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MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR AT GASTROESOPHAGEAL JUNCTION- A RARE CASE

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ABSTRACT

Malignant peripheral nerve sheath tumors (MPNSTs) are very rare and , represents 3 - 10% of all soft tissue sarcomas. Approximately half of all such tumors are diagnosed in patients with neurofibromatosis type 1 (NF1). The extremities are involved most commonly, and the patient's age is usually 20 - 50 years. We herein describe a case of 63 year old lady with gastroesophageal junction MPNST, which was diagnosed histopathologically after surgery. The patient underwent curative esophagogastrectomy with D2 lymph node dissection and Roux-en-Y esophagojejunostomy. The postoperative recovery was uneventful. The ideal adjuvant treatment protocol is yet to be decided due to the relatively limited number of cases of these tumours previously reported.

INTRODUCTION

A malignant peripheral nerve sheath tumour(MPNST) is a very rare tumour, with an incidence of approximately 1: 100,000 people per year [1]. The neoplasm arises from a nerve fibre and exhibits variable differentiation toward one of the cellular components of the nerve sheath.

Approximately 50-60% of MPNSTs develop in patients with neurofibromatosis type 1(NF1)[3]. MPNSTs behave aggressively, and the risks of local recurrence and metastasis are significant. The 5-year survival rate is 30-50% despite application of multi disciplinary therapy[4]. Patients are usually diagnosed at 20-50 years of age[5].

Case Report

A 63 year old diabetic lady presented with complaints of difficulty in swallowing solid food since 3 months. She gives history of abdominal distension and epigastric discomfort after food intake. Also she had history of loss of appetite and lost 5kgs weight in last 3 months. No history of hematemesis or malena. She is a known case of Type 2 Diabetes mellitus, and was on regular oral hypoglycemic agents.

On General examination she was pale and dehydrated. Abdominal examination was unremarkable.

On admission, laboratory data revealed her hemoglobin level of 7.7gm/dL, for which she received two units of packed red cells. Gastroduodenoscopy (figure 1B) revealed a distal esophageal growth 29cms from incisors, extending into stomach with normal overlying mucosa.

In fundus of stomach a fungating mass seen in continuation of the esophageal growth, along the greater curvature of stomach occupying entire fundus of stomach with sloughed overlying mucosa and surface friability.

Body of stomach, antrum , pylorus , first and second part of duodenum were normal. Multiple biopsies taken from the mass- reported as poorely differentiated malignancy.

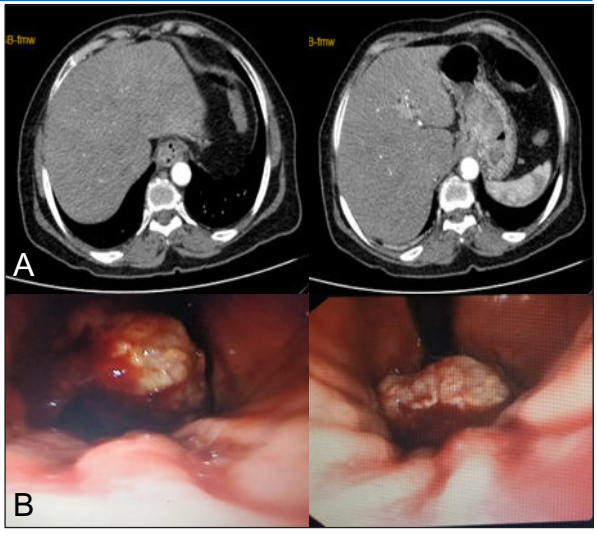

Figure 1: (A) CT revealed an enhancing mass at the lower end of esophagus extending through gastroesophageal junction into fundus of stomach. (B) Gastroduodenoscopy revealed a distinctly large proliferative mass arising from lower end of esophagus and extending on to fundus of stomach.

Contrast enhanced computed tomography of abdomen (figure 1A) showed Irregular wall thickening with loss of mural stratification noted involving the distal esophagus at the level of d9 vertebra extending through gastro-esophageal junction with a proliferative growth in fundus of stomach measuring 5.3x3.1x4.1cm (APxTRxCC). Lesion shows heterogenous enhancement following intravenous contrast administration. The lesion is seen to cause severe luminal narrowing at the level of esophagogastric junction without proximal dilatation of esophagus.

With a working diagnosis of Type III gastroesophageal junction tumour, patient was taken up for laparotomy, curative

esophagogastrectomy with D2 lymphnode dissection and Roux-en-Y esophagojejunostomy was done. Macroscopically polypoidal growth in esophagogastric junction extending into fundus of stomach distally and the lower esophagus proximally. Tumour measured 7x5.5x3.5 cm. The surface mucosa of the mass was ulcerated and it invaded serosa but not the adjacent structures. Totally 23 lymphnodes were retrieved and one node turned out positive for cancer cells. The surgical safety margin (proximal cut margin, 3.0 cm; distal cut margin, 15cms) was negative for tumour cells.

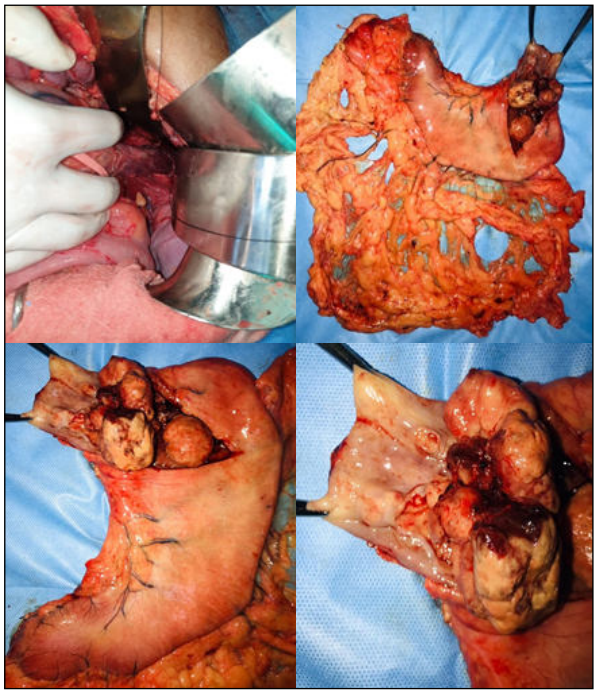

Figure 2: Macroscopically, the proliferative lesion was approximately 7.5x5.5cm in diameter and extending from lower esophagus to fundus of stomach.

On Microscopic examination, the tumor showed malignant spindle cells. The cytoplasm was scant, abundant with anisokaryosis. FNCLCC histologic grade 3 with Tumour differentiation score-2, The mitotis score-3 (10-19 mitoses per 10 high-power fields) and Necrosis score-1(<50% tumour necrosis). Margins were negative without any lymphovascular or perineural invasion.

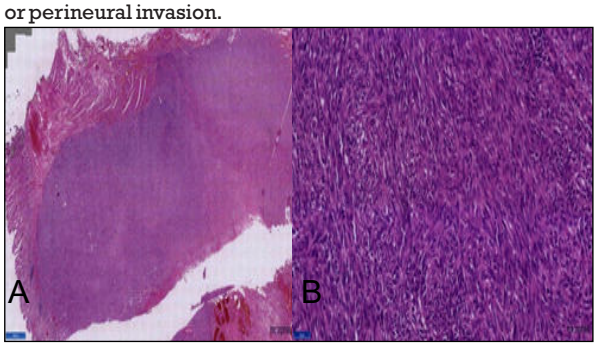

Figure 3: A, On low power field, The tumour is hypercellular with fascicular growth pattern. B. On high power field, spindle shaped cells with frequent mitotic figures.

On immunohistochemical staining, the tumor was negative for CD117& DOG 1 (rules out Gastro intestinal stromal tumour) ,P63 (rules out myoepithelial and basal cells), HMB45 (rules out melanoma), INSM1 and Smooth muscle Actin (rules out smooth muscle origin) but positive for S100 protein, EMA (focally positive). The Ki67 proliferation index was higher at 80%. Based on these findings, the tumor was identified as a malignant peripheral nerve sheath tumor - Grade 3

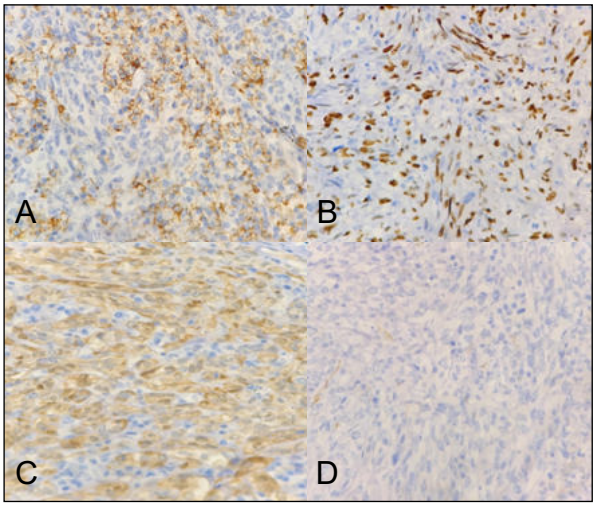

Figure 4: Immunohistochemical analysis showed that the tumour cells were focally positive for EMA(A) and S-100(C) but lack staining for DOG-1(D) and Ki-67(B) proliferation index was 80%.

Postoperatively, patient had an uneventful recovery and completed adjuvant chemotherapy (Adriamycin, Cyclophosphamide)

DISCUSSION

MPNST is typically associated with a poor outcome compared with those of other soft tissue sarcomas. The recurrence rate is as high as 40%, and the most common metastatic sites are the lungs and the bone [2]. The 5- year survival rate ranges from 30 to 50% [4].Tumor size, tumor site, and microscopically incomplete resection explain causes of poor outcomes in these patients. MPNST is associated with schwannomatosis and TP53 mutations and is confirmed at high frequency in NF1. The lifetime risk of MPNST in NF1 is between 9–13%. Gastric MPNSTs are extremely rare with only a few case reports (Table 1). In the gastrointestinal tract MPNST presents with hemorrhage or obstruction.

Literature Review

Table 1: Previous Case Reports Of Gastric MPNST

S.No.	Author	Journal	year
1.	Bees NR et al[6]	British Journal of Radiology	1997
2.	Loffeld RJ et al[7]	European Journal of Gastroenterology-Hepatology	1998
3.	Akira Watanabe et al[8]	Case Reports-Gastroenterology	2011
4.	Masashi Takemura et al [9]	Journal of Medical case reports	2012
5.	Wun Young Kim et al[10]	International Journal of Surgical Pathology	2015
6.	Subbbiah Shanmugam et al[11]	Journal of Medical Science and Clinical Research	2017

In view of limited incidence, and regulation of MPNST conception, there is a paucity of data in the literature regarding prognostic factors, incidence, and long term outcome in MPNST, especially in stomach. Of the English literature (searched in PubMed), from 1980 until now, there have been only 6 case reports of gastric MPNST[7-12] . Our case was the only case reported to affect gastroesophageal junction.

MPNSTs display unique clinicopathological characteristics. It is extremely difficult to diagnose MPNST. Much of the difficulty in diagnosing MPNST is the lack of specific neural

differentiation biomarkers[3]. It may occur sporadically or in association with Neurofibromatosis type 1(NF-1). Approximately 25-50% of observed MPNSTs occur in patients with NF-1. Most patients with MPNST have a small, truncating mutation in the NF-1 gene that is associated with an 8% to 13% risk of developing MPNST[13]. However in our case, the patient was not associated with neurofibromatosis. As it is difficult to make diagnosis of MPNST and exclude probable disease, many immunohistochemical stains including CD117, DOG 1, P63, HMB45, INSM1 and Smooth muscle Actin, S100 protein and EMA were used. Some neural markers, such as S-100, CD56 and protein gene product 9.5 are considered sensitive markers for peripheral nerve sheath tumors. S100, which is traditionally regarded as the best marker for MPNST, has limited diagnostic utility and is positive in only about 50-90% of the tumors [6]. MPNSTs per se lack sufficiently specific and sensitive immunohistochemical marker. So, in many cases the diagnosis of MPNST essentially becomes a diagnosis of exclusion.

MPNSTs are very aggresive and survival is poor. Like other soft tissue sarcomas, MPNSTs recur locally and spread hematogenously[13]. Treatment of choice for MPNST is curative surgical resection with negative margins. Radiation therapy and adjuvant systemic chemotherapy are important in addition to surgery in improving local control. Although improvement in local control have been seeen with adjuvant radiation therapy, the only one study out of Milan, Italy, has been ableto demonstrate that lack of radiation threapy predicts decreased disaese specific survival[14]. Inspite of aggressive surgery and adjuvant therapy, the prognosis for patients with MPNST is still poor, with the 5 year survival rates ranging from 35%-50%.[3]

In some reports, large tumour size(10cms) and a lack of S-100 staining were identified as important prognostic factors for the development of distant metastsis in patients with localised MPNST[3]. In our case, the mass was less than 10cm and positive for S-100, and we predict to have better prognosis compared with other MPNST cases. However, application of the results is limited because the reports are originated from all MPNSTs, not only stomach.

CONCLUSION

MPNST involving the gastroesophageal junction is an extremely rare case. R0 resection constitute the prime modality of treatment. Lymphadenectomy is done selectively. Adjuvant treatment is decided on the merit of individual cases after discussing in Tumour board.

In addition, careful histopathological and immuno histochemical review is very important to confirm the diagnosis of MPNST.

Declaration of Conflicting Interests

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