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Case Report

Gastric Malignant Peripheral Nerve Sheath Tumor – A Rare Mesenchymal Tumor in the Era of C-Kit

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Abstract
Malignant tumors of stomach other than carcinomas are less common. The more frequent of these are lymphomas and Gastrointestinal stromal tumors. A malignant peripheral nerve sheath tumor (MPNST) of stomach is extremely rare and only five cases have been reported in literature so far. Here we report a case of a Gastric malignant peripheral nerve sheath tumor in a patient of neurofibromatosis.
Keywords: *Gastric MPNST, Malignant Peripheral nerve sheath tumor, Stomach Carcinoma, Neurofibromatosis*

Introduction

A malignant peripheral nerve sheath tumor (MPNST) is a very rare tumor, with an incidence of approximately 1:100,000 people per year [1]. WHO coined the term MPNST in 2002 to replace previously existing terms including malignant schwannoma, malignant neurilemmoma, and neurofibrosarcoma [2]. 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) [4]. MPNSTs behave aggressively, and the risks of local recurrence and metastasis are significant. The 5-year survival rate is 30 - 50% despite application of multidisciplinary therapy [5].

Case Report

A 52 year male known case of neurofibromatosis, presented with dyspeptic symptoms and history of malena for 6 months duration. The patient had undergone partial cystectomy 12 years ago for leiomyosarcoma of the urinary bladder. Gastro duodenoscopy was done revealed proliferative growth in the fundus and body of the stomach. Rest of the stomach was normal first and second parts of duodenum were normal. Multiple biopsies

from the growth were done – reported as poorly differentiated adenocarcinoma. Computed tomography of the abdomen showed gastric wall thickening, no significant perigastric nodes, liver normal, no ascites.

With a working diagnosis of carcinoma stomach, patient was taken up for laparotomy, subtotal gastrectomy with D2 lymph node dissection was done (figure 1). Post-operative biopsy was poorly differentiated carcinoma. Immunohistochemical studies revealed– focal positive staining for S100, negative for CD117, SMA, CK 7, CK 20, CD34, CD 45& Chromogranin A, Ki 67 was 40% (Figure 3). A diagnosis of epithelioid variant of Malignant Peripheral Nerve Sheath Tumor was arrived at (Figure 2). All nodes sampled were negative for malignancy, tumor excision margins were clear. The patient had an uneventful recovery and is on follow up for the past three months.

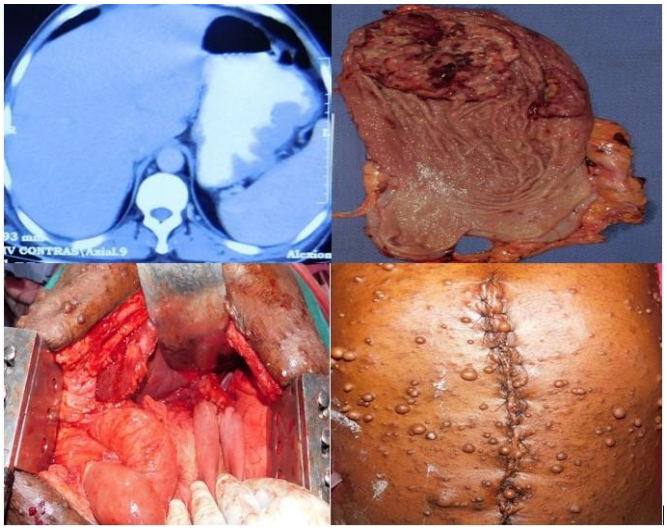

Figure 1: Top left: CT showing growth in the gastric fundus, Top right: Gastrectomy specimen, Bottom left: Residual gastric pouch, Bottom right: Abdomen shoeing multiple neurofibromatosis

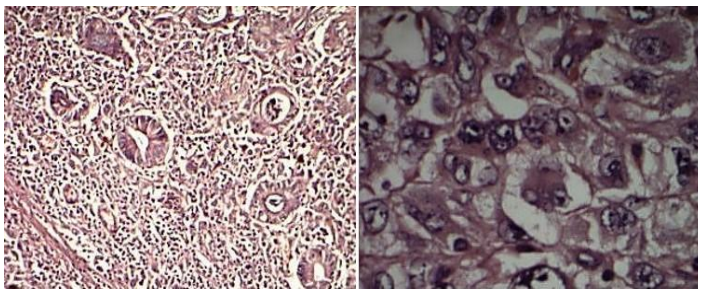

Figure 2: Histopathological features: Left: Gastric glands, Right: Epithelioid cells

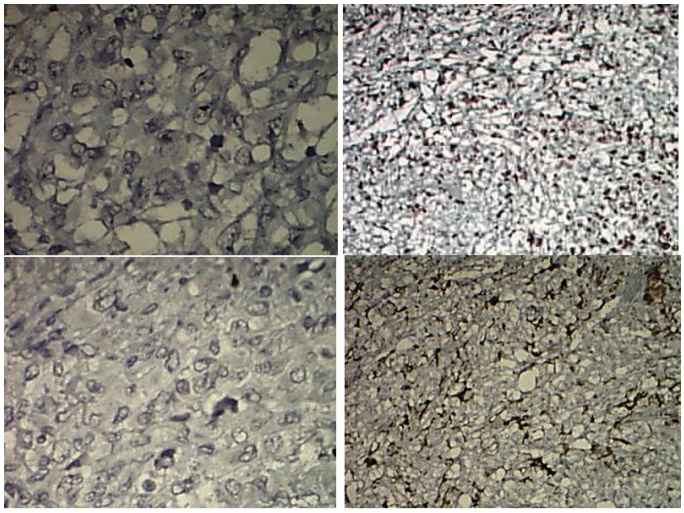

Figure 3: Top left: IHC- Cytokeratin negative, Top right: High Ki67 (40%), Bottom left: C-kit negative, Bottom right: Focal S-100 positive

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 [3]. The 5- year survival rate ranges from 30 to 50% [5]. Tumor size, tumor site, and microscopically incomplete resection explain causes of poor outcomes in these patients.

Only half of these are shown to exhibit schwannian differentiation by immunohisto-chemical methods. MPNST is associated with schwannomatosis and TP53 mutations and is confirmed at high frequency in NF1. It appears to be only increased in NF2 amongst those that have been irradiated. 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. The ideal adjuvant treatment protocol is yet to be decided due to the relatively limited number of cases of these tumors previously reported.

Table 1: Previous case reports of Gastric MPNST

S.No.	Author	Journal	year
1.	Bees NR et al [12]	British Journal of Radiology	1997
2.	Loffeld RJ et al [13]	European Journal of Gastroenteroly – Hepatology	1998
3.	Akira Watanabe et al [14]	Case Reports Gastroenterology	2011
4.	Masashi Takemura et al [15]	Journal of Medical case reports	2012
5.	Eun Young Kim et al [16]	International Journal of Surgical Pathology	2015

Akira Watanabe et al in 2011 reported a case of a spindle cell tumor in the body of the stomach treated with laparoscopic partial gastrectomy, with the pathological diagnosis of MPNST established post operatively.

Mashasi Takemura et al (Japan)in 2012 reported a case of Gastric MPNST in a 70 year old male treated with distal gastrectomy and D2 lymph node dissection.

Kim et al (Korea) in 2015 reported a case of Gastric MPNST in a 48 year old male treated with subtotal gastrectomy and D1 lymph node dissection. Patient had a margin free excision and no adjuvant treatment was given. In both these instances the regional nodes were uninvolved by the tumor.

In our patient owing to the proximal location of the lesion in the fundus and body of the stomach, it was initially decided to proceed with a total gastrectomy, but intraoperatively owing to the exophytic polypoid nature of the lesion and absence of peritumoral infiltration, subtotal gastrectomy with a modified Billroth II anastomoses was done so that the patient ended up with a remnant gastric pouch giving superior reservoir function.

The CT features of MPNST include large heterogeneously enhancing mass with an irregular or infiltrative margin, invasion of adjacent organs or soft tissues [9,10]. Gastric MPNSTs must be differentiated from Gastric Schwannomas and GISTs. Schwannomas are biologically benign and patients have an excellent prognosis after surgical resection.

MPNST is generally characterized by alternating hypo- and hyper-cell areas or a diffuse growth pattern of spindle-shaped cells which are asymmetrical and fusiform with wavy or comma-shaped hyperchromatic nuclei, arranged in palisades or spiral shapes [11]. In about 15% of MPNSTs, epithelioid or heterologous differentiation can be found [11]; the later includes rhabdomyoblasts, smooth muscle, bone, cartilage, and neuroendocrine component. Additionally, MPNST with glandular differentiation must be differentiated from metastatic carcinoma.

Some neural markers, such as S-100, CD56 and protein gene product 9.5 are considered sensitive markers for peripheral nerve sheath tumors. S-100, 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 [7]. In high grade MPNST, only scattered, if any, tumor cells are S-100 positive [11]. Thereby, MPNSTs per se lack sufficiently specific and sensitive immunohistochemical marker. So, in many cases the diagnosis of MPNST essentially becomes a diagnosis of exclusion.

Complete surgical resection is the mainstay of treatment for MPNST. Incomplete surgical resection increases the risk of MPNST-specific death nearly six-fold [4]. Adjuvant radiotherapy may improve local tumor control; however, any evidence that survival is prolonged by radiotherapy is limited [8,10]. In case of inoperable tumors neoadjuvant radiotherapy may render complete excision possible [9]. Role of chemotherapy for MPNST was proved more in pediatric patients than in adults. The overall response rate to primary chemotherapy was reported as 45% in a group of pediatric MPNST patients [6]. First-line chemotherapy typically consists of a combination of ifosfamide and doxorubicin [1].

Conclusions

The following conclusions could be drawn based on this case report. In patients with a background with neurofibromatosis, Gastric MPNST should be regarded as a differential diagnosis for carcinoma, more so when the biopsy confirms a

poorly differentiated glandular histology. Confirmation should be sought with immunohistochemistry studies. Surgery with clear margins is the only potential curative option in such patients. The final diagnosis is confirmed by immunohistochemical studies, and it is essential to differentiate this entity from other benign mesenchymal tumors like schwannoma which has very good prognosis and gastrointestinal stromal tumors for which targeted therapies do exist. Regional nodes are not involved and hence node dissection may be avoided if there is no clinical or radiological nodal involvement. There being no recommendations on adjuvant treatment for gastric MPNST as the experience is limited, it has to be decided on case to case basis.

Acknowledgement: nil

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