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CASE REPORT

Esophageal Squamous Cell Carcinoma Metastatic to Umbilicus: a Case Report with Review of Literature

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Introduction

Esophageal cancer is the 8th most common malignancy worldwide and around 455,800 new cases and 400,200 deaths in 2012 were attributed to it. An alarming 80% of these cases occurred in developing countries [1]. According to WHO cancer statistics 2018, esophageal cancer is responsible for 4.9% of overall cancer-related deaths worldwide and 5.7% in India. The two major histological types not only differ in their origin but also in their incidence. Whereas, adenocarcinomas arise from lower 1/3rd of esophagus with frequency of 0.7/100,000; however, squamous cell carcinoma (SCC) arises from upper and middle 1/3rd region and occurs at rate of 5.2 per 100,000 [1]. Even though newer treatment modalities have developed, esophageal cancer still has dismal prognosis. The 5-year survival rates depend upon tumor stage at the time of diagnosis which warrants a thorough workup to look for metastatic disease, tumor invasion, and lymph node involvement. The origin of cancer has been divided in three regions, i.e., upper, middle, and lower 1/3 based on lymphatic drainage. The region involved has been directly included in the stage T2–T3 N0M0 for SCC of esophagus [2]. Presence of distant metastases at the time of presentation has been found in around 20–30% of patients with esophageal SCC. They are seen in liver (35%), lungs (20%), bones (9%), adrenal glands (5%), and, rarely, peritoneum and brain [3]. Metastasis to skin has been found between 1 and 9% among all cases of malignancies and only 10% of them affect the umbilical region [4]. Cutaneous metastasis from esophageal primary per se is very rare (< 1%) and rarer when it comes to SCC esophagus. The location of metastasis to skin from esophageal carcinoma is variable. The scalp, neck, and face have been reported as common locations [4]. Umbilical metastatic nodule is an important clinical sign, which signifies widespread metastasis and poor prognosis. After extensive search on PubMed and Google with mesh terms "umbilical nodule," "SCC esophagus," and "Sister Mary Joseph Nodule," we could find only four [Table 1] published cases in medical literature [5–8]. Here in, we report a case of esophageal SCC metastatic to umbilicus as a nodule along with review of published medical literature.

Case Report

Initially in the month of March 2017, our case, who is a 40-year-old male, presented with complaints of progressive dysphagia to solids as well as liquids for a period of 10 months. He was a beedi smoker (20 packs/day) and alcoholic for past 25 years. His upper GI endoscopy was done which revealed an ulcero-proliferative growth in the lower part of the esophagus. CT scan also showed circumferential thickening in lower 1/3 region, partly extending to the GE junction (GEJ). Esophageal biopsy from growth showed a moderately differentiated SCC. Whole body PET–CT (Fig. 1a, b) showed hyper metabolic soft tissue thickening of distal esophagus reaching up to GEJ with luminal narrowing (extent 7 cm and thickness 1.8 cm) along with involvement of left gastro-hepatic lymph node. The diagnosis of primary SCC of esophagus with metastasis to left gastro-hepatic lymph node was concluded. Preoperatively, the patient was given three cycles of chemotherapy including cisplatin and 5 fluorouracil which was completed in the month of September 2017. Initially, the patient got relieved, but after 2 months, symptom of dysphagia reappeared with more severity. A repeat PET CT scan showed progressive disease (post chemotherapy) with the

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Table 1 Cases of primary esophageal squamous cell carcinoma with metastasis to umblicus

S. no.	Year	Ref. no.	Case reports	Age in years	Location of primary/ histopathology	Stage at diagnosis	Time interval for recurrence	Metastasis to other organs	Size of the nodule
1	2004	Ref. no. 5	Dutta U et al.	65 years	Lower 1/3 of esophagus, squamous cell carcinoma	Not mentioned	2 years	Yes	Not mentioned
2	2007	Ref. no. 6	Wijekoon NS et al.	77 years	Lower 1/3 of esophagus, squamous cell carcinoma	Extensive mets present	2 months painful umblical nodule (no primary)	Yes	1.5 cm
3	2011	Ref. no. 7	Ge, Jheng-Siang and Yang et al.	64 years	Esophageal SCC; PDSCC	T3N0M0	6 months post surgery and CT and RT	Yes	Not mentioned
4	2016	Ref. no. 8	Mashimo Y et al.	74 years	Lower thoracic esophagus; poorly differentiat-ed SCC	T3N1M1b	Post 2 cycles of CT	Yes	2 cm
5	2018		Index case	40 years	Middle esophagus; MDSCC	T3N1M0	Post 8 months surgery	Yes	3 × 2 cm

extent increasing to 7.8 cm and max thickness to 2 cm (from 7 to 1.8 cm respectively). The patient was planned for Ivor–Lewis esophagectomy and was operated in the month of November 2017. Abdominal examination intra-operatively showed no ascites and no sign of liver or omental metastasis but multiple matted left gastric lymph nodes were noted. There were multiple adhesions of lung and parietal wall with tumor. Gross and histopathological examination of esophagectomy specimen showed ulcero-infiltrative growth circumferentially involving 4.5 cm of lower end of esophagus. The growth was diagnosed as squamous cell carcinoma. Tumor did not involve the gastroesophageal junction and

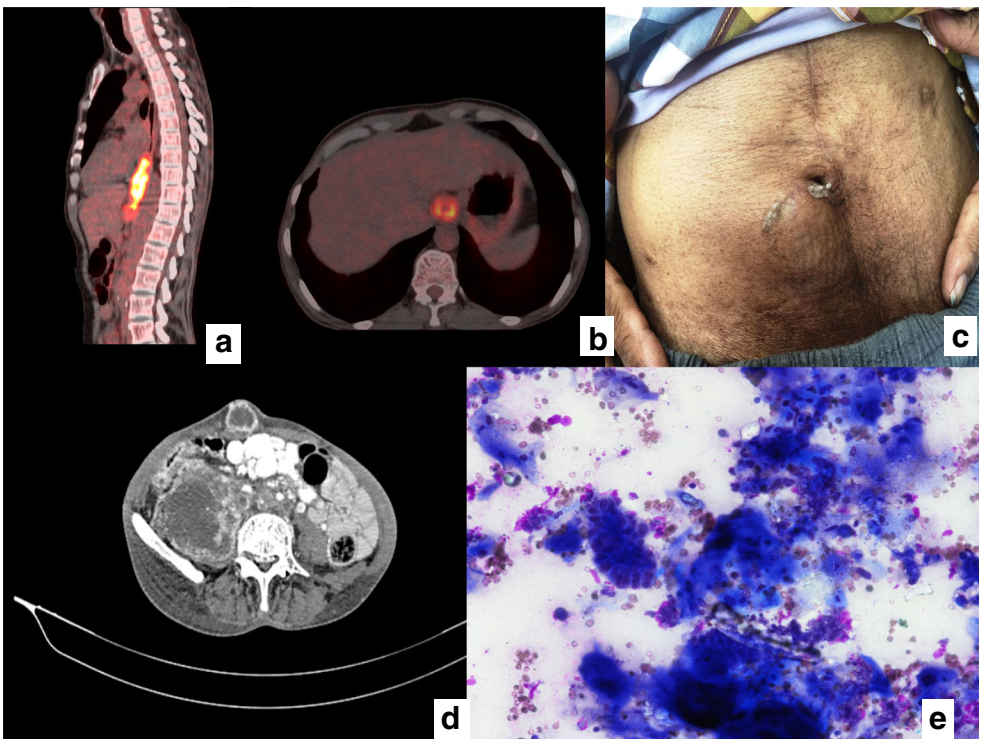

Fig. 1 **a** Sagittal section. **b** Transverse section—PET scan showing cancerous growth at lower end. **c** Clinical photograph of umbilical nodule. **d** CT scan of abdomen showing the presence of umbilical nodule. **e** Microphotograph of umbilical aspirate showing pleomorphic squamous cell carcinoma tumor cell and mature squamous cells. Giemsa 20X10

proximal and distal margins of esophagectomy specimen were free. Post-operatively, the patient was on regular follow-up.

After 8 months, he developed a subcutaneous nodule (Fig. 1c) in umbilical region. Abdominal CECT showed it measuring 3 × 2 cm (Fig. 1d). Ultrasound-guided fine needle aspiration was done from the nodule which showed metastatic tumor cells in a necrotic background. Tumor cells were arranged in clusters and scattered singly, having high N/C ratio, inconspicuous nucleoli, and moderate to scant ink blue cytoplasm which were consistent with metastatic SCC (Fig. 1e). Subsequently, on upper GI endoscopy, mucosal irregularity and bleeding just proximal to anastomotic site was noted. Endoscopic biopsy showed dysplastic squamous epithelium with ulceration along with acute inflammatory exudate. Over the next few weeks, the patient developed symptoms like sharp aching pain in the back, difficulty in breathing, swelling, and bilateral edema in lower limbs. Subsequent CECT revealed extensive metastasis involving the right kidney, lungs, mediastinal lymph nodes, and retroperitoneal nodes along with soft tissue and subcutaneous deposits in the gluteal region and anterior abdominal wall. There was also an infrarenal tumor thrombus extending up to the bilateral common iliac veins. Patient is now on palliative medications including oral morphine and gabapentin along with NSAIDS for pain control and better quality of life for a month but his condition is deteriorating.

Discussion

The global burden and incidence of esophageal cancer is expected to rise by as much as 140% by 2025 [9]. Adenocarcinomas of esophagus are on the rise in developed countries like the USA attributed to the dietary and lifestyle changes causing obesity and gastroesophageal reflux. However, SCC is the most prevalent histological subtype of esophageal cancer worldwide. Developing countries make up as much as 80% of the total esophageal cancer-related deaths worldwide. The area extending from Northeast China to the Middle East is known as the Asian esophageal cancer belt. A whooping 100 cases per 100,000 of esophageal SCC annually are reported from these areas [9]. Even though numerous advances have been made in screening, diagnostics, and treatment modalities over the past few decades, a 5-year survival rate for esophageal cancer is only 15–20% [9]. The contributing factors for overall survival are the extent of local spread and distant metastasis which warrants a thorough workup. Metastasis to distant organs is the leading cause of cancer-related deaths. Metastasis from esophageal cancer most commonly spreads to the liver, followed by lung, bone, and brain.

A study [10] evaluated published literature on metastasis from esophageal cancer and found that unique anatomical features of the esophagus, i.e., absence of serosal coating and presence of peri-esophageal adventitia, make it more prone for unexpected metastatic sites. It also concluded that around 2/3rd of cancer originate from the lower esophagus and 60% of them were from squamous cell carcinoma. Cutaneous etastasis is reported up to 5–10% in all visceral malignancies. Neoplasms that are prone to metastasize to skin are usually from breasts, lung, colon, and rectum [10]. In one study, Lookingbill et al. [11] analyzed 4020 cases of cutaneous metastasis and found only 3 of the cases to be of esophageal origin. On the other hand, Quint et al. [12] studied 838 cases of esophageal carcinoma and found only 2 cases metastatic to skin. Skin involvement is known to occur over the age of 60 years and the primary tumors are located in the lower third of esophagus [13]. However, the index case was a 40-year-old patient but the primary tumor was located in lower 1/3rd esophagus similar to other cases.

Sister Mary Joseph nodule (*SMJN*) is a name given to cutaneous metastasis from internal malignancies to honor Sister Mary Joseph, who first suggested a link between patients having abdominal malignant neoplasms and umbilical nodule. Dr. Hamilton Bailey first described this as SMJN in his book *Demonstrations of Physical Signs in Clinical Surgery* in the year 1949 [14]. Metastasis to the umbilicus can occur via direct contiguous extension, lymphatic or hematogenous spread. Umbilicus due to lack of muscle layer has anatomical susceptibility to metastasis. The only barriers between the umbilical skin and peritoneal tumor are transversalis fascia and linea alba [6]. SMJN almost always originates from a primary cancer of GI tract (35–65%) and genitourinary tract (12–35%). Other primary cancers have also been reported from lung, pancreas, liver, gallbladder, lymphoma, breast, kidney, penis, prostate, and testicles [14]. As many as 83% of all malignant tumors in the umbilical region are metastastic and out of these 15–29%, the primary site is unknown [14]. Histology of the metastatic umbilical tumor usually reveals adenocarcinomas, but rare reports of umbilical metastasis from sarcomas, mesotheliomas, and melanomas have also been seen [15]. Metastasis to the umbilicus from a primary esophageal squamous cell carcinoma is an extremely rare condition, and only 4 cases have been previously reported [Table 1] [5–8].

No distant metastasis at the time of diagnosis was present in our case similar to the case reported by Jheng et al. [7]. However, other two case reports had distant metastasis present at the time of diagnosis [6, 8]. The time period for secondary umbilical nodule ranged between 6 and 8 months after first diagnosis and beginning of treatment except in a single case where it is reported 2 years after treatment which could be probably due to the patient not being on follow-up [5]. All case reports including index case had extensive metastasis at the time secondary umbilical nodule. The survival time post umbilical metastasis was found to be variable but poor and ranging between 6 and 10 months. Hence, umbilical

metastasis points towards advanced disease and poor prognosis. SMJN as a sign should not be overlooked and if detected can change the future treatment protocol for the patients.

Conclusion

In a patient with a known malignancy, an umbilical nodule signifies possible spread or seeding of the primary tumor which can influence therapeutic decision-making. Presence of such a mass renders the patients inoperable and prevents unnecessary surgical interventions. Medical fraternity as well as patients must be made aware regarding SMJN, which is often overlooked and misinterpreted. However, it plays an important contributing factor to improve overall survival and management.

Compliance with Ethical Standards

Ethical Compliance The case has been reported with in compliance of institutional ethics protocol for hospital services.

Conflict of Interest The authors declare that they have no conflict of interest.

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