Warthin-like mucoepidermoid carcinoma of the parotid gland: case report

Limin Yan
Tangshan Gongren Hospital
Jinheng Xu
Tangshan Zhongxin Hospital
Liyun Liu
Tangshan Gongren Hospital
Xin Li (xinghaiwuxianmhx@sina.com)
Tangshan Gongren Hospital

Case Report

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Abstract

Warthin tumor (WT)-like mucoepidermoid carcinoma (WT MEC) resembles the histologic pattern of WT, and pathologists unaware of this possibility may misdiagnose it as squamous and mucoepithelial WT or WT malignant transfer into MEC (MEC ex WT). Here, we report a case of a 41-year-old Chinese woman with a solitary mass in the left parotid gland. In this case, microscopic observation revealed prominent lymph node stroma and multiple cystic structures similar to those seen in WT. It lacked the two layers of oncocytic epithelial tissue characteristic of WT. Considering the histological findings, we diagnosed this case as WT MEC. This case provides pathological and clinical features to differentiate from MEC ex-WT and WT with squamous and mucous epithelium. In conclusion, further observations and case reports will clearly define this tumor.

Introduction

Warthin tumor (WT) is a benign neoplasm of salivary gland origin, the second most common after pleomorphic adenoma. The WTs described to date are characterized by a bilayered glandular epithelium with a dense lymphocytic stroma and overlying acidophilic cytoplasm. Mucoepidermoid carcinoma (MEC), characterized as the most common malignant salivary gland neoplasm, is histologically defined by a mixture of three cell types: epidermal cells, intermediate cells, and mucous cells, which may be present in different proportions. In the diagnosis of salivary gland tumors, the term WT MEC was first formally proposed by Ishibashi and colleagues' group in 2015[1]. Because WT MECs are characterized by a close resemblance to the histological pattern of WT, this potential pitfall may go unnoticed and be misidentified as WT[2]. WT MEC is a rare neoplasm, only recently defined, and few cases have been described in the literature. In this study, we present one case of WT MET, a neoplasm arising in the parotid gland.

Case Report

On April 8, 2021, a 41-year-old Chinese woman with a painless mass behind her left ear visited Tangshan Gongren Hospital (Hebei, China) after a 3-day follow-up. Clinical examination revealed a 2.5 x 2 x 2 cm solitary mass arising from the left parotid gland; a CT scan (Fig. 1) revealed a 1.8 x 2.4 cm smooth rounded nodule with varying density and well-defined border. A lumpectomy of the left parotid gland was performed.

The excised tissue measured 3 x 2.5 x 2 cm and, according to gross findings, was an oval nodule with a smooth gray-brown surface (Fig. 2a). Microcapsule structures were also observed within the tumor, and the cross-section of the tumor was shiny (Fig. 2b). Microscopic examination revealed multiple cystic structures of varying size and shaped filled with a protein-like substance all around the tumor (Fig. 3a/b). An infiltration of lymphocytes with the formation of lymph follicles was evident around the cysts (Fig. 3c). The epithelium was multilayered and oncocytic but not malignant characeristcs, containing single scattered mucous cells (Fig. 3d/e). Some cysts were lined by only a single mucinous columnar

epithelium (Fig. 3f). It is noteworthy that small foci of tumor cells infiltrate and proliferate into the surrounding lymphoid stroma (Fig. 3g) and that the normal parotid ducts appeared only around the tumor, and only briefly. (Fig. 3h). On the other hand, no necrotic, keratinized squamous epithelium or bilayered oncocytes were observed.

Immunohistochemical analysis showed that the mucosa cells were positive for CK7 and CK8/18, and the neoplastic epidermal cells were positive for CK5/6, CK8/18, and p40; the cell proliferation index due to ki67 positivity was 5% for both the neoplastic epidermal and mucosal cells (Fig. 4).

Based on these results, the tumor was diagnosed as WT MEC. Based on the final histopathological diagnosis, a parotidectomy and selective ipsilateral neck dissection were performed. Postoperative pathology revealed no residual mass or lymph node metastasis. After one year of postoperative follow-up, there was no evidence of recurrence or metastasis, and no additional treatment was performed.

Discussion

In 2012, Rotellini et al.[3] proposed WT with myxoid and squamous metaplasia. In the same year, Mohapatra and Satyanarayana[4] reported MEC with numerous eosinophilic epithelia lacking typical epidermal, mesenchymal, and mucous cells and with extensive lymphocytic infiltration, which was considered WT MEC for diagnostic purposes. The term WT MEC was first formally proposed in the diagnosis of salivary gland tumors by Ishibashi et al[1] in 2015. Recently, several cases of mutant MEC, consisting of multilayered cuboidal eosinophils and abundant lymphoid tissue with germinal centers similar to the WT form, have been reported[5–6]. In salivary gland pathology, WT MEC is a rare tumor, and many tumors have been misdiagnosed as MT in the past due to the significant histologic similarities that exist between WT MEC and WT[7].

WT and MEC are neoplasms of salivary gland origin and can be characterized as two distinct neoplasms with different histologic diagnostic criteria and clinical features: WT is a clearly demarcated parotid tumor with a cystic structure and variable papillary shape histologically composed of (i) prominent lymphoid stroma and oncocytic epithelial elements; (ii) oncocytic epithelium consists of two layers of outer cuboidal basal cells with nuclei at the base and luminal epithelial cells with nuclei predominantly on the luminal side[8, 9]. On the other hand, MEC, the most common salivary gland malignancy, especially in young adults, typically aggregates epidermal cells, intermediate cells, and mucous cells, forming a solid or cystic pattern[8, 10]. When analyzed histologically, WT MECs observed under low power show a cystic structure of oncocytic epithelial cells with lymphoid interstitium, and their cellular arrangement and characteristics are strongly reminiscent of WT. The most important finding is that WT MECs lack the well-arranged, bilayered oncocytic epithelial tissue characteristic of WT[11]. In rare cases, perineural invasion and necrosis are also observed[12].Only 26 cases of WT MEC have been reported in the literature, including this case, since the first report by Ishibashi et al. in 2015[7, 11, 13]. The most common and predominant complaint is a painless mass, and all cases preferentially affect women and originate in the

parotid gland[11]. It is generally believed that this tumor appears in adults, but it can also occur in teenagers, as the broad age range is 13–60 years[11, 13]. The main pathologic differential diagnoses of MT MEC were WT with squamous and mucous epithelium metaplasia and malignant transformation of benign Warthin's tumor to MEC (MEC ex-WT).

In WT, the formation of squamous and mucous epithelium metaplasia may occur; transformation of WT is usually localized, with an increase in the epithelial layer and the formation of cystic structures covered with mucous and nonkeratinized squamous epithelial cells. However, WT MECs exhibit atypical cells and infiltrative growth and lack the well-arranged bilayered oncocytic epithelial tissue characteristic of WT[14]. The presence of double oncocytic epithelium (mucous and squamous epithelium metaplasia) is one of the most reliable histologic findings that distinguish metaplastic WT from WT MEC In addition, while the transformation of WT to the squamous epithelium is 7.5%, the presence of both mucous and squamous epithelium metaplasia in WT is extremely rare (0.2%)[5]. In addition, since MEC is more common in adults or teenage females but WT is more common in males in their 50s to 60s who are smokers[15], a differential diagnosis may be possible based on these clinical features. The most important finding is that WT, which has both mucous and squamous epithelium metaplasia, lacks the MAML2 rearrangement that is often present in WT MEC and conventional MEC[16]. The present case lacked bilayers of oncocytic epithelial tissue, and the epithelium was multilayered and contained single scattered mucous cells. In addition, there were small foci of tumor cells infiltrating and proliferating into the surrounding lymphoid stroma. Thus, based on this pathologic morphology, this case was diagnosed as WT MEC, but not as WT with mucous and squamous epithelium.

The most common malignant transformation from the epithelial component of WT may result in squamous cell carcinoma. Other malignant metastatic tumors from WT include oncocytic carcinoma, adenocarcinoma, and MEC[14]. Nevertheless, it is important to note that they can occur simultaneously in the salivary glands as collision tumors[17]. To support the diagnosis of MEC ex-WT, Seifert et al.[18] proposed four criteria: (i) the presence of a WT background, (ii) a transition zone between the epithelial components of WT and MEC, MEC ex-WT, (iii) invasive growth into surrounding tissues (iv) exclusion of metastasis of the extra salivary primary tumor to lymphatic stromal components. It is noteworthy that this can also occur in MAML2. In addition, WT generally occurs more frequently in older males; therefore, it is highly unlikely that MEC ex-WT occurs in children or teenagers. Rarely the epithelial portion of WT tumors can become malignant, but the cause of this is not yet fully understood. Stimulation by chronic local inflammation, hypoxia, and ischemia is thought to play an important role in the transformation from benign epithelium to atypical hyperplasia[4]. In the present case, there was no WT background or no transition zone between the epithelial components of WT and MEC. Therefore, we conclude that the final diagnosis in this case is WT MEC, not MEC ex-WT.

The most important diagnostic clue for WT MEC is MAML2 rearrangement by FISH analysis[1], which is specific for MEC and correlates with low- and intermediate-grade histology and improved prognosis[19]. Cytogenetic studies by Citak EC et al.[20], which characterize both MECs, have identified a specific

chromosomal translocation: t(11;19) (q21;p13), resulting in a new fusion oncogene, CRTC1-MAML2. Most recent studies have not reported MAML2 rearrangements in WT; in the study of Bieńkowski et al.[16], MAML2 rearrangements were not observed in 114 WT cases, including WT with squamous and mucous epithelium metaplasia. Although it is unfortunate that FISH analysis of MAML2 was not performed in this case, the diagnosis of WT MEC was possible based on typical histological features.

Current guidelines state that the treatment strategy for MEC is often to perform a total parotidectomy with some degree of neck dissection. In cases of high-grade tissue or positive resection margins, adjuvant radiation therapy should be considered[21]. To date, few cases have been reported with follow-up, but with regard to WT MEC in a 17-year-old female, there is one case of recurrence as a normal MEC 4 years later. However, like low-grade normal MEC, WT MEC appears to have a slow biological behavior[12], and no metastasis of WT MEC has been reported to date. In addition, most cases with WT MEC have been successfully treated with complete local excision. In the present clinical report, since the resection margins and lymph node metastasis were negative, postoperative adjuvant therapy was not performed, and no recurrence or metastasis was observed at 1-year follow-up.

Conclusions

In this clinical report, we describe a rare case of WT MEC and review the previously published literature on this tumor. Clinical and pathologic features may help in the differential diagnosis between WT MEC, WT with squamous and mucous epithelium metaplasia and WT MEC ex-WT., Detection of MAML2 rearrangements may also lead to an accurate pathology diagnosis. However, further observations and more case reports are needed to clearly define this variant.

Declarations

Ethics approval and consent to participate: Approved by the Ethics Committee of Tangshan Gongren Hospital, China.

Consent for publication: No applicable.

Competing Interests: The authors declare that they have no competing interests.

Author contributions: Limin Yan and Xin Li were major contributor in writing the paper; Xinheng Xu and Liyun Liu were responsible for picture collection.

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Availability of data and materials: The ariginal data and Pathological digital section will available upon request. Please send your inquiries to the first author.

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Figures

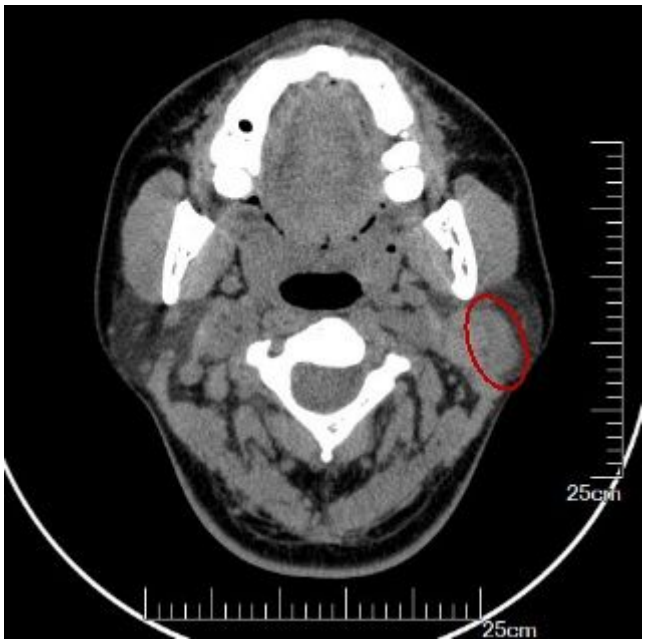

Figure 1

CT scan revealed a smooth rounded nodule with varying density and well-defined border in the left parotid gland (red circle).

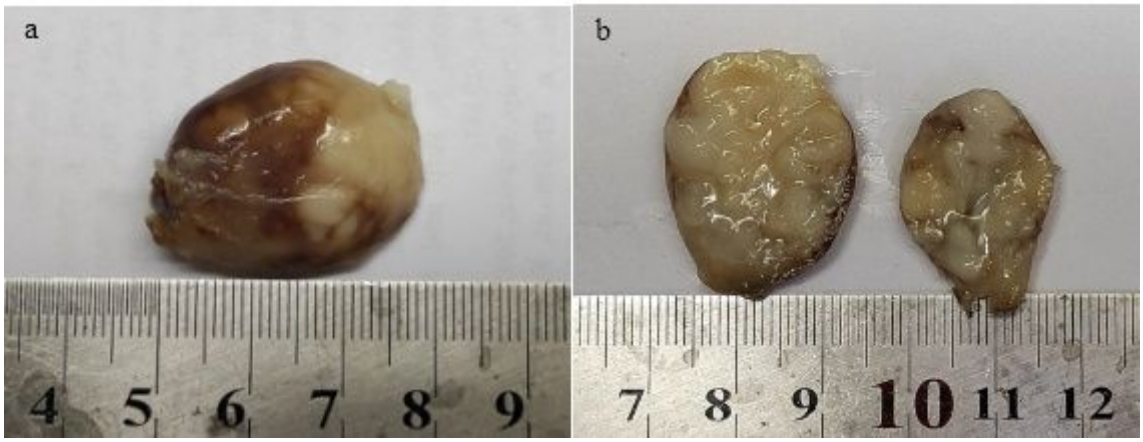

Figure 2

Gross examination. a, oval nodule with smoothly surface; b, the cross-section of the tumor was shiny and with microcapsule structures.

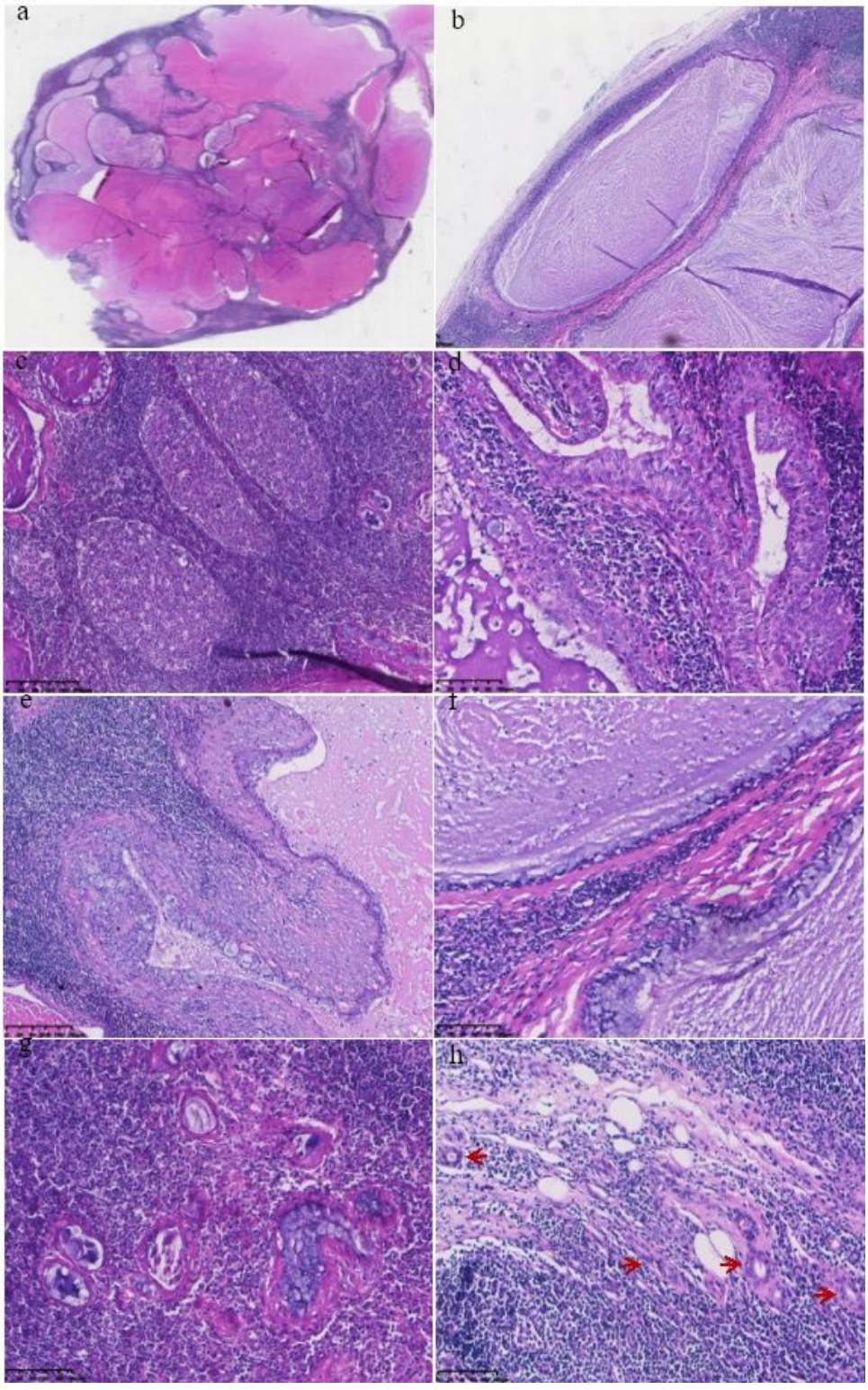

Figure 3

Microscopic examination. a, multiple cystic structures of varying size and shaped all around the tumor (H□E, 5X); b, cystic structures filled with a protein-like substance (H□E, 40X); c, prominent infiltration of lymphocytes around the cysts (H□E,100X); d/e, the epithelium was multilayered and oncocytic, containing single scattered mucous cells (d, H□E,200X; e, H□E,100X); f, cysts lined by only a single mucinous

columnar epithelium (H&E,200X); g, tumor cells infiltrate into the lymphoid stroma (H&E,200X); h, normal parotid ducts appeared around the tumor (red arrow, H&E,200X)

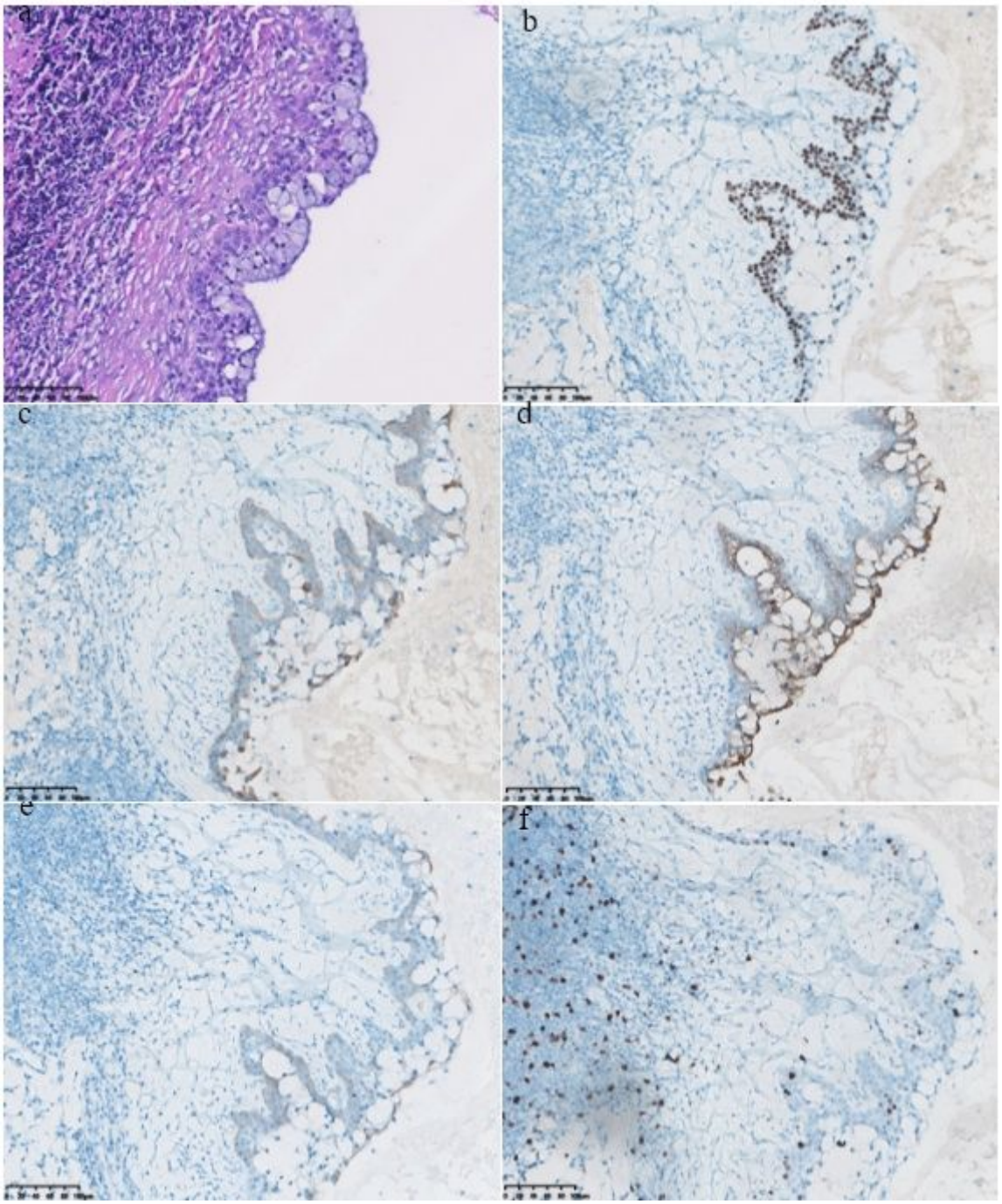

Figure 4

Immunohistochemical staining of the tumour. a, the neoplastic epidermal and mucosa cells in H&E staining (H&E, 200X). b, neoplastic epidermal cells were positive for P40 (IHC, 200X); c, neoplastic epidermal cells were positive for ck5/6 (IHC, 200X); d, neoplastic epidermal cells and mucous cells both positive for CK7 (IHC, 200X); e, neoplastic epidermal cells and mucous cells both weakly positive for CK8/18 (IHC, 200X); f, the proliferation index due to ki67 positivity was 5% (IHC, 200X).