Proximal-type epithelioid sarcoma of pharynx: A case report with immunohistochemical study

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Abstract Epithelioid sarcoma (ES) usually occurs in extremities. ES shows characteristic granulomatous morphologies, and its prognosis is not so poor. Proximal-type ES (PT-ES) is a variant of ES, and is characterized by central locations, severe atypical features, and poor prognosis. Both ES and PT-ES histologically show epithelial and sarcomatous patterns, and immunohistochemically express both vimentin and cytokeratins. A 77-year-old man presented with sore throat. The laryngoscope revealed a large polypoid tumor (4 × 3 × 4 cm) in upper pharynx, and a large biopsy was taken. The biopsy showed malignant epithelioid and spindle tumor cells. There were no apparent transitions between normal epithelial cells and tumor cells. The tumor consisted of malignant epithelioid and spindle cells with marked anaplasia. The tumor showed marked infiltrative features and lymphovascular permiations. Mitotic figures, atypical mitosis, and necrotic areas were present. No apparent features of sarcomas were seen. No rhabdoid cells were seen. Immunohistochemically, the malignant cells were positive for vimentin (3+, diffuse), CK AE1/3 (1+, focal), CK CAM5.2 (1+, diffuse), CK8 (1+, focal), CK18 (1+, focal), CD20 (1+, focal), p53 (3+, 84%), Ki-67 (labeling = 94%), CD68 (2+, only focal), and anti-trypsin (2+, only focal). They were negative for CK34BE12, CK5, CK6, CK7, CK14, CK19, CD99, CEA, CA19-9, CA125, EMA, S100 protein, NCAM, NSE, synaptophysin, chromogranin, α-smooth muscle actin, smooth muscle actin, desmin, CD34, CD31, CD45, D2-40, factor-VIII-related antigen, HMB-45, Melan-A, myoglobin, MDM2, CDK4, KIT, and PDGFRA. The author diagnosed this pharyngeal tumor as PT-ES, but the author cannot completely exclude the possibility of sarcomatoid carcinoma. The prognosis of patient was poor; the patient died of carcinomatosis 2 years after the manifestation.

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Introduction

According to WHO blue book [1], epithelioid sarcoma (ES) is defined as a distinctive sarcoma of unknown lineage showing predominantly epithelioid cytormorphology, affecting mainly adolescents and young adults. This tumor may be misdiagnosed as a benign lesion, especially as a benign granulomatous process [1]. Certainly, ES often
affects extremities especially in fingers and often shows granulomatous features. However, deep and central located more monotonous, atypical, aggressive variant is seen [2,3]. This is now called proximal-type ES (PT-ES). The PT-ES showed more atypical features, and some of them show rhabdoid features. The pathological diagnosis of classical ES is relatively easy, but the diagnosis of PT-ES of deep-located and situated in epithelial tissue is very difficult. In the epithelial tissue, PT-ES should be differentiated from sarcomatoid carcinoma (SC). This distinction is very difficult and the criteria have not been established.

In head and neck regions, of course, there have been no reports of ES. In addition, there have been only a few cases of sarcomatoid carcinoma (SC) in head and neck region including the pharynx [4,5]. The author herein reports a very rare case of PT-ES of pharynx, with immunohistochemical studies.

**Case report**

A 77-year-old man consulted our hospital because of sore throat. The tumor markers were within normal ranges. The laryngoscope revealed a large polypoid tumor (4 × 3 × 4 cm) in the upper pharynx, and a large biopsy was taken.

The biopsy contained non-tumorous respiratory epithelium and malignant tumor cells (Fig. 1A). No apparent transitions between the normal epithelium including surface respiratory and glandular epithelium and the tumor cells were seen. The tumor was medullary, and consisted of epithelioid malignant cells. However, spindle tumor cells were also seen in broad areas. The tumor showed marked infiltrative features. Lymphovascular permeations were noted. No apparent features of carcinoma were seen. No angiomatoid areas were seen. No storiform-pleomorphic pattern as seen in malignant fibrous histiocytoma (MFH) was seen, and no apparent features of other sarcomas were seen. No rhabdoid cells were seen. The tumor cells showed marked cellular atypia, numerous mitotic figures, and necrotic areas. Atypical mitotic figures were also scattered. The tumor cells showed relatively clear cytoplasm and had vesicular nuclei with prominent nucleoli. No pigment was seen. The histological diagnosis was sarcoma, sarcomatoid carcinoma (SC), amelanotic melanoma, or epithelioid sarcoma (EC).

An immunohistochemical study was performed by Envision Method and its variants, as previously reported [6-10]. Immunohistochemically, the malignant cells were

![Fig. 1](image-url) Histological findings of the pharyngeal tumor. A: Low power view. The specimens contain normal pharyngeal epithelium and malignant tumor cells. There are no transitions between the tumor and pharyngeal normal epithelial cells. The tumor has high grade atypia and high invasive features. HE, ×40. B: High power view. The tumor shows high grade atypia including hyperchromasia, numerous mitotic figures, vesicular nuclei, and prominent nucleoli. In this area, the tumor cells are round and are highly epithelioid with clear cytoplasms. HE, ×200. C: High power view of the pharyngeal tumor. These are spindle-shaped cells with high grade atypical features. Nevertheless, the tumor cells are somewhat epithelioid with focal clear cytoplasms. HE, ×200.
positive for vimentin (3+, diffuse) (Fig. 2A), cytokeratin (CK) AE1/3 (1+, focal), CK CAM5.2 (1+, diffuse) (Fig. 2B), CK8 (1+, focal), CK18 (1+, focal) (Fig. 2C), CK20 (1+, focal), p53 (3+, 84%) (Fig. 2D), Ki-67 (labeling = 94%), CD68 (2+, only focal) (Fig. 2E), and anti-trypsin (2+, only focal) (Fig. 2F). They were negative for CK34BE12, CK5, CK6, CK7, CK14, CK19, CK20, CD99 (MIC-2), CEA, CA19-9, CA125, EMA, S100 protein, NCAM, NSE, synaptophysin, chromogranin, α-smooth muscle actin (ASMA), smooth muscle actin (HHF-35), desmin, CD34, CD31, CD45, D2-40, factor-VIII-related antigen, HMB-45, Melan-A, myoglobin, MDM2, CDK4, KIT, and PDGFRA.

The author made the pathological diagnosis of proximal-type epithelioid sarcoma (PT-ES). The biopsy diagnosis, whole body examinations including CT, MRI, PET, endoscopes were done, and it was found that the patients had brain metastases and lymph nodes metastases of the head and neck. The patient was treated by chemotherapy and radiation, but the patient died of carcinomatosis 2 years after the presentation.

Discussion

The pathological diagnosis is the most important point in this case. The high grade malignancy of the present tumor was apparent. The histology showed high grade atypia, numerous mitotic figures including atypical mitoses, and necrotic areas. Much infiltrative features and lymphovascular permeation were seen. In addition, the immunohistochemistry showed high p53 expression and very high Ki-67 labeling (94%). Thus, the present tumor is very aggressive tumor.

The tumor cells expressed mesenchymal antigen, vimentin, and epithelial antigens CK AE1/3, CK CAM5.2, CK8 and CK18. EMA was negative. Thus, the present showed both epithelial and mesenchymal phenotypes. The present tumor is not amelanotic malignant melanoma, because the present tumor was negative for HMB45, S100 proteins, and melan-A. In addition, the present tumor appears not to be ordinary sarcomas, such as malignant peripheral nerve sheath tumor (MPNST), leiomyosarcoma (LS), angiosarcoma (AS), and malignant fibrous histiocytoma (MFH). These tumors can be excluded histologically and immunohistochemically. The present tumor is not neurogenic MPNST because of its different morphology as well as no immunoreactive neuroendocrine molecules (NSE, NCAM, synaptophysin, KIT, and PDGFRA) and negative desmin. The LS is unlikely because no expression of smooth muscle actins was seen. The LS (pleomorphic or dedifferentiated type) was unlikely because of age and because of negative MDM2, CDK4 and lipoblasts. The present tumor is different from RS because of the age and negative myoglobin. The tumor is not AS or lymphangiosarcoma because no vascular or microcystic patterns were seen and also because CD31, CD34, and D2-40 were negative. The present tumor is not MFH, because the common features of MFH, i.e., storiform-pleomorphic pattern, are not seen. Although the present tumor focally expressed CD68 and
anti-trypsin, these molecules are not specific for MFH. MFH is waste basket diagnosis. In any way, because the tumor cells expressed CK, all the above tumors were quite unlikely.

Thus, the remaining are sarcomatoid carcinoma (SC) and epithelioid sarcoma (ES). The present tumor is not classical ES, which shows characteristic granulomatous appearances. ES shows milder atypia in extremities, but proximal-type ES (PT-ES) exhibits severe anaplasia. This distinction appears very difficult or impossible. The present tumor was positive for vimentin and CK, thus showing both epithelial and mesenchymal lineage. However, as is well known, the myth of specificity of the 5 intermediate filaments was already destroyed. It is widely known that CK may be positive in mesenchymal tumors and vimentin in the epithelial neoplasms. However, these two antigens are now used to discriminate between carcinoma and sarcoma because no other methods for the discrimination are now available.

Certainly, the present tumor is either PT-ES or SC. If this tumor would be located in soft tissue free from epithelial cells, the diagnosis of PT-ES is easy. The problem is the location. Although the present tumor expressed both vimentin and CKs, the expression of vimentin is much more strong and diffuse than that of CKs. In addition, there were no merges between the tumor cells and normal pharyngeal epithelium is in favor of PT-ES. The histology is typical for PT-ES, though rhabdoid cells are absent. The rhabdoid cells are not prerequisite for PT-ES. On the other hand, the present case may be SC of the pharynx, a very rare condition. It seems that the discrimination between PT-ES and SC is very difficult or impossible. The author pushes the diagnosis of PT-ES only because of the histology and predominant vimentin intermediate filament.

The PT-ES has rarely investigated. In 1997, Guillou et al. [2] coined the term of proximal-type epithelioid sarcoma (PT-ES) and described clinicopathologies of 18 patients. The PT-ES is male dominant and occurs in relatively young persons with mean of 35 years. The sites of involvement were central soft tissues. The mean size was 4 cm. Immunohistochemically, the expressions of vimentin, CK, and EMA were seen. The PT-ES may be positive for desmin, CD34, and smooth muscle actin. Expressions of HMB45 and CEA were exceptional. S100 and CD31 were consistently negative. Rhabdoid phenotype was occasionally seen in histological and ultrastructural studies. The differential diagnoses were classical ES, epithelioid MPNST, extrarenal rhabdoid tumor, melano-

ma, RS, and undifferentiated carcinoma. The biological behavior of PT-ES was not good; the prognosis ranged from 4 months to 8 years with a median of 19 months. Thus, the PT-ES shows much poorer outcome than classical ES.

In 2001, Hasegawa et al. [3] reported 20 cases of PT-ES. In their cases, male predominance and young age (mean 40 years) were recognized. Of the 20 cases, 17 were located in central soft tissue and 3 were located in mucosa where epithelial cells are present. The mean size was 8 cm. The tumor frequently showed rhabdoid phenotype. Immunohistochemically, all cases were positive for vimentin and CK20. EMA was recognized in 85%, CD34 in 45%, CD99 in 25%, desmin in 15%, smooth muscle actin in 15%, p53 in 80%, and Ki-67 > 30% in 70%. The prognosis was poor; local recurrence was seen in 65% and metastases in 65%. Large tumor size and early metastases were independent poor prognostic factors.

The author has no conflict of interest.

References