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Original Article

Clear cell sarcoma of soft tissue in right parapharyngeal region: report of a rare case

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Abstract: Clear cell sarcoma (CCS), initially named malignant melanoma of soft parts, is a rare malignant neoplasm typically involving deep soft tissue of the extremities, in close proximity to tendons and aponeuroses. Here we describe a case of clear cell sarcoma of the right parapharyngeal region in a young female aged 20 years. MRI detected a mass about 4.4 cm×3.4 cm×3.0 cm, located in the right parapharyngeal area and between the external pterygoid and the medial pterygoid. Microscopically, most of the tumor cells were epithelioid with palely eocinophilic cytoplasm arranged in sheets. Pleophorism of tumor cells were not marked. Immunohistochemical analysis shows that the tumor cells were positive for vimentin, S-100, HMB45 and MelanA, and negative for AE1/AE3, actin-sm, desmin, CD117, TFE-3, and P63. Ki67 index was about 5%.

Keywords: Clear cell sarcoma, clear cell sarcoma of soft tissue, parapharyngeal region, malignant melanoma, alveolar soft part sarcoma

Introduction

Clear cell sarcoma of soft tissue is a rare sarcoma, which represents about 1% of all sarcomas [1-5]. It mainly affects young adults between the ages of 20 and 40 years with a female predominance [1-9]. It was originally described by Enzinger et al and designated as malignant melanoma of soft parts because it shows melanocytic differentiation [1-4]. However it differs from cutaneous malignant melanoma by virtue of its soft tissue location in association with tendons and aponeuroses [1-5]. Clear cell sarcoma usually occurs in deep soft tissues in the extremities and involvement of the head and neck region is rare [1-5]. Here we present a rare case of clear cell sarcoma in the right parapharyngeal region in a 20-year-old female. The mass was about 4.4 cm×3.4 cm×3.0 cm and located between the external pterygoid and the medial pterygoid. Most of the tumor cells were epithelioid, with palely eocinophilic cytoplasm, arranged in sheets. The tumor cells were positive for vimentin, HMB45, MelanA, and S-100.

Case presentation

Clinical history

A 20-year-old female referred to our hospital because of right pharyngeal pain for 2 months. The pain was intermittent and without incentive. The patient reported no pharyngeal foreign body sensation, choke when drinking, dysphagia, dyspnea, fever or significant changes in body weight. She received no treatment before. Laryngoscope showed diffuse shallow ulcers on the membrana mucosa laryngis and right parapharyngeal area bulging. The chest X-ray showed no abnormality.

Materials and methods

Specimens resected were fixed with 10% neutralbuffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4 μm-thick sections and were dewaxed in xylene and rehydrated stepwise in descending ethanol series. Then the sections were boiled in citrate buffer (pH 6.0). Endogenous peroxidase activity and non-specific binding were blocked with 3% H_2O_2

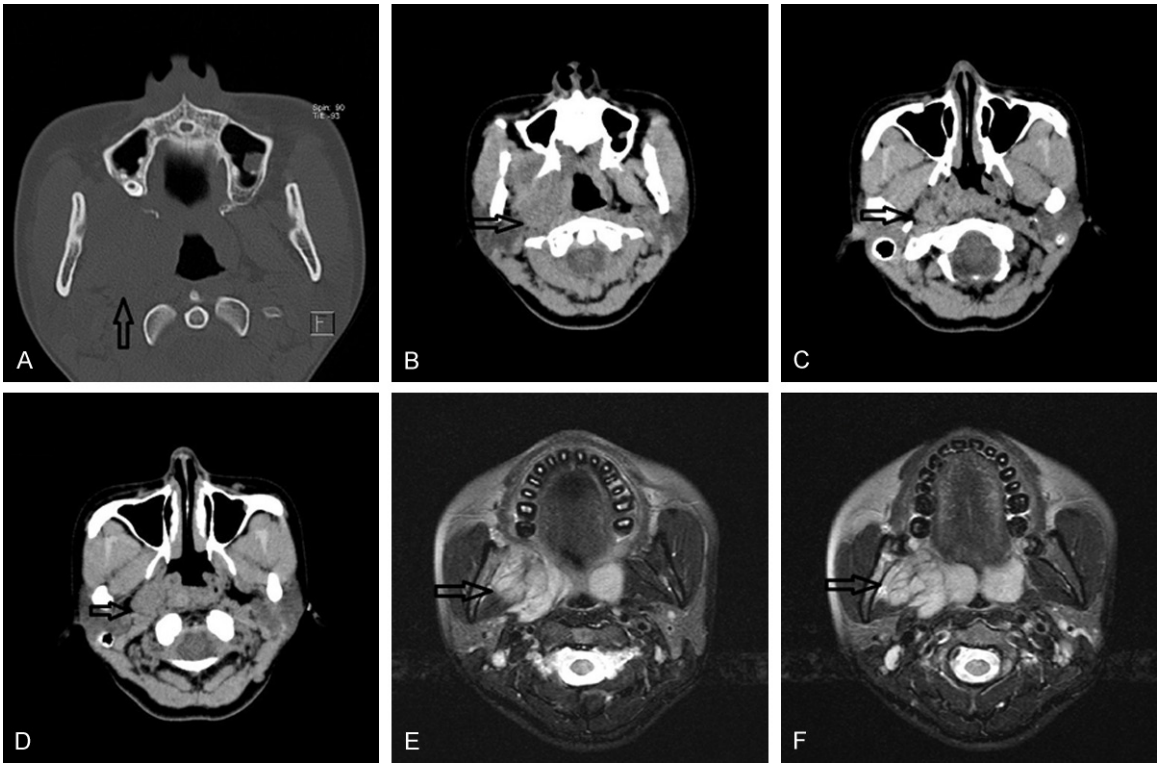

Figure 1. Imaging of the tumor. The CT detected the lesion but the border is not clear. We can know only an approximate location of the mass from the image (black arrow) (A). The enhancement CT detected the mass (black arrow) more clearly (B-D). The tumor was most clearly found in the MRI imaging (black arrow) (E, F).

and non-immune sera, respectively. The sections were incubated with the following primary antibodies: actin-sm (1:50, DAKO), AE1/AE3 (1:50, DAKO), CD117 (1:50, DAKO), CD34 (1:100, DAKO), desmin (1:50, DAKO), HMB45 (1:50, Abcam), Ki67 (1:200, DAKO), Melan-A (1:50, DAKO), P63 (1:100, DAKO), S-100 (1:50, DAKO), TFE-3 (1:100, Abcam), and vimentin (1:200, DAKO) overnight at 4°C. The catalyzed signal amplification system (Maixin Biotechnology, Fuzhou, Fujian, China) was used for staining of these proteins according to the manufacturer's instructions. The antibodies were detected by a standard avidin-biotin complex method with biotinylated secondary antibodies (Maixin) and an avidin-biotin complex (Maixin), and developed with diaminobenzidine. Counterstaining was done lightly with hematoxylin, and the sections were dehydrated in alcohol before mounting.

Results

Imaging and gross features

CT and MRI detected a parapharyngeal mass (**Figure 1**) in the patient. The mass was located in the right parapharyngeal area and between the external pterygoid and the medial pterygoid, and about 4.4 cm×3.4 cm×3.0 cm (vertical diameter, transverse diameter, anteroposterior diameter) (**Figure 1E**, **1F**). The medial pterygoid was wrapped and pressed and the borderline became unclear. The relative parapharyngeal interspace disappeared. No destruction was found in adjacent bones. The surgical information indicates that the upper pole of the mass reached the scull base and was very difficult to be separated. A nodule about 6.5 cm×4.5 cm was removed. Grossly the tumor was firm and grey-white and the border was well-circumscribed and pushing.

Microscopic features

Tumor cells were diffusely and densely attributed (**Figure 2**). Characteristic nested growth pattern and collagenous bands were focally present in this case. Most of the tumor cells were round or polygonal arranged in sheets (**Figure 2A**). In some areas the tumor cells were spindle and storiform-like architectures were formed (**Figure 2B**). The tumor cells infiltrated

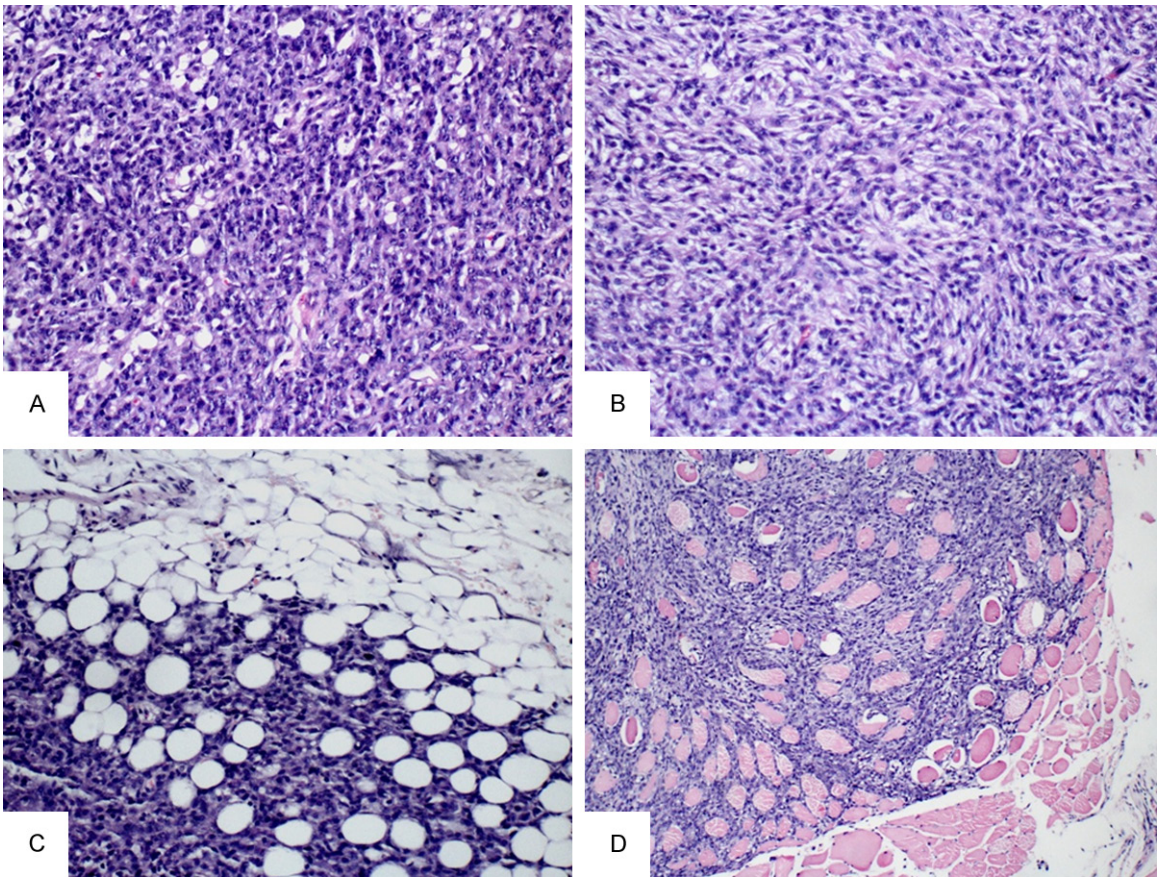

Figure 2. Microscopic findings of the tumor: architecture and growth pattern. Most of the tumor cells were arranged in sheets (A) (In some areas storiform-like architectures were formed (B). The tumor cells infiltrated into the adjacent adipose tissue (C) and muscle tissue (D).

into the adjacent adipose tissue (**Figure 2C**) and muscle tissue (**Figure 2D**). Most of the tumor cells were epithelioid, with palely eocinophilic cytoplasm (**Figure 3A**). A minority of tumor cells showed true clearing cytoplasm (**Figure 3B**). The nuclei of the cells were vesicular and had macronucleoli. Nuclear atypia was not prominent. The mitotic activity was lower and <5 mitoses/50HPF. A few areas with spindle tumor cells presented as seen in **Figures 2B** and **3C**. Marked nuclear pleomorphism only presented in a few areas of the tumor tissues (**Figure 3D**).

Immunophenotype

Immunohistochemical analysis shows that the tumor cells were diffusely positive for vimentin, HMB45, and MelanA, focally positive for S-100 (nuclear immunostaining), and negative for actin-sm, CK (AE1/AE3), CD117, CD34, desmin, P63, and TFE-3 (**Figure 4**). CD34 immunostaining indicates abundant capillaries in tumor tissues. Ki67 index was about 5% (**Figure 4**).

Discussion

Clear cell sarcoma is a rare sarcoma with consistent melanocytic differentiation which was first described by Enzinger et al and designated as malignant melanoma of soft parts because of its immunohistochemical resemblance to malignant melanoma [1-4]. It represents about 1% of all sarcomas and mainly affects young adults between the ages of 20 and 40 years with female predominance [1-5]. It occurs most commonly in the extremity, especially in the foot/ankle region which accounts for about 40% of cases [1-5]. Involvement of the head and neck region is rare. Here we report a rare case of clear cell sarcoma in the right parapharyngeal region in a 20-year-old female, who referred to our hospital for right pharyngeal pain for 2 months. Laryngoscope showed right

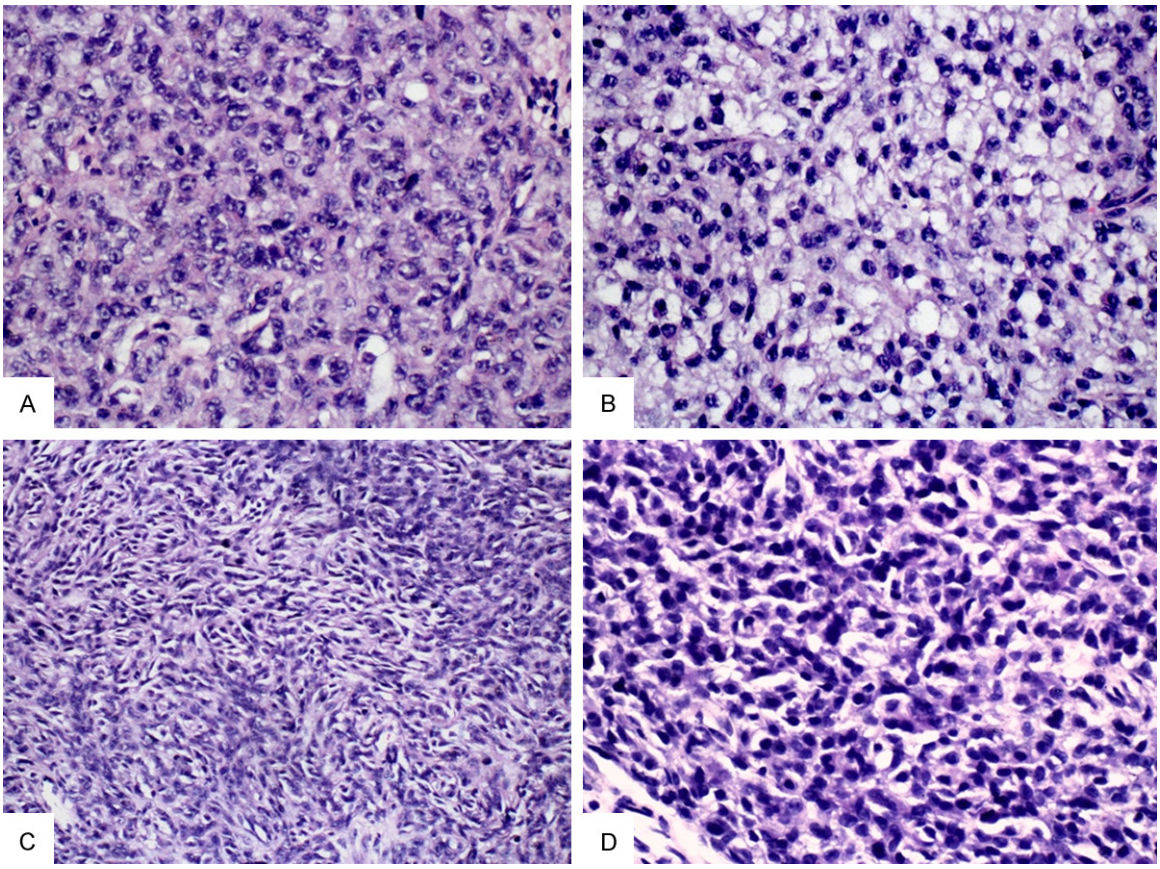

Figure 3. Microscopic findings of the tumor: morphological features. Most of the tumor cells were epithelioid, with palely eocinophilic cytoplasm (A). A minority of tumor cells showed true clearing cytoplasm (B). The nuclei of the cells were vesicular and had macronucleoli (A, B). Nuclear atypia was not prominent. The mitotic activity was lower. A few areas with spindle tumor cells presented (C). Marked nuclear pleomorphism only presented in a few areas of the tumor tissues (D).

parapharyngeal area bulging and CT and MRI detected a parapharyngeal mass about 4.4 cm×3.4 cm×3.0 cm.

Microscopically, the tumor is usually at least focally separated into nests by fibrous bands. The neoplastic cells vary from epithelioid to spindle with clear-to-pale eosinophilic cytoplasm. Nuclei of the tumor cells are vesicular, with prominent nucleoli. However, mitotic activity is usually minimal [5]. In this case, most of the tumor cells were epithelioid. A few areas with spindled tumor cells also existed. Cytoplasm of the tumor cells was mainly palely eocinophilic and only a minority of tumor cells showed true clearing cytoplasm, which is a common cytological feature of this kind of tumor. The tumor cells in this case infiltrated adipose tissues and muscle tissues, showing aggressive growth pattern.

Tumor cells of clear cell sarcoma often show melanocytic differentiation and stain positive for the melanocyte immunohistochemical markers HMB-45 and S-100 [1-5]. The tumor is thought to derive from neural crest cells [1-5]. These markers are helpful for distinguishing clear cell sarcoma from epithelial tumors and synovial sarcomas. The tumor cells of the current case were positive for HMB-45, Melan A, and S-100, but negative for CK and CD117. One of the main differential diagnoses of clear cell sarcoma is metastatic malignant melanoma [10]. Recently, Garcia et al suggested that CD117 immunoreactivity, which was positive in metastatic melanoma, but not in clear cell sarcoma, may be useful for differentiation of these tumors [8].

About 33-50% of all the patients that suffer from clear cell sarcoma experienced pain above

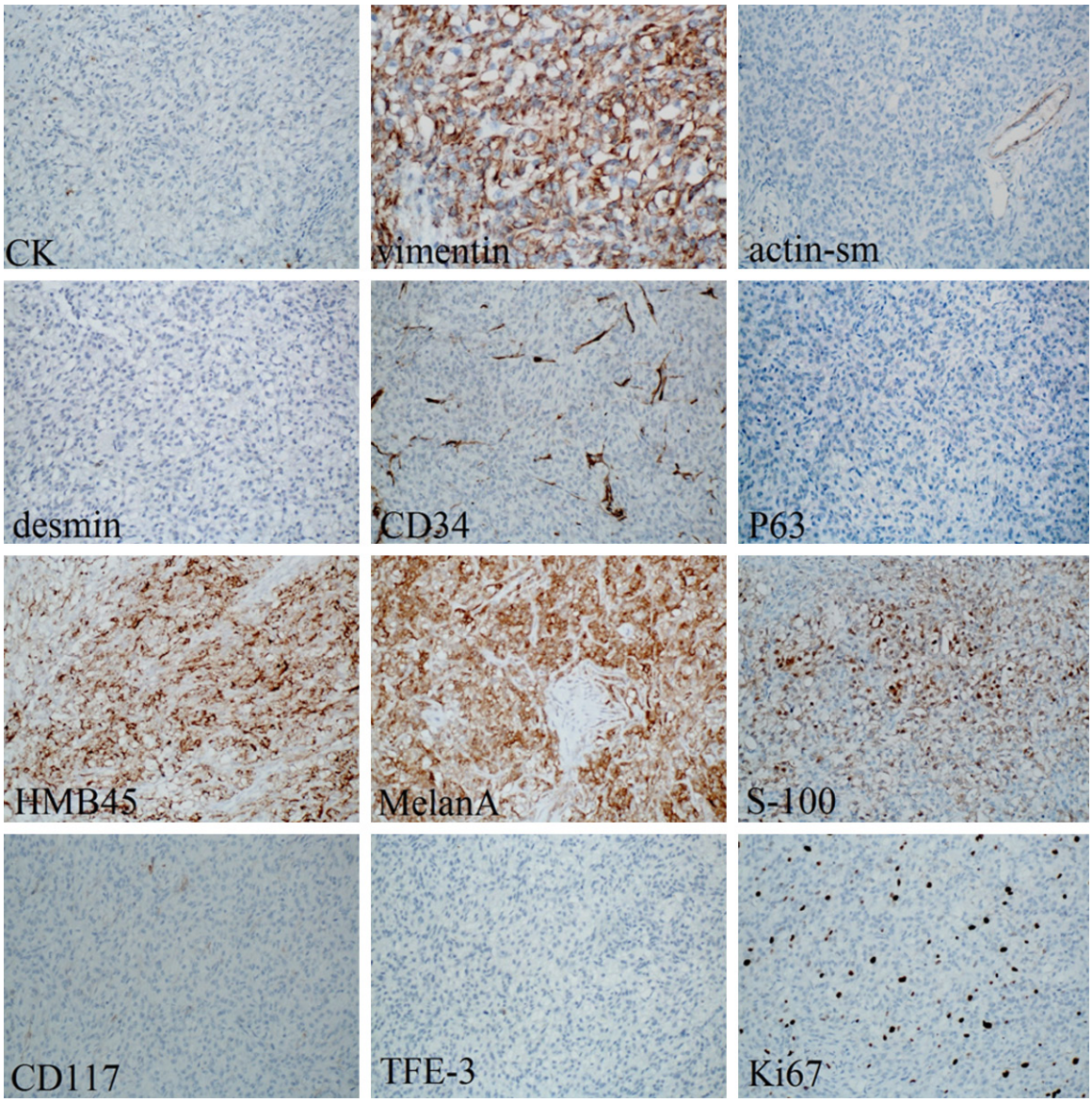

Figure 4. Immunohistochemical examination. CK (AE1/AE3) was negative in tumor cells. Vimentin was strongly and diffusely positive. Actin-sm, desmin, CD34, and P63 were negative in tumor cells. HMB45 and Melan A were diffusely positive and S-100 was focally positive in tumor cells. CD117 and TFE-3 were negative. Ki67 index was about 5%.

the tumor site [11]. In this case, the patient experienced a right pharyngeal pain for about 2 months. The overall prognosis for clear cell sarcoma is poor with a 5-year survival rate about 50% to 65%, though patients may have an unpredictable course of the disease [12-19]. Necrosis is considered as a poor prognostic factor [18], which was absent in the current case. Recurrences of the tumor occur in about 20% of patients and risk for metastasis increases after multiple recurrences [12-19]. Late metastases are quite common and need to be paid attention to because that most patients are young people, as in the current case.

Conclusion

Clear cell sarcoma is a rare sarcoma with consistent melanocytic differentiation. Malignant melanoma is one of the main differential diagnoses of clear cell sarcoma. Overall prognosis for clear cell sarcoma is poor and late metastases are needed to be paid attention to because the tumor mainly affects young adults.

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Disclosure of conflict of interest

None.

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