

Case Report

Synovial sarcoma arising in the posterior pharyngeal wall confirmed by molecular detection of *SYT* gene split: case report

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Abstract: Synovial sarcoma is a primitive mesenchymal tumor which occurs most frequently in soft tissues. Some unusual locations of synovial sarcoma could lead to diagnostic challenges. In this study, we reported a case of primary synovial sarcoma arose in the posterior pharyngeal wall. X-ray examination showed a space-occupying lesion in the post-pharyngeal wall. Frozen section and conventional histopathological diagnosis suggested that it could be mucinous-rich fibroblastic tumor. Immunohistochemistry results showed that vimentin was diffusely expressed in tumor tissue. However, epithelial membrane antigen (EMA) was expressed focally. To further identify the tumor, *SYT* gene split, a specific characteristic of synovial sarcoma cells was detected using FISH. It was found that over 10% of tumor cells had *SYT* gene split in the nucleus. In combination with the morphology and immunohistochemistry results, it was finally diagnosed with monophasic synovial sarcoma, which occurs at a very unusual site.

Keywords: Synovial sarcoma, molecular pathology, *SYT* gene

Introduction

As a primitive mesenchymal tumor, synovial sarcoma accounts for up to 10% of all soft tissue sarcomas [1]. It occurs most frequently in adolescents and young adults with poor prognosis [2]. However, novel targeted therapeutic methods for synovial sarcoma are still lacking and extremely needed.

Generally, synovial sarcoma arises most commonly in the vicinity of large joints [2, 3]. However, some unexpected locations of synovial sarcoma, such as heart [4], kidney [5], lung [6], the head and neck, pleura and abdomen, could lead to diagnostic challenges. Synovial sarcomas contain a chromosome translocation at t(X;18)(p11.2;q11.2), producing the fusion of *SYT* gene on 18q with the *SSX* gene on Xp, which could be detected by reverse transcription polymerase chain reaction or fluorescence in situ hybridization (FISH) [6, 7]. Thus, using molecular analysis could improve the diagnosis of synovial sarcoma, particularly in

tumors developed at unusual sites. Here, we reported a case of primary synovial sarcoma arose in the posterior pharyngeal wall which was confirmed by molecular detection of *SYT* gene split.

Clinical history

A 45-year-old woman presented to a local hospital in 2009 with neck pain. X-ray examination showed a space-occupying lesion in the post-pharyngeal wall. The patient had been followed-up with computed tomography (CT) scan in 2010. Contrast-enhanced CT scan of the neck showed a soft tissue mass in the left post-pharyngeal wall. The mass was clinically suspected to be a vascular tumor. Moreover, cartilage tumor or ectopic thyroid gland is unable to be excluded. However, the woman did not receive any therapy. Meanwhile, her snoring became worse since 2011, accompanied by an increase in cough following rapid swallowing. The patient was then referred to the authors' Institution in 2012 at the age of 48 years old. Whole-body

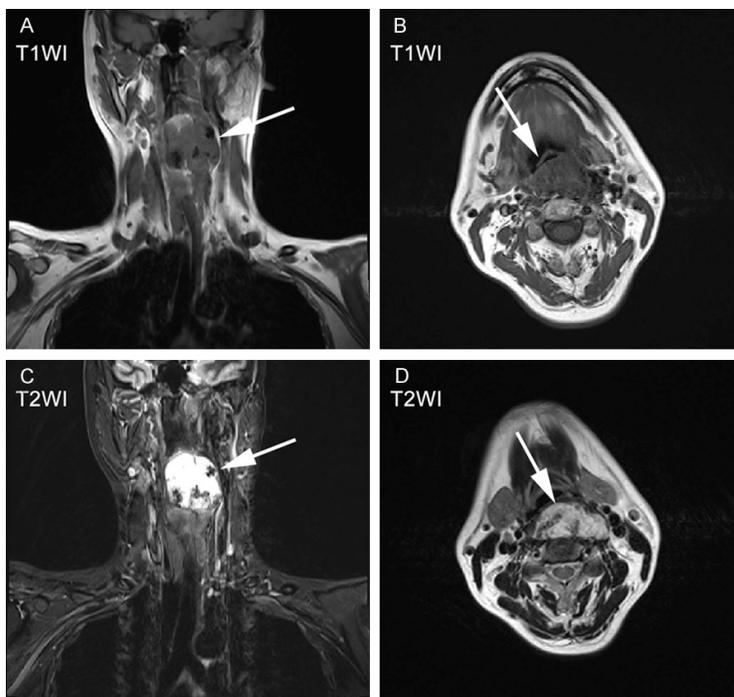


Figure 1. MR images (tumor masses are indicated by white arrows). A: T1-weighted MR image scanning with coronal; B: T1-weighted MR image scanning with axial position; C: T2-weighted MR image scanning with coronal; D: T2-weighted MR image scanning with axial position.

magnetic resonance imaging (MRI) revealed a tumor located in front of the second to the fifth cervical vertebrae. It showed an oval soft tissue mass shadow in retropharyngeal and parapharyngeal space; the tumor had a middle-density signal in the T1-weighted images and high-density signal in the T2-weighted images. Meanwhile, there was striped calcification in tumor, and the tumor had clear boundaries (**Figure 1**). Physical examination detected a palpable mucosal protrusion in the region of post-pharyngeal wall, and the mass was not freely movable. However, no precise diagnosis could be made. The past and family history was unremarkable. Even more, laboratory data were normal.

After consultation with the patient and her family, tumor resection was performed based on a suspected diagnosis of malignancy. Surgical incision was made to open the retropharyngeal space; the tumor was in contact with but not infiltrates the post-pharyngeal wall and the prevertebral soft tissue. Then the tumor was completely excised, frozen section and conventional histopathological diagnosis were undertaken. After surgery, the patient did not

receive any adjuvant therapy, such as radiotherapy or chemotherapy. The patient is surviving with no evidence of recurrent or metastatic disease by CT scan or local physical examination three years postoperatively.

Materials and methods

Immunohistochemistry

Immunohistochemistry (IHC) analysis was performed on paraffin-embedded tumor tissue using an automated IHC staining system (Roche Benchmark XT). The antibodies used in this study were purchased from Maxin Biotech. Co., Ltd. (Fuzhou, China).

Break-apart rearrangement FISH

SYT break-apart rearrangement FISH was carried out using a GLP *SYT* (18q11.2) Dual Color Break-Apart Rearrangement Probe kit (GP medical, Beijing, China) following the manufacturer's protocol with some modifications. Briefly, 4 μ m paraffin sections were treated with *SYT* FISH probe mixture, and then the sections were counterstained by DAPI dyes (Sigma-Aldrich, CA, USA).

Using fluorescence microscope (Olympus, Tokyo, Japan), the FISH signals were observed in each tumor cell nucleus. Normal tumor cell nucleus showed paired red 5'-*SYT* signal and green 3'-*SYT* signal overlapped yellowish signals, while *SYT* gene break nucleus showed one overlapped and two separate fluorescent signals. When the ratio of *SYT* gene break nucleus to total tumor cell nucleus was greater than 7%, the tumor was considered to have a *SYT* gene break, which was an important characteristic of synovial sarcoma.

Results

Pathological findings

Gross and pathological findings: Grossly, the tumor measured 8*5*3 cm and lobulated. On the cut surface, it was whitish gray to red in

Synovial sarcoma diagnosed by SYT gene

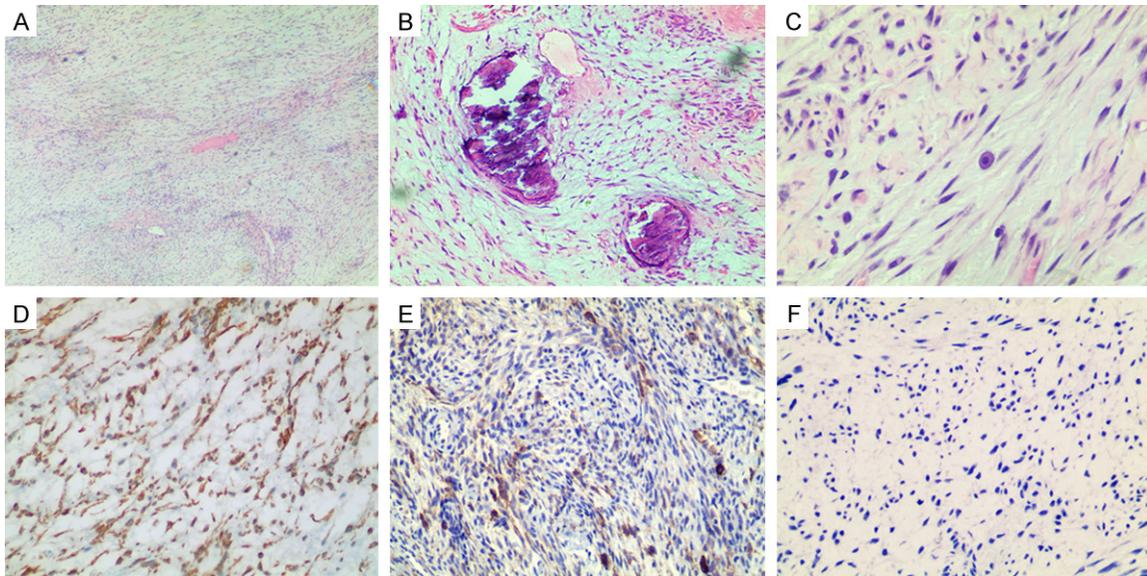


Figure 2. (A) Synovial sarcoma showing nodular proliferation of spindle-shaped fibroblastic tumor cells and poorly differentiated small round cells, accompanied by extensive myxematous portions (40 \times); (B) Calcification (100 \times) and (C) mast cells (indicated by black arrows, 400 \times) were identified by H&E staining; Immunohistochemical results showed (D) vimentin (200 \times), (E) EMA (200 \times), (F) CK8/18 (200 \times).

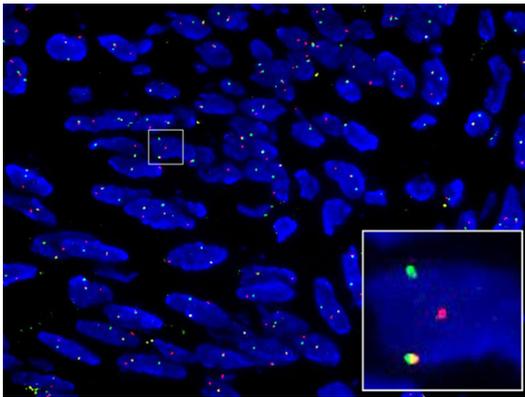


Figure 3. Two separate fluorescent signals in tumor cell nucleus of the monophasic fibrous areas showed SYT gene split. Magnification $\times 1000$, white boxes showed representative SYT gene split nucleus.

color and elastic hard to moderately soft in consistency, accompanied by some areas of calcification and some areas showing the characteristic features of mucinous degeneration. Microscopically, the tumor displayed nodular proliferation of spindle-shaped fibroblastic tumor cells and poorly differentiated small round cells, accompanied by extensive myxematous portions (**Figure 2A**). Calcification (**Figure 2B**) and mast cells (**Figure 2C**) were observed focally. Meanwhile, mitotic figures and cellular atypism were not remarka-

ble (**Figure 2A-C**). Immunohistochemically, the tumor cells were diffusely positive for vimentin (**Figure 2D**) while epithelial markers such as epithelial membrane antigen (EMA) was focally expressed (**Figure 2E**). However, cytokeratin 8/18 (CK8/18, **Figure 2F**), CD34, Cytokeratin 7, cytokeratin 19, smooth muscle actin, actin, desmin and S-100 (Data not shown) were negative in both the spindle-cell and round-cell components. Meanwhile, the Ki-67 index of the tumor was $<5\%$. Pathological findings led to a suspected diagnosis of synovial sarcoma. However, this diagnosis could not be fully confirmed. Other soft tissue tumors and spindle cell squamous carcinoma should be considered in the differential diagnosis.

FISH: We confirmed the diagnosis by additional cytogenetic analysis, which revealed the presence of SYT gene split by FISH. As synovial sarcoma was considered as one part of the differential diagnosis, we sought to detect the presence of SYT gene split, a specific characteristic of synovial sarcoma cells. In normal non-neoplastic stromal cells without the SYT gene split, there were two fusion orange signals. However, tumor cells carrying the SYT gene break revealed one fusion orange, one red and one green signal in nucleus. In the present case, over 10% of the tumor cell nucleus carried one fusion orange and two sepa-

Synovial sarcoma diagnosed by SYT gene

rate fluorescent signals in tumor cells of the monophasic fibrous areas (**Figure 3**). All experiments were approved by Ethic Committee of the First Affiliated Hospital of Nanjing Medical University. The informed consent had been obtained from the patient and her relatives.

Discussion

Synovial sarcomas could be classified into three types in pathological diagnosis, including the classical biphasic type, monophasic type and poorly differentiated type [8]. In which, classical biphasic type could be relatively easy to diagnose as it is composed of representative epithelial and spindle cells. However, the differentiation is ambiguous in the other two types of synovial sarcomas. Meanwhile, although synovial sarcomas occur most commonly in the deep soft tissue of the thigh and knee joints, some rare cases occurred in other sites have also been reported. These facts improve the difficulty of diagnosis of synovial sarcomas.

Synovial sarcoma occurs rarely in pharynx, and less synovial sarcoma arose in pharynx have been reported previously. Only 4 cases arose in posterior pharyngeal wall had been reported [9-12]. In the present case, the tumor showed homogeneous patterns of spindle cells under microscope. Meanwhile, poorly differentiated small round cells were also observed. Thus, immunohistochemistry was performed to distinguish this tumor from other tumors which had similar spindle cell types. In this case, vimentin staining was positive while EMA showed local but not diffusely positive in tumor cells. Therefore, taken together with the morphological results, the major differential diagnosis of the tumor could be fibrosarcoma, myopericytoma, malignant peripheral nerve sheath tumor (MPNST) and synovial sarcoma. Further results showed that the tumor cells were negative for S-100, muscle-specific actin, desmin and CD34. It is reported that S-100 is diffuse expressed in MPNST [13], while CD34 is positive in fibrosarcoma [14]. Therefore, in combination with morphological and immunohistochemical results, we eventually excluded fibrosarcoma, myopericytoma and MPNST.

It is known that synovial sarcoma occurs most commonly in adolescents and young adults. Thus, considering the age of the patient,

although synovial sarcoma might be the most possible diagnosis from above presented diagnoses, further evidence for confirming this diagnosis is still needed. Recently, tumor-specific chromosomal translocation has been frequently used in the pathological diagnosis, especially soft tissue sarcomas. In synovial sarcoma, SYT gene on 18q chromosome could translocate with SSX genes on chromosome Xp, including SSX1, SSX2 and SSX4. Thus, this chromosomal translocation could be used as molecular marker to confirm the pathological diagnosis of synovial sarcomas by various techniques such as RT-PCR and FISH analysis. In which, FISH could be performed in archival paraffin-embedded samples, which made it more convenient in pathological diagnosis. Thus, SYT break-apart rearrangement FISH was performed to confirm the diagnosis of this present case. In this case, paired split SYT gene signals has been exclusively observed in the tumor cells of the monophasic fibrous components, supported the diagnosis of synovial sarcoma.

In conclusion, using SYT break-apart rearrangement FISH, we confirmed a diagnostically difficult case of synovial sarcoma occurred in posterior pharyngeal wall. It also occurred in an unusual age since synovial sarcoma arises commonly in adolescents and young adults. This study suggested that in the diagnosis of synovial sarcoma developed in some unusual sites, FISH should be considered for the detection of synovial sarcoma chromosomal translocation.

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Disclosure of conflict of interest

None.

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