Case Report

Sarcoma esophagus: A case report and review of literature

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ABSTRACT

Synovial sarcoma (SS) is an uncommon mesenchymal malignant neoplasm that occurs mainly in extremities. Sarcoma of the esophagus is a rare neoplasm and comprises 0.1–1.5% of all esophageal tumors. Only a few cases have been reported from the Indian context. We report a case of SS occurring in the esophagus of a 35-year-old male and managed with radical radiotherapy alone. We also want to highlight the histopathological and immunohistochemistry profile which aid in its accurate diagnosis. Molecular testing for SS18-SSX was done for confirmation.

Key words: Esophagus, Immunohistochemistry, Radiotherapy, Synovial sarcoma

Squamous cell carcinoma and adenocarcinoma are the most common histological variety of esophageal cancer. Rare histology includes sarcoma, lymphoma, and melanoma. Sarcoma of the esophagus comprises 0.1–1.5% of all esophageal tumors [1]. Among sarcoma, the most common is carcinosarcoma followed by leiomyosarcoma. The diagnosis of primary synovial sarcoma (SS) of the digestive tract becomes more difficult and requires confirmation by molecular analysis. The treatment and survival for esophageal carcinoma are well studied in the literature, but the treatment for sarcoma and its survival is not defined due to the low incidence of the disease. Surgery, wherever possible, remains to be the mainstay of treatment [2] but not all the patients with sarcoma esophagus underwent surgery. Some patients also offer radiotherapy (RT) either radical or palliative and the role of chemotherapy is still controversial. Hence, it is necessary to report these rare cases, its treatment, and outcome so that we can offer the best possible treatment for this rare disease and improve the outcome.

We are reporting a rare variety of esophageal cancer; biphasic SS, its clinical presentation, diagnosis with aid of immunohistochemistry (IHC), and the treatment outcome. This case report highlights the unusual histopathological presentation in esophageal cancer patient. As there are no standard predefined guidelines for the treatment of such patients, these anecdotal case reports may help in future management.

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CASE REPORT

A 35-year-old male with no known comorbidities and nil family history of cancer presented to our outpatient department in August 2018 with a complaint of Grade II dysphagia for 2 months. On examination, the patient was well nourished and had an average built. His vitals were stable.

His hematological and biochemical profile were normal. On endoscopic examination, an exophytic tumor was seen in the cervical esophagus. Multiple core biopsies of the lesion obtained and sent for the histopathological examination.

Histopathological examination revealed biphasic SS, Fédération Nationale des Centres de Lutte Contre Le Cancer Grade-II (Fig. 1a) arranged in fascicles. Moderate nuclear pleomorphism was noted. The mitotic rate was 7–9/10 high-power field. Necrosis was absent.

On IHC, tumor cells were positive for AE1/AE3 (occasional Cell), CD 99 (Fig. 1b), BCL2, EMA (focally positive), and negative for S100, CD 34 (Fig. 1c), SMA, Desmin, C-kit, DOG1, PXA8, and p63. INI1/SMARB1 showed characteristic weak staining with a mosaic pattern. Reverse transcription-polymerase chain reaction for SYT-SSX translocation detected two peaks, one at 97 bp indicating general translocation for SYT-SSX and one at 143 bp indicating chimeric fusion transcript for SYT-SSX1 translocation. These findings further confirmed the diagnosis of SS. Computerized tomography scan (CT scan) of the neck, thorax, and abdomen (Fig. 2) done to complete metastatic workup shows

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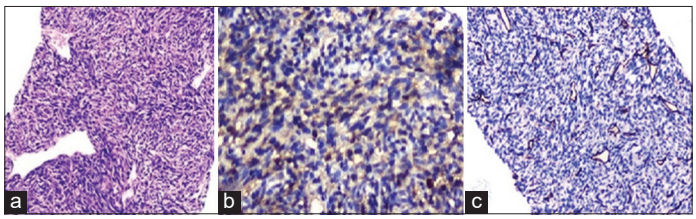

Figure 1: (a) Sheets of spindle cells with hemangiopericytoma like pattern (H&E, ×100); (b) CD99: Tumor cells showing membranous positivity (IHC, ×100); (c) CD34: Negative staining of tumor cells, note the endothelial cells lining the blood vessels showing positive staining (IHC, ×100)

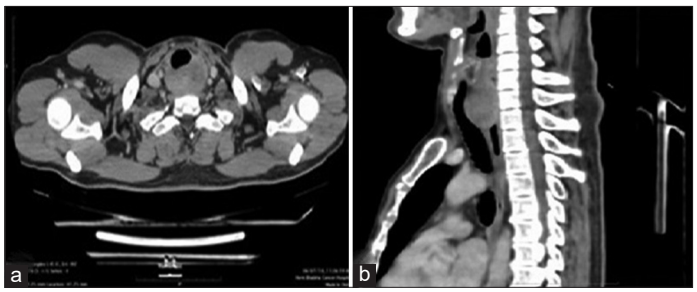

Figure 2: Computed tomography scan showing an exophytic mass arising from cervical esophagus. (a) Axial view; (b) sagittal view

5.2 cm×3.2 cm sized exophytic lesion arising from the cervical esophagus lies in the trachea-esophageal groove. No evidence of nodal or systemic metastasis was present. After metastatic workup, the case was discussed in the multidisciplinary joint clinic of our hospital.

After discussing the case in the multidisciplinary joint clinic, he was treated with radical RT considering the location of the disease. He received radical RT to the cervical esophagus with 1 cm margin circumferentially and 3 cm margin craniocaudally. Elective nodal irradiation was avoided (considering no evidence for elective nodal irradiation for sarcoma esophagus) using volumetric arc therapy with image guidance (IGRT) with 6 MV photon energy to a dose of 70.20 Gy in 39 fractions at 1.8 Gy per fraction daily. Chemotherapy was not given, neither concurrent nor adjuvant.

He was started on celecoxib 200 mg twice daily for 18 months after 3 months of completion of RT. He was on regular follow-up every 3 months. On the first follow-up (post-RT 3 months), the positron emission tomography-CT (PET-CT) scan showed metabolically inactive residual disease of 1.5 cm × 1.6 cm × 5.1 cm, no distant metastasis, and dysphagia relived completely. Six months post-RT endoscopy was suggestive of no residual lesion. He continued taking celecoxib and was clinically asymptomatic.

After 16 months post-RT in February 2020, he presented with complaints of hoarseness of voice for 15 days. CT scan of the neck and thorax suggestive of increased in the size and extent of the exophytic lesion arising from the cervical esophagus, measuring 5.8 cm×3.8 cm which was previously 4.7 cm×2.5 cm. PET CT showed mildly avid exophytic mass in the cervical esophagus 3.9 cm×7 cm×5.2 cm abutting the left lobe of the thyroid, with infiltration into the upper trachea SUV 3.6 suggestive of residual/recurrent sarcomatoid tumor and indeterminate pleural-based nodule in the lower lobe of the left lung SUV 1.5. He developed rapidly progressive dysphagia and breathlessness. Upper gastroduodenoscopy was not able to perform due to stricture. He underwent feeding jejunostomy in view of progressive dysphagia. He was planned for palliative chemotherapy, ifosfamide, and doxorubicin. After three cycles of chemotherapy, he is asymptomatic and having Grade 0 dysphagia.

DISCUSSION

More than 95% of esophageal malignancies are of epithelial in origin either squamous cell carcinoma or adenocarcinoma. Sarcoma esophagus is a rare variety that occurred in 0.1–1.5% of patients [1]. They may be divided into tumors with mixed epithelial and spindle cell characteristics such as carcinosarcoma and pure sarcomas of mesenchymal origin such as leiomyosarcoma. Carcinosarcomas occur more frequently than pure sarcomas. Carcinosarcoma, first named by Virchow in 1865, is more common and consists of intermingled malignant epithelial and sarcomatous components, both of which are known to metastasize. Like squamous cell carcinoma of the esophagus, carcinosarcomas occur most commonly in middle-aged and elderly males with a history of smoking and/or alcohol use [3,4]. It has been suggested that carcinosarcomas have a better prognosis than squamous cell carcinomas.

Pure sarcomas of the esophagus are very rare. The most common of these is leiomyosarcoma. Leiomyosarcomas usually occur in the middle or distal portions of the esophagus, where smooth muscle is located. They may be polypoid or infiltrating and has better long-term survival than squamous cell carcinoma. Leiomyosarcoma has a slow and indolent clinical course, followed by late recurrence, and eventual death of patients from the disease. Hematogenous metastasis was the cause of most of the cases of tumor recurrence and death [5].

Usually, the patients present at a younger age than carcinoma. The median age at diagnosis is 58 years (26–76 years) and has slightly more predilection for males [6]. The most common symptom is progressive dysphagia but may present with unusual symptoms such as epigastric pain, vomiting, and anemia.

On endoscopy, sarcomas are mostly seen as polypoid and exophytic mass lesions and rarely as an ulcerative lesion. Sometimes may present as malignant stricture. CT may show an inhomogeneously enhancing intramural mass. Depending on the degree of histological differentiation and relative prominence of the two cellular elements, SS forms a continuous morphologic spectrum and can be classified into the biphasic SS, monophasic fibrous SS, and poorly differentiated SS. Characteristic histologic finding of SS is often a biphasic pattern accompanied by an epithelial component and spindle cell region. SS is difficult to diagnose purely on the basis of histological appearance, IHC aid in diagnosis.

SS has undifferentiated spindle cells similar in appearance to SS in other areas but overt mesenchymal differentiation showing smooth muscle, cartilage, or bone formation. Epithelial cells in

biphasic SS consistently express EMA and keratins, in particular (7, 8, 14, 18, and 19 including keratin 20) [7]. Neoplastic cells also show immunoreactivity for vimentin, Bcl-2, and CD99 with focal immunoreactivity for S-100 protein and are negative for CD34 and desmin. Almost all morphological subtypes express a specific t(X;18)(p11.2;q11.2) chromosomal translocation. X;18 translocation is a sensitive marker and is demonstrated in 70–90% of SS. The specific t(X; 18) (p11.2; q11.2) results in the fusion gene product SYT-SSX [8]. This translocation results in three alternative fusion products of the SYT gene (on chromosome 18) with either SSX1 or SSX2 or SSX4 gene (on chromosome X). This translocation is 100% specific for SS. A unique pattern of decreased INI1 immunoreactivity with high specificity (100%) and sensitivity (86%) for SS distinguishes it from its histologic mimics.

We did a literature review to understand the incidence, treatment, and outcome of sarcoma esophagus which is summarized in Table 1 [9-14]. Even in the Indian context, we found only two cases of spindle cell sarcoma [15,16] and one case of leiomyosarcoma involving the esophagus [2], which is summarized in Table 2. About 85–90% of SS occurs in the extremities, especially around large joints followed by the head-and-neck region. SSs rarely involve the esophagus. Reported examples arising in the digestive tract are rare, only 11 case reports of primary esophageal SS including one case report of gastroesophageal junction involvement [17]. Esophageal SS mostly involved the cervical or proximal esophagus.

The primary differential diagnosis of biphasic SS in the digestive tract is carcinosarcoma. The age ranges for both tumors overlap; however, carcinosarcoma tends to present at an older age than SS. Carcinosarcomas of the esophagus are most common in the middle third of the esophagus while SS has been restricted to the proximal esophagus.

By IHC, the epithelial and mesenchymal elements of carcinosarcoma and SS can have essentially the same pattern of reactivity with antibodies directed against epithelial markers and vimentin. However, SS often expresses neuroectodermal antigens. CD99 expression has been demonstrated in 46–100% of SS. The differential diagnosis of monophasic fibrous or poorly differentiated SS of the digestive tract includes benign and malignant gastrointestinal stromal tumor and leiomyosarcoma.

There is no consistent treatment policy and it is difficult to make treatment recommendations due to the scarcity of cases. The treatment of choice for esophageal sarcomas has traditionally been radical surgical resection [2]. Esophagectomy/esophagogastrectomy is the surgery of choice wherever surgery is possible. In inoperable cases of esophageal sarcomas, RT may play an important role as a primary modality of treatment. Our

Table 1: Cases of different esophageal sarcoma in the international studies

Histology	Incidence	Treatment	Survival
Carcinosarcoma	0.63% [9]	Esophagectomy with mediastinal and abdominal lymph node dissection. Followed by adjuvant radiotherapy or adjuvant chemotherapy	5-year overall survival 44.8% Median survival time 43 months
	1 case report [10]	Subtotal esophagectomy with cervical, thoracic, and abdominal lymph node dissection, and reconstruction using the stomach	Overall survival of 8 months
	1 case report [11]	Transthoracic total esophagectomy with wide lymph node dissection, gastric interposition, and posterior mediastinal esophagogastrostomy.	Died during post-operative period
	2 case reports [12]	No definitive treatment	-
Synovial sarcoma nearly 10 cases reported [17]	1 case report [13]	Transhiatal total esophagectomy with gastric pull-up through the posterior mediastinum and cervical esophagogastric anastomosis Adjuvant chemotherapy (ifosfamide, etoposide, and mesna every 3 weeks for 6 courses) Adjuvant RT (54 Gy in 30 fractions)	Disease-free survival 4 months Overall survival 18 months
	1 case report [12]	Low cervical esophagectomy with local excision of the tumor Adjuvant radiotherapy 60 Gy	Overall survival 6.5 years
	1 case report [8]	Vagotomy, antrectomy, and a Billroth II procedure	Disease-free survival 21 months
Leiomyosarcoma	0.5% [14]	Subtotal esophagectomy with esophagogastroplasty and anastomosis in the lower cervical region	Disease-free survival 14 months Overall survival 20 months
Liposarcoma	Very rare	-	-
Myxofibrosarcoma	Very rare	-	-
Ewing's sarcoma	Very rare	-	-
Granulocytic sarcoma	Very rare	-	-
Histiocytic sarcoma	Very rare	-	-
Schwannoma	Very rare	-	-
Epithelioid sarcoma	Very rare	-	-
Rhabdomyosarcoma	Very rare	-	-

Table 2: Case reports available from the Indian context

Histology	Age at presentation	Treatment	Survival	Author
Leiomyosarcoma	40 years male	Ivor Lewis esophagectomy	7 years (DFS)	Pramesh *et al*. [2] (2003)
Spindle cell sarcoma	55 years female	Radical radiotherapy to 66 Gy	2 years (DFS)	Lokesh *et al.* [15]
Spindle cell sarcoma	63 years male	Palliative radiotherapy 46 Gy/23 # followed by adjuvant 4 cycles of chemotherapy (Doxorubicin + Ifosfamide)	1 year 8 months (OS)	Patricia *et al*. [16]
Synovial sarcoma	35 years male	Radical radiotherapy to dose of 70.20 Gy/39# at 1.8 Gy/#	16 months (DFS)	Present study (2020)

OS: Overall survival, DFS: Disease-free survival

patient was treated successfully with radical RT and was disease free for 16 months.

CONCLUSION

SS esophagus is a rare variety; we found only two cases reported in the Indian context and ours is the third case. It usually presents at an early age, our patient was presented at 35 years of age. It can present with uncommon symptoms such as epigastric pain, vomiting, and anemia, although our patient presented with a common symptom of dysphagia. Histopathology examination is diagnostic for spindle cells but needs IHC to differentiate it from other types of sarcoma (leiomyosarcoma, RMS, and schwannoma). SYT-SSX translocation and INI1 are a specific marker for SS. Our patient was disease free for more than a year after receiving radical RT before developing a recurrence. We need more cases to understand the biology of such rare disease, its optimum treatment, and outcome.

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