

Salivary Duct Carcinoma with Invasive Micropapillary and Rhabdoid Feature Arising in the Submandibular Gland

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Salivary duct carcinoma (SDC) is a high-grade malignant salivary gland tumor associated with poor prognosis, frequent recurrence, and metastasis. An 82-year-old man presented at the department of oral and maxillofacial surgery at Tokai University Hospital with a painless swelling in the right submandibular region that had been there for 20 years. On presentation, an elastic hard tumor, 50 × 50 mm in size, was observed in the submandibular region. Diagnostic imaging was performed, and a malignant tumor in the submandibular gland was suspected. The suspected tumor was excised and postoperative radiotherapy and adjuvant chemotherapy were performed. Despite this treatment, the patient died of multiple metastases 12 months postoperatively. SDCs are often diagnosed as carcinoma ex pleomorphic adenomas and multiple variants and subtypes exist. This case was histopathologically rare in terms of the coexistence of invasive micropapillary and rhabdoid features.

Key words: Salivary duct carcinoma, rhabdoid feature, invasive micropapillary feature

INTRODUCTION

Salivary duct carcinoma (SDC) is a malignant salivary gland tumor that was first reported by Kleinsasser *et al.* in 1968 [1]. SDC exhibits a histological similarity to infiltrating mammary duct carcinoma [2]. SDC is histologically similar to invasive mammary ductal carcinoma and is characterized by cribriform and central necrosis known as “comedo necrosis.” In addition, immunostaining frequently provided positive results for androgen receptor (AR) and gross cystic disease fluid protein 15 (GCDFP-15).

It represents a rare tumor with an estimated incidence of 1%-3% among all malignant salivary gland tumors. SDC is often observed in men and occurs more commonly in those aged >50 years [3-6]. The parotid gland is most commonly involved; however, submandibular, sublingual, minor salivary gland, maxillary and laryngeal tumors have also been reported [3-6]. Pain and facial palsy are commonly observed as subjective symptoms [7-13]. The carcinogenic process includes *de novo* and/or *ex pleomorphic adenoma* and has relatively longer clinical histories [14]. However, when it exacerbates, it presents as a rapidly growing mass, which develops aggressively with possibilities of early distant metastases, local recurrence, and high mortality. The local recurrence rate of SDC is 30% and lymph node metastasis rate is 60%, while the distant metastasis rate is 30%-70% [2, 4-6].

Recently, it has been reported that subtypes such as sarcomatoid variant [15, 16], invasive micropapillary variant [17], and mucin-rich variant [18] exist in SDC.

In this study, we encountered a case of SDC with the

coexistence of invasive micropapillary and rhabdoid feature. This case may contribute to elucidating the process of SDC development.

CASE REPORT

An 82-year-old man was presented to the Department of Oral and Maxillofacial Surgery, Tokai University Hospital, with swelling in the right submandibular region for 20 years. The submandibular region was grown over 3 months. Clinical examination revealed a painless hard mass measuring 55 × 45 mm that was detected in the right submandibular region. Enhanced computed tomography (CT) showed a tumor exhibiting internal calcification and an enhanced margin within the right submandibular gland (Fig. 1). With the diagnosis of a right submandibular gland tumor, tumor resection was performed under general anesthesia. Frozen section diagnosis conducted during the operation showed the presence of a malignant salivary gland tumor arising from the submandibular gland. Therefore, neck dissection (American Joint Committee on Cancer level I to V) was additionally performed. The extracted tumor was gray-white to yellow-brown, and its core was solid. Consequently, the histopathological diagnosis was SDC. Metastasis was noted in 30 cervical lymph nodes. Postoperative radiotherapy (whole neck, 50 Gy) and adjuvant chemotherapy (docetaxel 60 mg/m², cisplatin 60 mg/m², 5-fluorouracil 600 mg/m² × 5 days: TPF therapy) were administered. Ten months postoperatively, CT revealed multiple metastases in the lung and spines and subcutaneous to the precordium. Radiotherapy (30 Gy/40 Gy) was administered to the metastasized spine and the

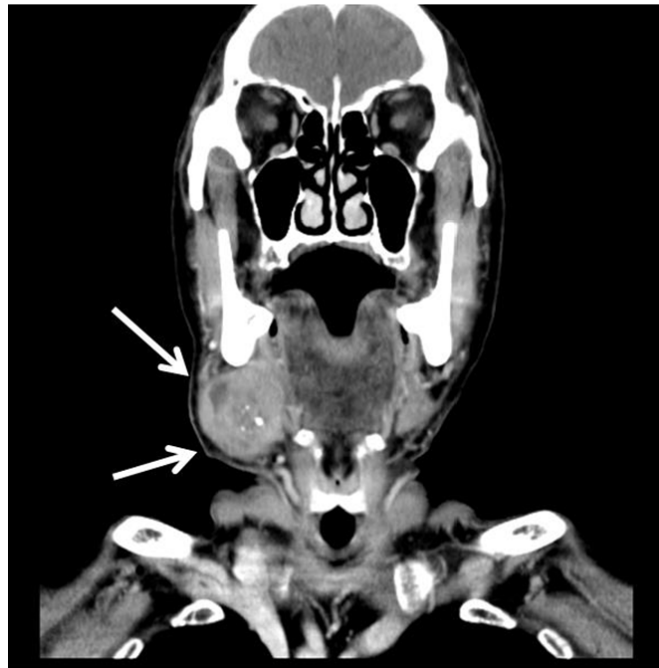


Fig. 1 Contrast-enhanced coronal CT image: There was a tumor associated with calcification in the right submaxillary gland, showing contrast effects along the periphery (arrow).

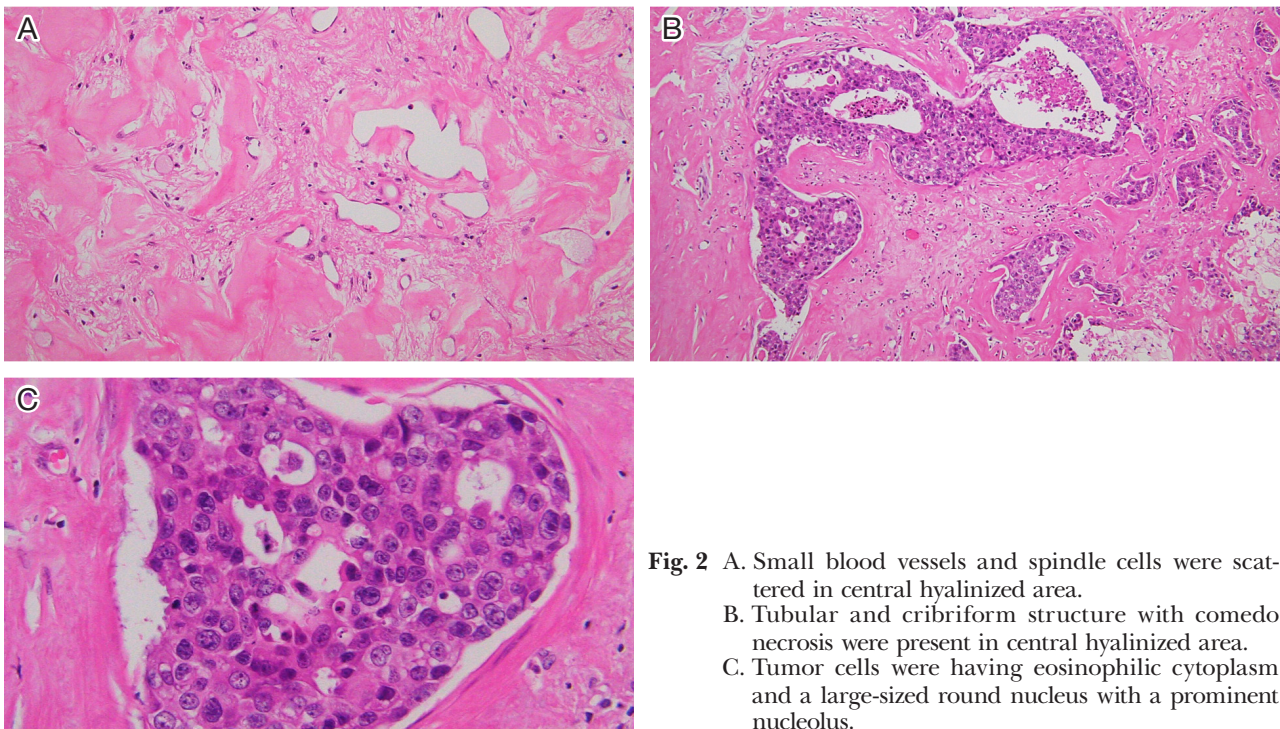


Fig. 2 A. Small blood vessels and spindle cells were scattered in central hyalinized area.
B. Tubular and cribriform structure with comedo necrosis were present in central hyalinized area.
C. Tumor cells were having eosinophilic cytoplasm and a large-sized round nucleus with a prominent nucleolus.

subcutaneously metastasized precordium to alleviate pain. Although the procedure relieved the patient's pain, he died 12 months after the operation.

Histopathological findings

A 60 × 45 × 40 mm-sized tumor in right submandibular gland was resected. On cut surface, greyish-white, irregular-shaped solid mass with central hyalinized area was observed. Histologically, central hyalinized area showed glassy stroma with scattered small blood

vessels and spindle cells (Fig. 2A). Chondroid or myxoid stroma was absent. In part, tumor cells having eosinophilic cytoplasm and a large-sized round nucleus with a prominent nucleolus proliferated in tubular and cribriform structure with comedo necrosis (Fig. 2B, 2C). Surrounding solid area showed a proliferation of tumor cells in diffuse, trabecular and micropapillary structure. Two types of tumor cells were seen. One had eosinophilic cytoplasm and a large-sized round nucleus with a prominent nucleolus in trabecular and micro-

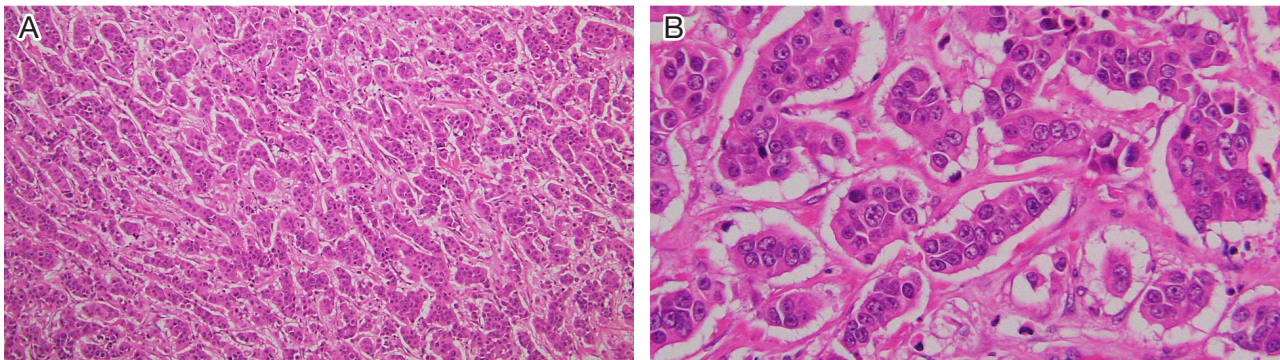


Fig. 3 A. Trabecular and micropapillary structure were present around hyalinized area.
B. Tumor cells were having abundant eosinophilic cytoplasm and a large-sized round nucleus with a prominent nucleolus.

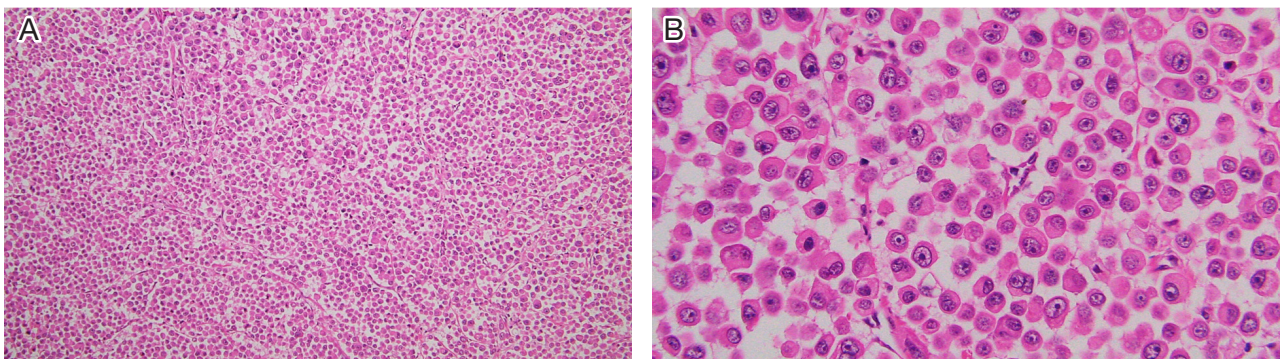


Fig. 4 A. Diffuse pattern were present around hyalinized area.
B. Tumor cells were having abundant eosinophilic cytoplasm and a large-sized nucleus displaced in periphery of cell, indicating rhabdoid cells.

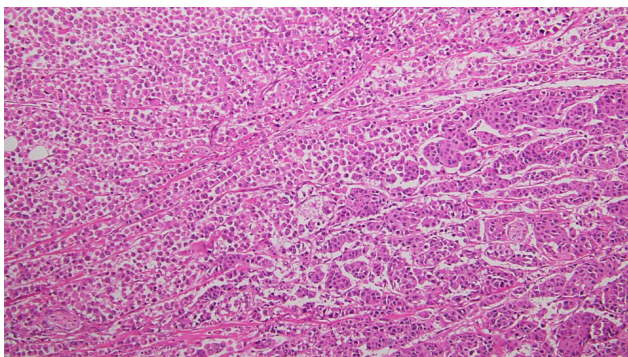


Fig. 5 Transitional area was observed in diffuse, trabecular and micropapillary structure.

papillary structure (Fig. 3A, 3B), and another had abundant eosinophilic cytoplasm and a large-sized nucleus displaced in periphery of cell in diffuse pattern, indicating rhabdoid cells (Fig. 4A, 4B). Transitional area of these two was present (Fig. 5). A diagnosis of SDC with invasive micropapillary and rhabdoid feature was made. In immunohistochemistry, Tumor cells in tubular, cribriform, trabecular and micropapillary structure were positive for human epidermal growth factor receptor 2 (HER2), focally positive for androgen receptor (AR) and gross cystic disease fluid protein 15 (GCDFFP15) and negative for vimentin (Fig. 6 and 7). Rhabdoid cells in the diffuse pattern were positive for AR, HER2 and GCDFFP15 and negative for vimentin (Fig. 8). These staining pattern correspond to that of a SDC. Spindle cells in central hyalinized area were positive for Actin-SM (SMA), p63 and S-100 protein (S-100), suggesting atrophic myoepithelial cells (Fig.

9). It is considered that central hyalinized area was remaining pleomorphic adenoma (PA). Regarding the cervical lymph node metastasis, both two types of tumor cells in diffuse, trabecular and micropapillary structure were observed (Fig. 10).

DISCUSSION

Recently, it has been reported that subtypes such as sarcomatoid variant [15, 16], invasive micropapillary variant [17], and mucin-rich variant [18] exist in SDC.

Invasive micropapillary variant is a variant of SDC described by Nagao *et al.* in 2004. It is histologically characterized by a small nest in the area of infiltration and its surrounding gap. Cervical lymph node metastasis was observed in almost all patients and comparison of the 2-year survival rate with conventional SDC indicated the prognosis to be significantly poor [17]. This patient was not diagnosed as an invasive micro-

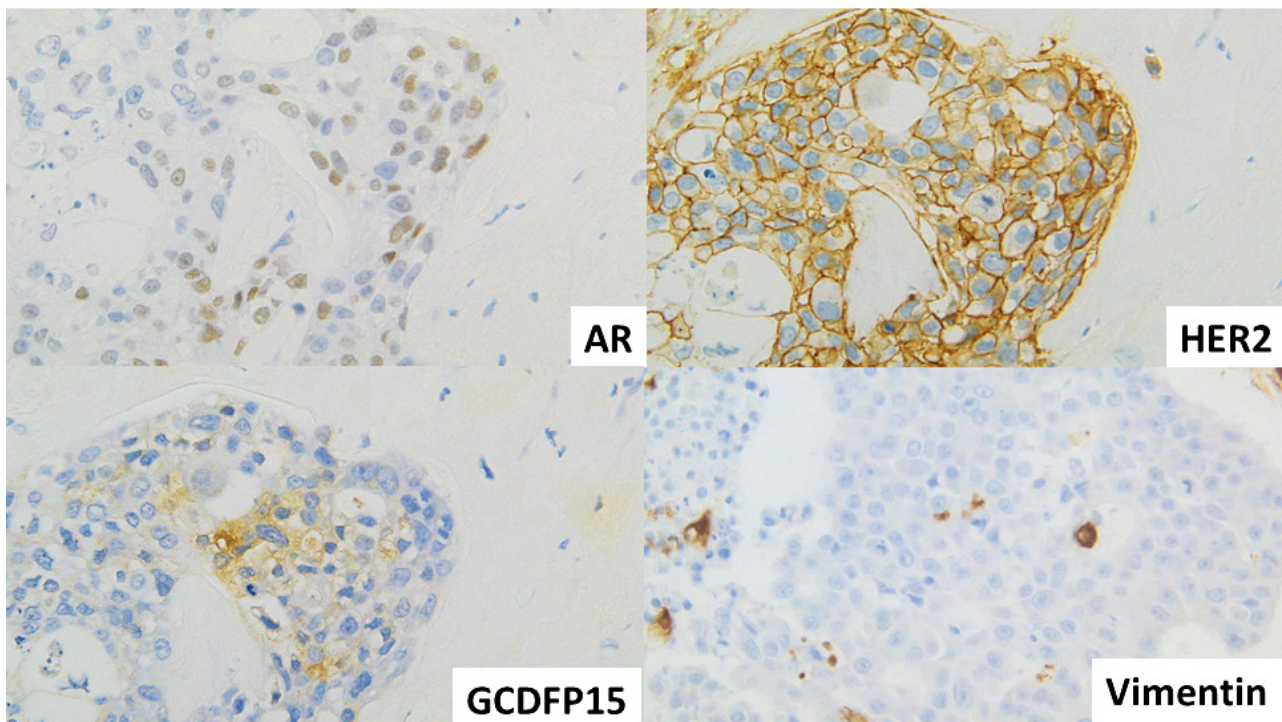


Fig. 6 In immunohistochemistry, tumor cells in tubular and cribriform structure were positive for HER2, focally positive for AR and GCDFP15 and negative for vimentin.

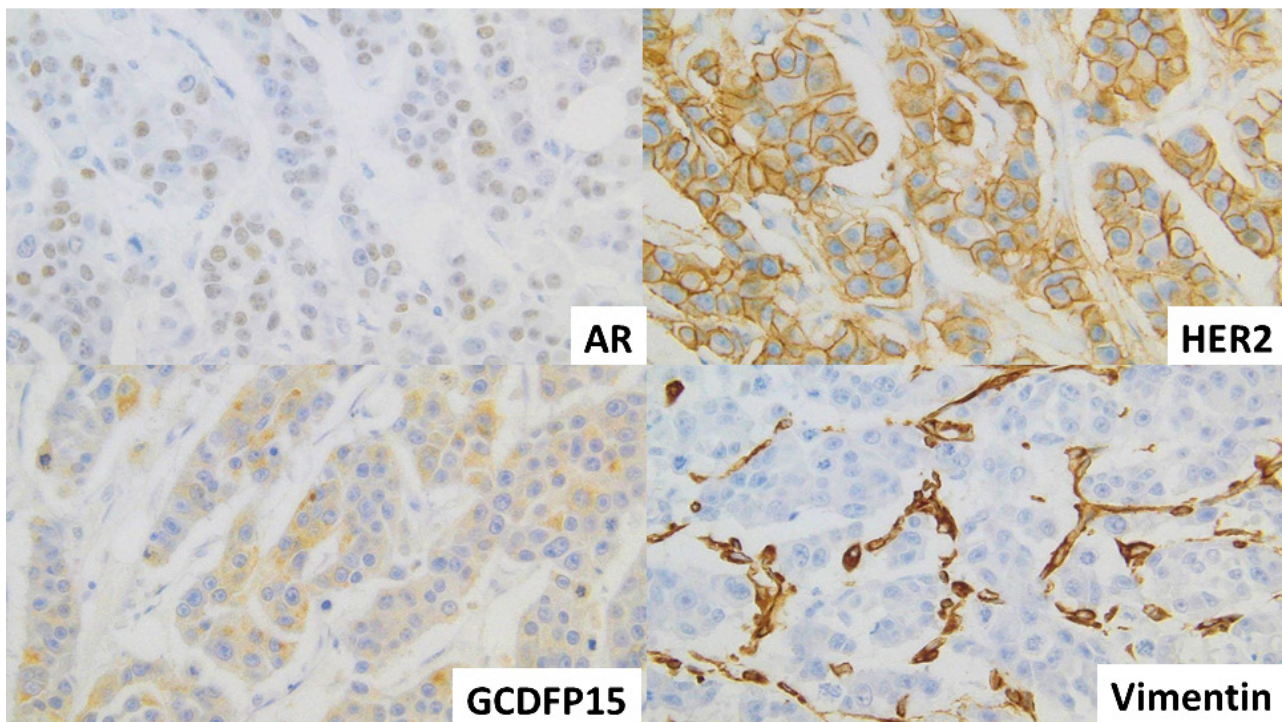


Fig. 7 In immunohistochemistry, tumor cells in trabecular and micropapillary structure were positive for HER2, focally positive for AR and GCDFP15 and negative for vimentin.

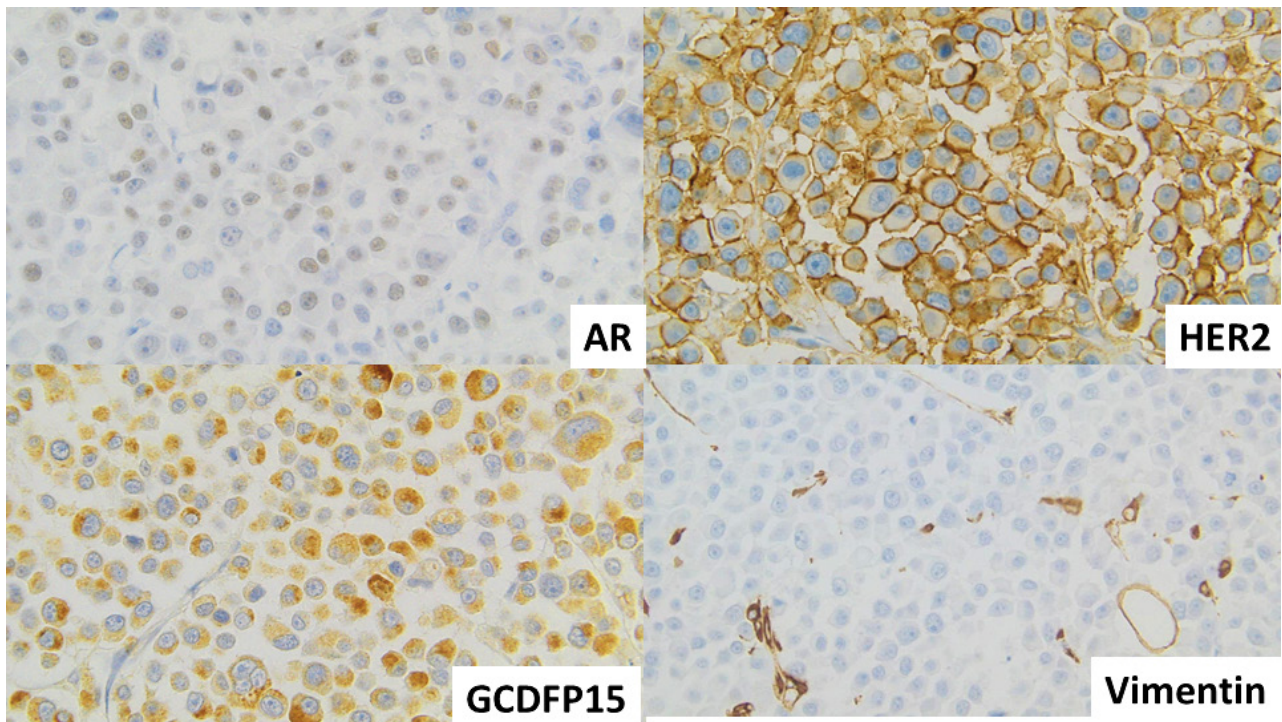


Fig. 8 In immunohistochemistry, rhabdoid cells in diffuse pattern were positive for AR, HER2 and GCDFP15 and negative for vimentin.

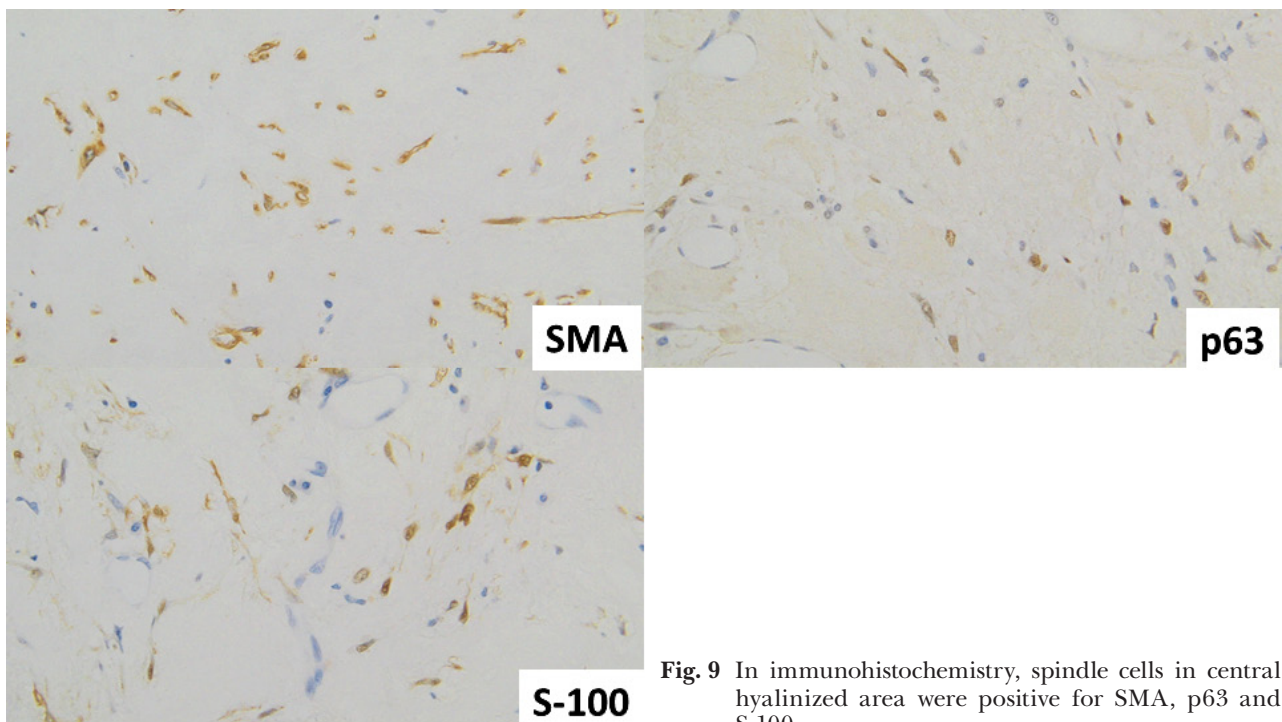


Fig. 9 In immunohistochemistry, spindle cells in central hyalinized area were positive for SMA, p63 and S-100.

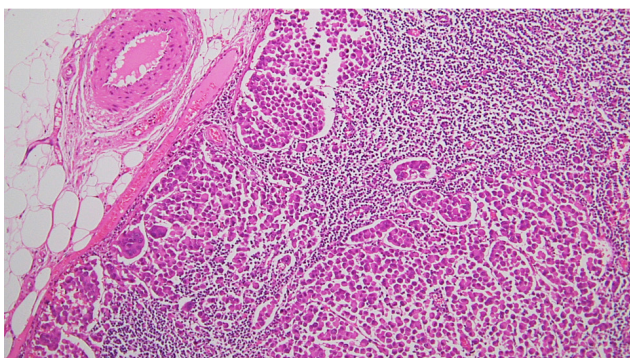


Fig. 10 Both two types of tumor cells in diffuse, trabecular and micropapillary structure were observed in cervical lymph node metastasis.

papillary variant. However, his condition seemed to be similar to invasive micropapillary variant in terms of poor prognosis, resulting in lymph node or distant metastasis.

In addition, SDC rhabdoid feature represents a rare type of SDC reported by Kusafuka *et al.* in 2014 [19]. It develops at a rate of 0.4% of overall SDC commonly in men. The most common site for its development is the parotid gland, followed by the submandibular gland. The condition frequently represents ex pleomorphic adenoma [20]. Its prognosis is poor. This patient met the aforementioned conditions. The immunohistochemical examination provided positive results for AR, GCDFP-15, cytokeratin (CK), and HER-2 and a negative result for vimentin.

Moreover, Kusafuka *et al.* have described that because of no or an aberrant expression of E-cadherin and beta-catenin, the rhabdoid feature of SDC represents a rare subtype of SDC rather than a sarcomatoid variant SDC [20].

Because this patient also had a negative result for vimentin, it may be appropriate to consider that he had the morphological rhabdoid feature.

This patient presented with an interesting histological image of coexistence of invasive micropapillary and rhabdoid feature. Currently, to our knowledge, there is no report on SDC with coexistence of two features, and this case is extremely rare.

There is no effective treatment procedure for treatment of SDC other than operative treatment and postoperative radiation therapy [21–27]. In the present case, the patient underwent chemotherapy (TPF therapy) in addition to postoperative radiation therapy. TPF therapy is frequently administered in the head and neck region; however, there have been few reports on salivary gland cancer and therefore, the effect is unknown [28]. However, since multiple cervical metastases were confirmed in this case and poor prognosis was expected, TPF therapy was added to postoperative chemoradiotherapy.

Therefore, the cervical region was controllable with postoperative treatment and distal metastasis could not be prevented. SDC is a cancer with an extremely poor prognosis, and there is an urgent need for the development of treatments. The present case tested immunohistochemically positive for HER-2/AR. Therefore, it was considered that molecular-targeted agents against HER-2 and AR were effective [29–30]. Although the incidence rate of SDC is low, it is planned to conduct clinical studies of drugs, including molecular-targeted agents against SDC in a limited number of patients. As SDC derived from pleomorphic adenoma occurs more commonly, it was considered necessary to provide operative treatment for benign salivary gland tumor early without leaving it untreated.

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CONFLICT OF INTEREST

None of the authors have any conflict of interest to be reported.

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