

Case Report

Rare case of primary esophageal synovial sarcoma with (x;18) translocation presenting as dysphagia

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ABSTRACT

Synovial sarcoma (SS) in young adult mainly involves periarticular region of the extremities. Synovial sarcomas are exceedingly rare neoplasms of the digestive tract. In this report, we describe a very rare occurrence of primary SS of the esophagus in a 30-year-old female. Patient presented with dysphagia. Endoscopy showed submucosal esophageal polyp. Piecemeal polypectomy was done. Histologically, the tumor demonstrated biphasic morphology with epithelial and mesenchymal component. Tumor cells expressed pancytokeratin, bcl-2 and CD99 antigens. Differential diagnosis of synovial sarcoma and epithelial mesenchymal biphasic tumor was made. Cytogenetics was done to confirm the diagnosis of SS. It showed translocation (x;18). Synovial sarcomas are very rare tumor entities, particularly in the gastrointestinal tract and are likely to be mistaken with other more common tumors such as gastrointestinal stromal tumors.

Keywords: Synovial sarcoma, Cytogenetics, Translocation (x;18), Biphasic tumor

INTRODUCTION

Adenocarcinoma and squamous cell carcinoma comprises 95% of esophageal epithelial malignancy.¹ Sarcomas are a rare entity along with melanoma and lymphoma. Varied histologies of sarcomas are reported such as carcinosarcoma (both epithelial and mesenchymal elements), synovial sarcoma, leiomyosarcoma, myxofibrosarcoma, Ewing's sarcoma, granulocytic sarcoma, histiocytic sarcoma, schwannoma, rhabdomyosarcoma and epithelioid sarcoma.² Synovial sarcoma (SS) is a malignant mesenchymal tumor most commonly seen in extremities followed by soft tissue of head and neck, mediastinum, lungs, pleura, heart, mesentery and retroperitoneum.³ Rarely primary SS have been documented with gastrointestinal tract (GI) tract. It can cause diagnostic dilemma with other spindle cell tumors. We report a rare case of primary SS of the esophagus,

suspected histologically and was confirmed by immunohistochemistry and cytogenetics.

CASE REPORT

A 30 year female patient presented with complaints of progressive dysphagia, epigastric discomfort and weight loss for duration of one month. Her physical examination was unremarkable. Routine laboratory investigations were normal. Endoscopy showed large submucosal esophageal polypoidal lesion preoperatively. Large pedunculated polyp seen in esophagus with stalk at post cricoid region measuring 5×2×1.5 cm (Figure 1). Piecemeal polypectomy was done which histologically showed only mesenchymal component. After which total polypectomy was done. Histologically polypoidal lesion lined by stratified squamous epithelium with focal ulceration covered by fibrinopurulent exudate. Focal hyperplastic lining seen. Underneath show submucosal lesion showing

biphasic population epithelial and mesenchymal component. Spindle cells are arranged in fascicles, bundles having spindle shaped vesicular nuclei inconspicuous nucleoli and mild nuclear atypia with eosinophilic cytoplasm. Other type of cell population admixed with the spindly components is the epithelial component which is arranged in focal glandular and papillary structures (Figure 2).

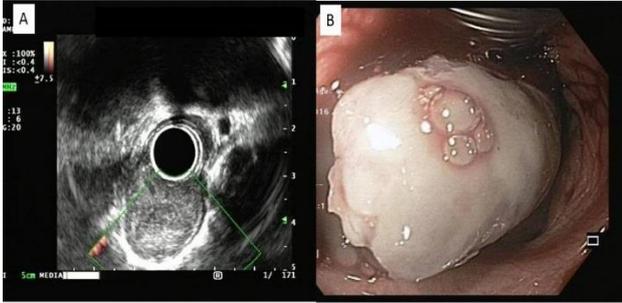


Figure 1: (A) Endoscopic USG-large polypoidal hyperechoic lesion arising from submucosal layer of esophagus, and (B) video endoscopy-large submucosal oesophageal polypoidal lesion. Lesion measures 5×2×1.5 cm.

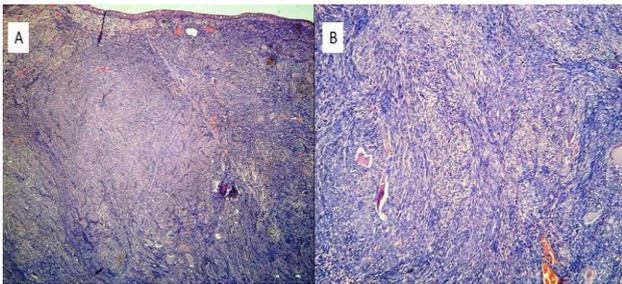


Figure 2: (A) Polypoidal lesion lined by stratified squamous epithelium subepithelium showing tumour with biphasic population of epithelial and mesenchymal component, H&E 4x, and (B) spindle cells are arranged in fascicles, bundles having spindle shaped vesicular nuclei inconspicuous nucleoli with mild nuclear atypia and eosinophilic cytoplasm. The epithelial component is arranged in focal glandular structures, H&E 20x.

Base of the polyp was free. Both vertical and horizontal margins were free. No lymphovascular invasion seen. Based on above feature provisional diagnosis of spindle cell neoplasm with focal admixed epithelial component was made. Immunohistochemistry was performed, (Figure 3) tumor cells expressed pancytokeratin, Bcl 2, CD 99, TLE1 and were negative for SMA, DOG 1 and CD34. Ki 67 showed focal moderate high positivity of upto 40% within the glandular component and spindle component (Figure 4). Correlating with immune profile, diagnosis of synovial sarcoma was made. Cytogenetics study was done to confirm the diagnosis using FISH with dual color deoxyribonucleic acid (DNA) probes, a green probe for the

X centromere and a red probe for a region in the middle of the 18 long-arm (18q21). Fluorescence in situ hybridization (FISH) test showed synovial sarcoma (SS18/SYT)18q11.2 gene rearrangement with 60% cells positive for 1O1G1Y signals, 20% cells positive for 1O2G3Y signals and 20% cells positive for 2O2G1Y signals (O=orange, G=green, Y=yellow). It showed t (X; 18) (p11.2; q11.2) resulting in fusion of the SYT gene at 18q11 with either the SSX1 OR SSX2 gene (Figure 5). Detection of this translocation is highly specific for synovial sarcoma. Patient is receiving chemotherapy and radiotherapy and is under follow-up.

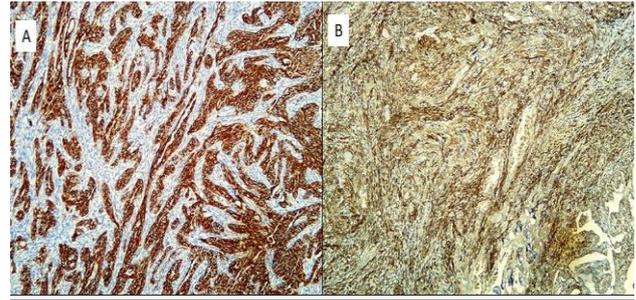


Figure 3: Immunohistochemistry (A) tumour cells positive for Pan cytokeratin, highlighting epithelial component, (B) tumour cells positive for BCL2, highlighting mesenchymal component.

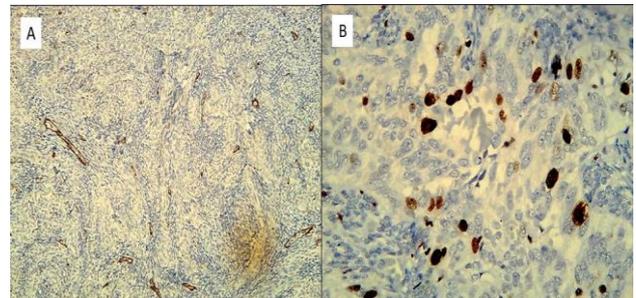


Figure 4: Immunohistochemistry (A) and (B) tumour cells are negative for A, SMA. B, Ki67 shows focal moderate high positivity within the glandular and spindle component.

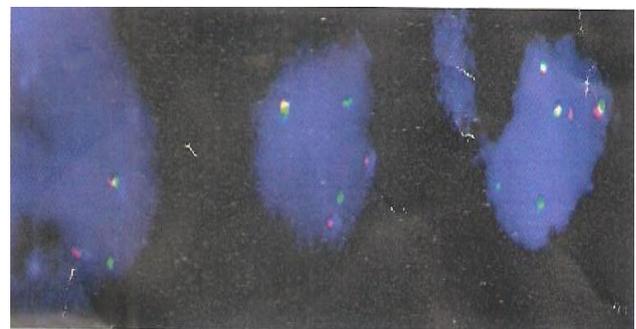


Figure 5: Fluorescence in situ hybridization (FISH) test- positive for synovial sarcoma (SS18/SYT) 18q11.2 gene rearrangement in 50 interphase nuclei.

Table 1: Common histological subtypes of esophageal sarcoma with immunohistochemistry.

S. no.	Subtype	Histological features	Immunohistochemical features
1	Synovial sarcoma ⁷	Biphasic morphologic features; spindle cells and gland-like epithelial structures. Monophasic; Hypercellular fascicular architecture with little intervening stroma.	Positive for vimentin, epithelial (EMA, CK7, AE1/3), bcl-2, and neuroectodermal (CD56, CD57, CD99) markers. Along with X;18 translocation on FISH
2	Leiomyosarcoma ⁸	Fascicular growth pattern with bundles intersect at right angles. Nuclei are cigar-shaped and blunt-ended with variable atypia, often with cytoplasmic vacuoles at both ends of nuclei.	Strongly positive for SMA, negative for cytokeratin.
3	Sarcomatoid carcinoma ⁹	Predominantly anaplastic spindle cells resembling fibrosarcoma or leiomyosarcoma. Occasional giant or multinucleated malignant fibrohistiocytoma-like cells.	Epithelial component is cytokeratin positive and mesenchymal element exhibits strong immunoreactivity with vimentin actin and desmin.
4	Epithelioid sarcoma ¹⁰	Uniform plump small to medium sized cells with eosinophilic cytoplasm, spindle cells can also be identified and often appear more conspicuous at the periphery of a nodule. Mild nuclear atypia with vesicular chromatin and small nucleoli.	Positive for epithelial and mesenchymal markers, such as cytokeratin, epithelial membrane antigen (EMA), vimentin and CD34
5	Carcinosarcoma ¹¹	Invasive epithelial component may be adenoid basal, adenoid cystic, basaloid squamous cell or keratinizing squamous cell. Sarcomatous component usually homologous resembling fibrosarcoma often with prominent myxoid change.	Positive for cytokeratin, vimentin, smooth muscle actin, and p53.
6	Ewing's sarcoma ¹²	Sheets of densely cellular areas with light and dark small round, uniform cells with scant clear cytoplasm, divided into irregular lobules by fibrous strands.	MIC2/CD99 positive

DISCUSSION

Esophageal sarcomas are rare and are of uncertain histology.² Sarcomas of the esophagus, comprise 0.1–1.5% of all esophageal tumors. Synovial sarcoma is very rare with nearly 14 reported cases, of which twelve were polypoid and located in upper and mid esophagus while two were submucosal in origin. Thirteen of these cases were biphasic and only one showed monophasic histology.⁴

Esophageal sarcoma mostly occurs in 26-76 years of age and median age of 58 years. Patients most commonly present with dysphagia, weight loss, chest discomfort, burning retrosternal pain, nausea, and vomiting.^{2,3,5} Endoscopically esophageal sarcoma present as polypoid and exophytic masses and rarely as ulcerating tumour. Barium studies may show large intramural mass or areas of luminal narrowing or filling defect. Computed tomography (CT)/magnetic resonance imaging (MRI) may show in homogeneously enhancing mass.²

18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is a useful imaging modality in the evaluation of both primary and recurrent soft-tissue sarcoma lesions with results superior than both CT scan or MRI alone.⁶

Synovial sarcoma of esophagus has undifferentiated spindle cells similar in appearance to synovial sarcoma in other areas. They are of two histological subtypes. The monophasic type consists of spindle cells alone and need be differentiated from other spindle cell tumors. The biphasic subtype, which is more common consists of epithelial cells admixed with spindle cells in different proportions. Confirmation of diagnosis by morphology alone is difficult and hence, immunohistochemistry is essential. The most common differential diagnosis and their immunohistochemical features are described in Table 1. Synovial sarcomas have biphasic morphologic findings and are positive for vimentin, epithelial (EMA, CK7, AE1/3), bcl-2, and neuroectodermal (CD56, CD57, CD99) markers. Because of overlap of morphology and immunohistochemistry, like vimentin and CD 99 being positive in synovial sarcoma and Ewing's sarcoma, molecular analysis helps in definitive confirmation.

t(X;18) is a sensitive marker and is demonstrated in 70 to 90% of synovial sarcomas. The specific t(X; 18)(p11.2; q11.2) results in the fusion gene product SYT-SSX. Novel SS18-SSX fusion-specific antibody provide high sensitivity and specificity for the diagnosis of synovial sarcoma.¹³ The histologic subtype and biological nature of the tumor is closely related to the SSX gene transcript type. SS18-SSX1 is the most common fusion subtype, followed

by SS18-SSX2, and SS18-SSX4 is very rare. SS18-SSX1 tumors tend to associate with the biphasic subtype showing a higher tumor cell proliferation and a higher risk of distant metastases. However, SS18-SSX2 tumors are usually monophasic with a low tumor cell proliferation activity and benign clinical course.

Factors affecting survival are age of patient (<25 years), size, location, pattern of growth, absence of poorly differentiated component and completeness of resection. Singer et al found that synovial sarcomas smaller than 5 cm had 100% 10-year survival.⁷ This suggests that synovial sarcoma may behave differently in different sites. The more favourable prognosis associated with synovial sarcoma versus other oesophageal neoplasms has been attributed to early onset of symptoms, resulting in prompt diagnosis and a lower propensity for tumour invasion. As in typical squamous cell carcinoma, early detection and treatment by surgical resection are needed to produce significant long-term survival.²

Surgery is the mainstay of treatment. Oesophagectomy/oesophagogastrrectomy is the surgery of choice. Even if metastases are present, a palliative resection can still be performed.

Endoscopic resection is another surgical option available for patients with localized lesions with an adequate wide margin in addition to adjuvant chemotherapy and/or radiotherapy.

In patients with advanced unresectable tumor and metastasis, the role of adjuvant radiotherapy and chemotherapy is controversial. However, doxorubicin and ifosfamide could be the mainstay chemotherapy of choice.¹⁴ Marine-derived antineoplastic drug and multitarget agent, Trabectedin has been found effective in translocation-related sarcomas, including synovial sarcoma by inducing apoptosis and cell cycle arrest.¹⁵

Studies with genetically engineered T lymphocytes and immunotherapeutic vaccines are under trial. Palliative procedures like stenting to relieve dysphagia improve quality of life.

CONCLUSION

Sarcomas are rare entity among all esophageal malignancies. Synovial sarcoma has some unique histologic features, and is exceedingly rare in the esophagus. Complete resection of lesion is important to identify the morphology. The surgical management of this tumor in the esophagus is unclear, and the prognosis remains to be clarified. Molecular analysis plays an important role in diagnosis of these unusual tumors at unusual site.

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REFERENCES

- Golioto M, McGrath K. Primary lymphoma of the esophagus in a chronically immunosuppressed patient with hepatitis C infection: case report and review of the literature. *Am J Med Sci.* 2001;321(3):203-5.
- Patricia S, Saikat D, Rajesh B, Rajesh I, Selvamani B, Subhashini J. Rare Cause of Stricture Esophagus-Sarcoma: A Case Report and Review of the literature. *Case Rep Gastrointest Med.* 2011;192423.
- Butori C, Hofman V, Attias R, Mouroux J, Pedeutour F, Hofman P. Diagnosis of primary esophageal synovial sarcoma by demonstration of t(X;18) translocation: a case report. *Virchows Arch.* 2006;449(2):262-7.
- Sasaki. K, Noda. M, Tsuruda, Y. Primary monophasic synovial sarcoma of the cervical esophagus confirmed by detection of the SS18-SSX2 fusion transcripts: case report and literature review. *Surg Case Rep.* 2020;6:176.
- Lokesh V, Naveen T, Pawar YS. Spindle cell sarcoma of esophagus: a rare case presentation. *J Cancer Res Ther.* 2010;6(1):100-1.
- Ioannidis JP, Lau J. 18F-FDG PET for the diagnosis and grading of soft-tissue sarcoma: a meta-analysis. *J Nucl Med.* 2003;44(5):717-24.
- Billings SD, Meisner LF, Cummings OW, Tejada E. Synovial sarcoma of the upper digestive tract: a report of two cases with demonstration of the X;18 translocation by fluorescence in situ hybridization. *Mod Pathol.* 2000;13(1):68-76.
- Adad SJ, Etchebehere RM, Hayashi EM. Leiomyosarcoma of the esophagus in a patient with chagasic megaesophagus: case report and literature review. *Am J Trop Med Hyg.* 1999;60(5):879-81.
- Raza MA, Mazzara PF. Sarcomatoid carcinoma of esophagus. *Arch Pathol Lab Med.* 2011;135(7):945-8.
- Maggiani F, Debiec-Rychter M, Ectors N, Lerut A, Sciot R. Primary epithelioid sarcoma of the oesophagus. *Virchows Arch.* 2007;451(4):835-8.
- Nakagawa S, Yabusaki H, Tanaka O. Rapid-growth carcinosarcoma of the esophagus arising from 0-IIc squamous cell carcinoma after definitive chemoradiotherapy: a case report. *Esophagus.* 2009;6:123-6.
- Maesawa C, Iijima S, Sato N, et al. Esophageal extraskelatal Ewing's sarcoma. *Hum Pathol.* 2002;33(1):130-2.

13. Baranov E, McBride MJ, Bellizzi AM. A Novel SS18-SSX Fusion-specific Antibody for the Diagnosis of Synovial Sarcoma. *Am J Surg Pathol.* 2020;44(7):922-33.
14. Lee SH, Chang MH, Baek KK. High-dose ifosfamide as second- or third-line chemotherapy in refractory bone and soft tissue sarcoma patients. *Oncology.* 2011;80(3-4):257-61.
15. Demetri GD, von Mehren M, Jones RL. Efficacy and Safety of Trabectedin or Dacarbazine for Metastatic

Liposarcoma or Leiomyosarcoma After Failure of Conventional Chemotherapy: Results of a Phase III Randomized Multicenter Clinical Trial. *J Clin Oncol.* 2016;34(8):786-93.

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