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International Journal of Otorhinolaryngology and Head and Neck Surgery
*Alhatem A et al. Int J Otorhinolaryngol Head Neck Surg. 2019 Nov;5(6):1694-1697*
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

**Case Report**

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20194952

# Out-of-the-box soft tissue tumor: pediatric synovial sarcoma of larynx

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**Received:** 17 July 2019
**Revised:** 05 September 2019
**Accepted:** 09 September 2019

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## ABSTRACT

Synovial sarcoma (SS) is a very rare, aggressive, mesenchymal neoplasm that displays both spindle cell and epithelial histologic characteristics. To our knowledge, there are only 20 documented cases of primary laryngeal SS in the English language literature among all age groups and only three case reports among the pediatric population. Due to its rarity, recognition of this laryngeal neoplasm is often very difficult, and diagnosis relies heavily on immunohistochemistry and its unique translocation between chromosome X and 18 [t(X; 18) (p11.2; q11.2)]. The treatment of SS typically involves a multimodal approach with surgery, chemotherapy, and radiation but despite these options the prognosis remains poor. Here we report the fourth laryngeal SS pediatric patient along with a review of all SS published cases in children. The current report is not only presenting the youngest patient with laryngeal SS but also the pediatric patient with the longest survival.

**Keywords:** Synovial sarcoma, Larynx, Pediatric pathology, Translocation (X; 18)

## INTRODUCTION

Synovial sarcoma (SS) is a very rare, aggressive, mesenchymal neoplasm that displays both spindle cell and epithelial histologic characteristics.[1] SS typically occurs in the lower extremities of adults; however, it has the potential to originate in almost any region of the body including the head and neck. To our knowledge, there are only 20 documented cases of primary laryngeal SS in the English language literature among all age groups.[2]

Although found within its name, synovial sarcoma is relatively unrelated to the synovium in origin, phenotype, and ultrastructure. In the head and neck, SS is thought to arise from pluripotent mesenchymal cells.[3] There are two distinct histologic forms: monophasic and biphasic. Both types are characterized by monomorphic spindle cells with tapering nuclei and poorly defined cytoplasm, often arranged in fascicles within a collagenous stroma.[3] The biphasic SS has the additive features of discernable glandular or solid epithelial structures.[4] Both, however, often contain some extent of stromal calcification.[3]

To our knowledge there are only three case reports in the English language literature among the pediatric population (Table 1).[2,5,6] Here we report the fourth laryngeal SS pediatric patient along with a review of all SS published cases in children. The current report is not only presenting the youngest patient with laryngeal SS but also the pediatric patient with the longest survival.

## CASE REPORT

A 10-year-old boy presented, in another institution, with a laryngeal mass and was diagnosed as rhabdo-myosarcoma (RMS) by biopsy. He was treated with chemo and radiation. Eleven years later, he presented to our hospital with a recurrent laryngeal mass and

hemorrhage. CT neck imaging showed left subglottic mass (Figure 1a). He underwent neck angiogram and embolization of a branch of facial artery. Repeat laryngeal biopsy at our institution revealed a spindle cell neoplasm without obvious glandular component. Spindle cells were bland without any nuclear pleomorphism and rare mitoses were evident. The tumor cells were immunoreactive to vimentin, Bcl 2, and Calponin, but negative to SMA, CD34, desmin, myoglobin, MyoD1, and positive for CK AE1/AE3 (focally) and EMA (Figure 2). Chromosomal analysis revealed t(x;18) (p11.2; q11.2) translocation (Figure 3a). FISH analysis identified SS18 gene rearrangement and RT-PCR detected SYT/SSX2 fusion gene (Figure 3b-c). These findings supported the diagnosis as monophasic synovial sarcoma (SS). Slides from the other institution were reviewed, revealing misinterpretation of the immunohistochemistry and leading to establish SS diagnosis.

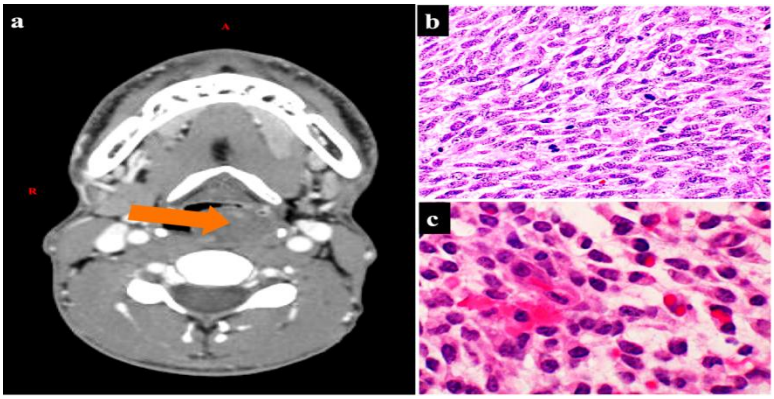


**Figure 1: CT imaging showing (a) the subglottic laryngeal mass; (b) histopathologic findings of spindle cell rhabdoid morphology of SS as diagnosed afterwards; (c) compared to rhabdoid morphology of SS as initially diagnosed as rhabdomyosarcoma.**

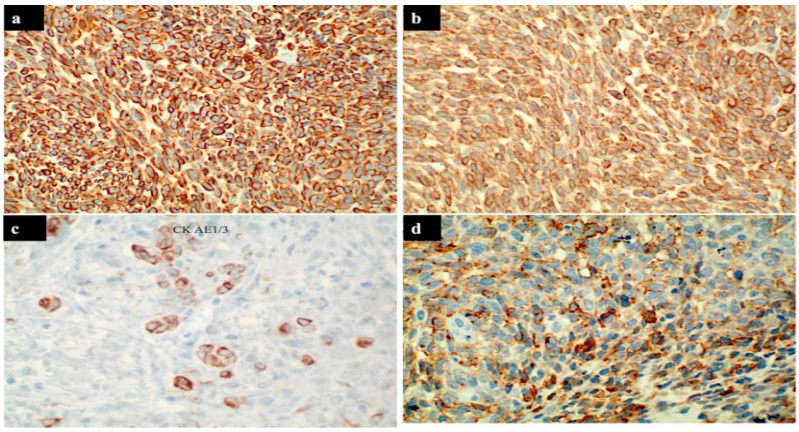


**Figure 2: Immunohistochemical studies showing positivity of (a) vimentin, (b) BLC 2, (c) cytokeratin and (d) EMA as usually found in SS.**

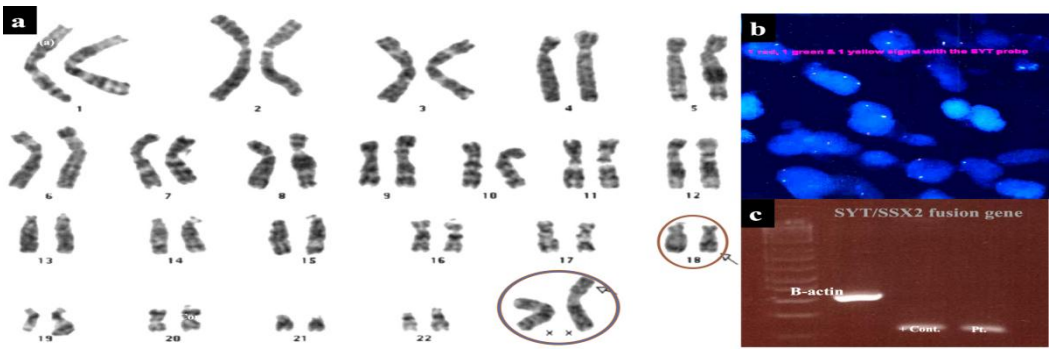


**Figure 3: Ancillary studies confirming the diagnosis of SS showing (a) chromosomal translocation t(x;18), (b) FISH and (c) RT-PCR.**

**Table 1: Comparison of known published cases of laryngeal SS in children.**

| Case | Reference | Age/ sex | Anatomic location | Immuno-staining used | Other ancillary studies used | Treatment | Follow up |
|---|---|---|---|---|---|---|---|
| 1 | 1 | 11/M | Aryepiglottic fold | EMA, CD99 | Cytogenetics (t(X;18)) | Chemoradiotherapy, Total laryngectomy | 6 years disease free. |
| 2 | 2 | 14/M | Bilateral arytenoids | Reticulin, PAS, Desmin, Myosin, SMA, S100, Factor VIII-related antigen, Vimentin, a-1-anti-trypsin, low molecular weight cytokeratin | None | Total laryngectomy, chemotherapy | Recurrence after 7 years. Disease free after 10 months. |
| 3 | 3 | 16/F | Supraglottic region | Bcl2, Vimentin, CD99 | None | Mass excision, Radiotherapy | Unknown |
| 4 | Our case | 10/M | Left Supraglottic, aryepiglottic fold | CK AE1/AE3, EMA, Vimentin, Bcl2, Calponin, SMA, CD34, CD99, Desmin, Myoglobin, MyoD1 | RT-PCR, Cytogenetics (SYT gene, t(x:18), (18q 11.2 translocation), Chromosomal analysis | Embolization, Chemo-Radiation, Total Laryngectomy | 15 years then lost follow up |

The patient was given ifosfamide chemotherapy and remained in remission for three years with unchanging MRI and PET scan, till presenting with bleeding and multiple local recurrences. He underwent total laryngectomy at an outside institution, followed by a local recurrence in the nasopharynx at our institution and lost follow up.

## DISCUSSION

SS is a rare, aggressive mesenchymal neoplasm that displays both spindle cell and epithelial histologic characteristics.[1] About 80% of SS occurs in the extremities, while only 3-9% occurs in the head and neck, where most commonly targets the hypopharynx and rarely the larynx.[3] Most individuals with laryngeal SS are male and are diagnosed in their third decade of life.[4]

Morphologically, as per WHO classification, SS can be biphasic or monophasic with variable morphology showing spindle and/or epithelial cellular characteristics. Both types are characterized by monomorphic spindle cells with tapering nuclei and poorly defined cytoplasm, often arranged in fascicles within a collagenous stroma.[4] The biphasic SS has the additive features of discernable glandular or solid epithelial structures.[7] Both, however, often contain some extent of stromal calcification.[4]

Due to its rarity, recognition of this laryngeal SS is often very difficult, and diagnosis relies heavily on immunohistochemistry and cytogenetics.[1] Eighty percent of SS have a specific t(x;18) (p11.2; q11.2) chromosomal abnormality, leading to fusion of the SSX gene with the SYT gene, which contributes to morphology and outcome.[3,4] Third of cases are monophasic or SSX2, 2/3 of cases are biphasic or SSX1, and rare cases are SSX4. Local recurrence is 45% of adults' head and neck SS, 33% metastasize, and 50% survive for 2 years.[7,8] No data is available for pediatric cases, nevertheless, children have a better prognosis, particularly when the tumor is small with bland morphology, rare mitoses and no necrosis. Transducin like enhancer of split 1 (TLE1) (nuclear stain) is considered a very specific marker for SS.

First published case of pediatric SS in the larynx diagnosed in bilateral aryntenoids in 14-year-old male, using morphology and immunohistochemistry (IHC).[5] The disease-free survival (DFS) was 10 months with a recurrence after 7 years.[5] Another case reported SS in supraglottic region in 16-year-old female, using morphology and IHC, with unknown DFS.[6] The third known case was reported in aryepiglottic fold in 11-year-old male, utilizing morphology, IHC and cytogenetics with 6-years DFS.[2] Our case was diagnosed in 10-year-old male in the left supraglottic and aryepiglottic fold,

utilizing morphology, IHC, cytogenetics, reverse-transcriptase-polymerase chain reaction (RT-PCR), and chromosomal analysis, with 14-years DFS.

Current guidelines for laryngeal SS treatment follow general practices specific to soft tissues sarcomas: adequate excision and adjuvant radiotherapy when appropriate, with or without adjuvant chemotherapy.[9,10] The prognosis of SS is poor, with the 5-year survival rate is approximately 70% and the 10-year survival rate is approximately 50%.[8,11] Lymph node dissection has not been shown to be necessary in previous cases.[6,10,12] Previous literature reports as much as 80% local recurrences in cases with inadequate surgery that did not receive adjuvant radiotherapy.[9] Similar to the previous pediatric cases, our case received local excision, chemotherapy, and radiotherapy. The patient eventually necessitated and underwent total laryngectomy, similar to two previous cases in pediatric patients.[2,5] While complete surgical excision followed by postoperative radiotherapy is the standard of care among the adult population, the use of adjuvant chemotherapy is still controversial.[1] However, as seen in the previous cases, ifosfamide has shown benefits for selected patients.[1,5,6]

## CONCLUSION

We reported a fourth case of laryngeal SS in a youngest pediatric patient with the longest survival. Morphologically monophasic SS can present as a small blue cell or spindle cell neoplasm and it can be a diagnostic challenge. Besides morphology ancillary studies such as immunohistochemistry and molecular studies are essential for the definitive diagnosis.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

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**Cite this article as:** Alhatem A, Farber N, Baredes S, Mirani N. Out-of-the-box soft tissue tumor: pediatric synovial sarcoma of larynx. Int J Otorhinolaryngol Head Neck Surg 2019;5:1694-7.