surgical margin.

By immunohistochemistry study, the tumour cells were diffusely immunoreactive for oestrogen receptor, progesterone receptor, CK7, GCDFP-15, mammaglobin and EMA (Fig. 2A-C). Chromogranin A and synaptophysin highlighted a significant number of tumour

cells with moderate to weak expression (Fig. 2E-F). EMA also decorated occasional luminal formation. The myoepithelial cells were highlighted by P63. The patient underwent a second excision a month later as the deep margin was involved. Subsequent report showed no residual malignancy was found. He was under a three-monthly follow up with the surgical team.

## DISCUSSION

Tumours of the skin adnexal in general and particularly the sweat gland constitute a heterogeneous group of neoplasms with a wide morphological spectrum. In term of histogenesis, sweat gland tumours predominantly show apocrine or eccrine differentiation, but they can also have areas of follicular and sebaceous differentiation.<sup>4</sup> This is due to the embryologic derivation of the apocrine glands, hair follicles

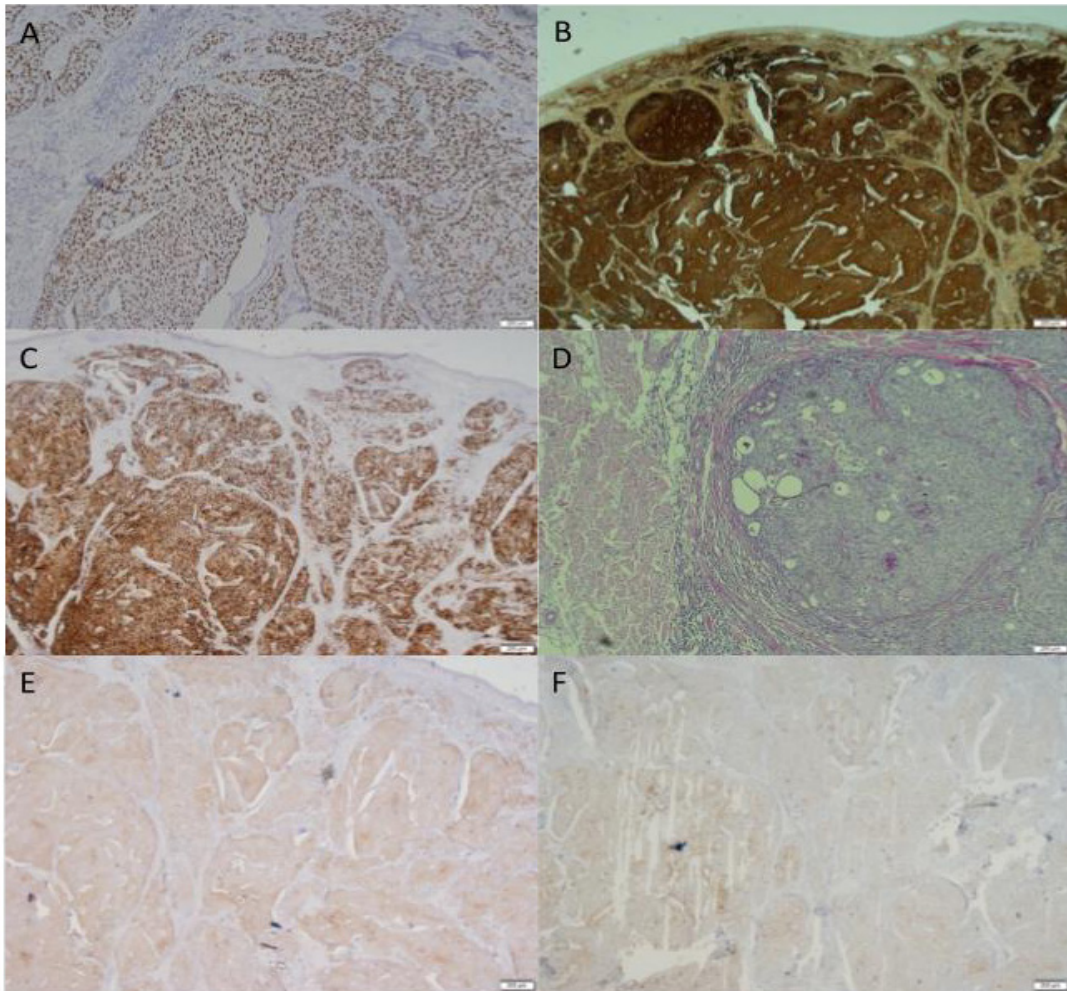


FIG. 2: The tumour cells are diffusely immunoreactive for ER (A, x100), GCDFP-15 (B, x40) and mamaglobin (C, x40). The focal areas of intracellular and extracellular mucin are highlighted by mucicarmine stain (D, x100). The tumour cells are also weakly to moderately immunoreactive for chromogranin A (E, x40) and synaptophysin (F, x40). All magnifications are original microscope magnification.

and sebaceous glands from the common folliculosebaceous-apocrine unit. Some of the entities are site-specific and derive from specific anatomical structures such as glands of Moll and anogenital mammary-like glands.

Some of the sweat gland tumours are quite unique, which are morphologically analogous to the extracutaneous counterparts, namely salivary glands and breast. The entity that we report here fall into the latter category. In the recent WHO Classification of Skin Tumours, EMPSGC is defined as a low-grade neuroendocrine neoplasm with cutaneous analogue of solid papillary adenocarcinoma of the breast.<sup>1</sup> The entity was first introduced by Flieder *et al.* in 1997, in which have been confirmed by immunohistochemistry and ultrastructural analysis study to share similar

phenotype of the breast counterpart.<sup>5</sup> Since then, there are less than 60 cases have been reported in English language literature and none from Malaysia.

EMPSGC shows a well-circumscribed uni- to multinodular tumour, with solid and cystic lobules some of which with papillary configuration. The tumour cells are uniform, medium-sized, with round to oval-shaped cells, stippled chromatin pattern and abundant cytoplasm. Intracellular mucin is seen within a subset of tumour cells as well as a small amount of extracellular mucin. Areas of in-situ carcinoma are observed in some tumours and in 50% of cases are associated with small foci of conventional mucinous adenocarcinoma.<sup>3</sup>

Immunohistochemical profile supports

neuroendocrine differentiation and breast origin. They are positive for ER, PR, GCDFP-15, chromogranin A, and synaptophysin. The intensity of expression of neuroendocrine markers varied from case to case. Myoepithelial markers highlighted carcinoma-in-situ and very useful in differentiating metastasis from the breast because the latter is lacking in-situ component.

The morphology and immunohistochemical profile show similarities between EMPSGC and solid papillary carcinoma of the breast (SPCOTB), thus making the former considered to be a cutaneous analogue of the latter. Both tumours are characterised by their bland histological appearance, mucin production either intracytoplasmic or extracellular, exhibition of endocrine differentiation and positivity for ER and PR.<sup>3,5</sup> In fact, one should rule out the possibility of metastatic SPCOTB before considering the diagnosis of EMPSGC. In most cases, closed clinico-pathological correlation is required to differentiate these two conditions and considered to be the gold standard.

This tumour, in the absence of mucinous adenocarcinoma shows excellent prognosis after excision with clear margins. The tumour can recur, but distant metastases of EMPSGC have not been documented to date.<sup>6</sup>

## CONCLUSION

EMPSGC is an uncommon, site-specific and newly described malignant sweat gland tumour which appears morphologically identical to solid papillary carcinoma of the breast. In most cases, combined immunohistochemistry that consists of ER, PR, neuroendocrine markers and mucin stain together with the exclusion of breast primary will give a correct diagnosis.

*Conflict of interest:* The authors declare that there is no conflict of interests regarding the publication of this paper.

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