Case Report

GIST – A Mimicker: A Case Report

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ABSTRACT

Mesenchymal tumours in the gastrointestinal tract have long been problematic in terms of diagnosis, prognosis and therapy. But recent advances in Immunohistochemistry (IHC) and related therapies have allowed more specific diagnoses. Histopathological examination and the IHC study can correctly identify gastrointestinal stromal tumours (GIST) that are positive for c-KIT. The Imatinib drug which blocks the c-KIT receptor shows remarkable efficacy in the treatment of GIST.

We hereby report a case of GIST in a very young male patient who was admitted with a history of pain in the abdomen and recurrent vomiting since 6 months. The clinical examination revealed gastric outlet obstruction. This case report highlights the difficulties which were encountered in the pre-operative diagnosis, where the barium meal and ultrasound (USG) examination findings reported it as a pseudocyst/pancreatic abscess and the CT findings reported it as leiomyoma/lymphoma of the stomach. The histopathological examination of the partial gastrectomy specimen with the tumour tissue showed features which were suggestive of GIST. The IHC study for c-KIT was positive, thus confirming the diagnosis of GIST.

Key Words: Mesenchyme, Tumors, GIST

INTRODUCTION

Gastrointestinal stromal tumours (GIST), a different histopathological group of intestinal tumours which are derived from the mesenchyme, are seen rarely. They arise most commonly from the stomach which account for ~1% of all the gastric malignancies [1]. Their origin has been proposed to be the intestinal cells of Cajal. The mainstay of the primary treatment for GIST is R0 resection. Approximately 95% of the GISTs express a mutation in the *C-KIT* proto-oncogen [1,2]. A tyrosine kinase inhibitor, Imatinib mesylate, which blocks the KIT proteins, is the main agent for targeted adjuvant and neoadjuvant treatment. Risk assessment after the resection determines the need for adjuvant Imatinib treatment [3].

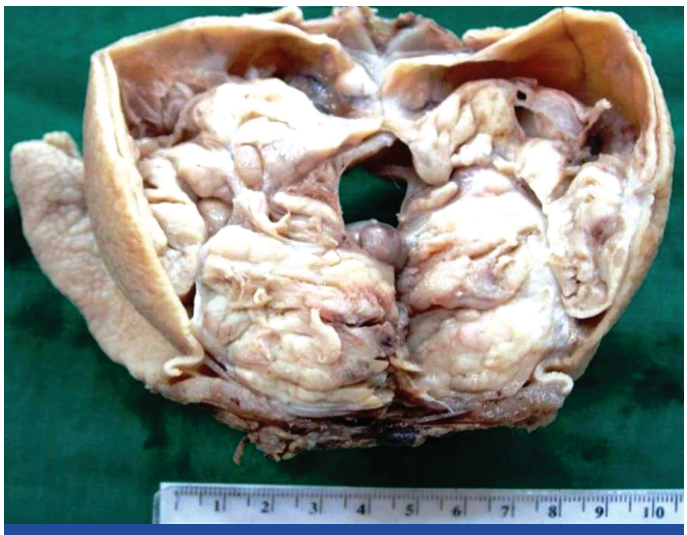
CASE REPORT

An adolescent male of 18 years was admitted with a history of abdominal fullness and distension. His past history was not significant. His general physical examination, vital signs and his respiratory, cardiovascular and central nervous system examination findings were normal. His per abdominal examination revealed a diffuse, vague, nontender swelling in the epigastrium. However, visible gastric peristalsis was not seen. The complete haemogram and serum amylase findings were within normal limits. The barium meal and USG investigation reports suspected a pseudopancreatic cyst/ pancreatic abscess. The CT findings suspected a leiomyoma/ lymphoma of the stomach. The clinical impression of a gastric outlet obstruction syndrome was made and the patient was posted for laparotomy.

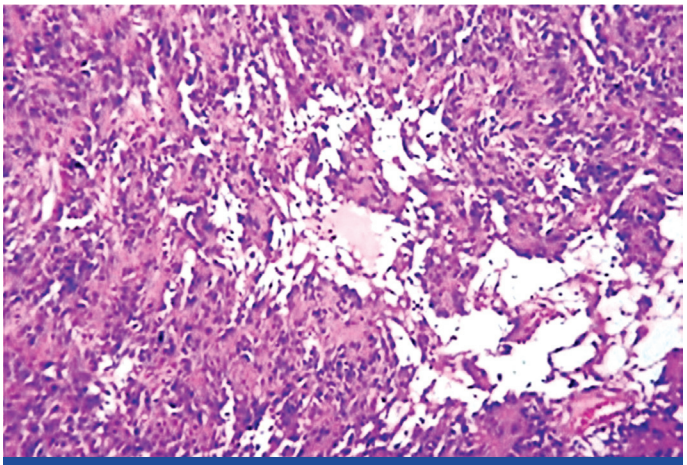
Gross Examination of the specimen: We received a partial gastrectomy specimen which showed a 8x6cm submucosal tumour of a predominantly gray white solid area. Focal areas of cystic change were also seen [Table/Fig-1]. The periantral lymph nodes were not enlarged significantly.

The histopathological examination of the multiple sections showed an irregular tumour which was invading the muscle layers. The tumour cells were arranged in interlacing bundles and fascicles and in diffuse sheets and nests (Table/Fig-2). Few areas showed a neurilemmoma like and other areas showed a vascular pattern with a myxoid background. The individual cells were predominantly of the spindle cell type with a few epithelioid types. No atypical mitosis, areas of necrosis and haemorrhage were noted. IHC was carried out, which revealed that CD 117 was positive and factor VIII was negative (Table/Fig-3&4).

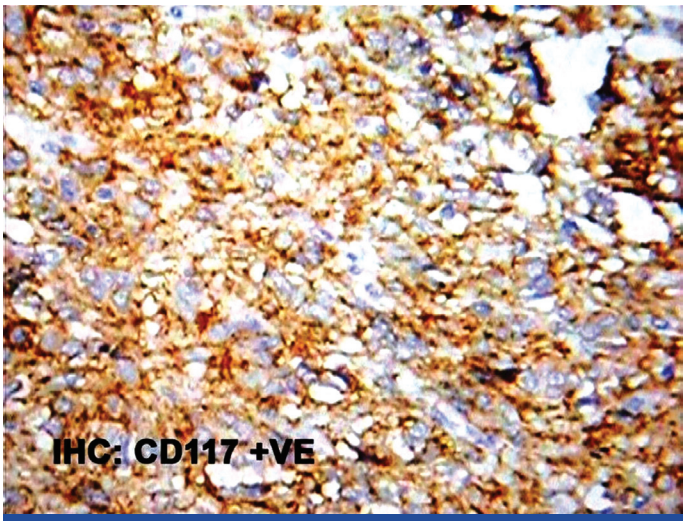
The final diagnosis was GIST of the stomach – the intermediate type. The postoperative follow up was uneventful.



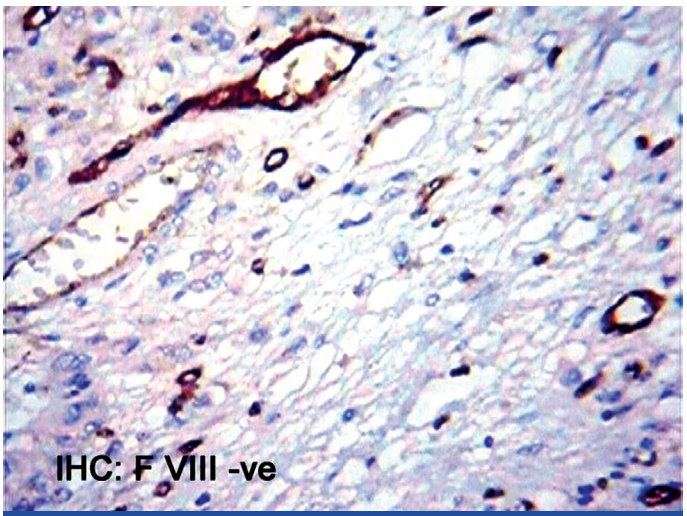
[Table/Fig-1]: Partial gastrectomy specimen showing submucosal tumor with gray white solid areas



[Table/Fig-2]: Tumor cells arranged in interlacing bundles and diffuse sheets with myxoid background (H and E stain, 10 X magnification)



[Table/Fig-3]: IHC showing CD 117 positivity



[Table/Fig-4]: IHC showing factor VIII negativity

DISCUSSION

Gastrointestinal stromal tumour (GIST) is the most common mesenchymal tumour of the gastrointestinal tract. GISTs have long been problematic in terms of diagnosis, prognosis and therapy. Most of them used to be classified wrongly as leiomyomas, leiomyosarcomas or leiomyoblastomas, based on the false belief that their origin was the smooth muscle [1]. Following the improvements in electron microscopy and in the immunohistochemical methods, it was shown that they originated from the intestinal pacemaker cells (the Cajal cells) [2]. The Cajal cells have both muscle and nerve cell properties and they are located in the submucosa, the muscularis mucosa and the myenteric plexus in the gastrointestinal system. GISTs can be diagnosed more easily and thus, major surgical resections can be prevented and the patients can be cured by using minimally invasive procedures [1,2,4].

Most of the GISTs are detected in the 6th or 7th decades of life, while only 10% are detected in those below 40 years of age. Although GISTs can be seen in any part of the gastrointestinal system, it has been reported that more than 50% of the cases are located in the stomach followed in order by the colorectum and the small intestine [1]. The commonest symptoms of gastric GISTs are haemorrhage and pain. Larger GISTs were found to have a tendency to grow lobulated and exophytic, whereas the smaller ones had a tendency to grow into the lumen. It is difficult to predict their metastatic potential, because malignity does not have any obvious clinical and pathological findings. All types of GISTs are considered to have malignant potential. Especially, the small intestinal GISTs have more potential for becoming malignant than the colonic and the gastric ones. Unlike the gastric adenocarcinomas, routine lymphadenectomy is not recommended unless there is no suspicion of intraoperative lymph node (LN) metastasis [5].

In general, the spindle cell type predominates over the epithelioid type. The malignant potential of GISTs depends on the tumour size and the mitotic counts. In the very low malignant risk group, the tumour size is less than 2 cm and the mitotic counts are less than 5 per 50 high power field (HPF). In the low malignant risk group, the tumour size is 2cm to <5cm and the mitotic counts are <5/50 HPF. In the intermediate risk group, the tumour size is 5cm to <10cm, and the mitotic counts are <5/50 HPF. In the high risk group, the tumour size is >10 cm, and the mitotic counts are >10/50 HPF. The other important histological properties are necrosis and ulceration. Especially, coagulation necrosis is thought to be related to the malignant behaviour. Recurrence and death were more common in the patients in the high-risk group, and these patients needed additional treatment [6].

Recent advances in the studies on the *KIT* gene and the *platelet derived growth factor receptor-α (PDGFRA)* gene have shown that GISTs are associated with the gain-of-function mutations of the KIT gene and less frequently with those of the PDGFRA gene [7]. The Cajal cells express the KIT protein (CD117) and CD34. In practice, the immunohistochemical demonstration of KIT and/or CD34 is a hallmark in the diagnosis of GIST in more than 90% of the GIST cases [7,8]. KIT-negative GIST is present. In practice, positive KIT and/or CD34 is enough to diagnose the lesions as GIST. In the KIT-negative cases, a genetic analysis of *KIT* and *PDGFRA* is necessary [9].

Surgery remains the mainstay of treatment in the patients with localized, resectable GISTs. It has recently been shown that the resection of the tumour and a microscopic negative surgical border is also sufficient. Lymphatic metastasis rarely occurs (0–3.4%) in patients with GIST. Lymph node (LN) dissection should be considered for patients with any suspicion of nodal metastasis. The most common locations for the metastasis are the liver, peritoneum, bones and lungs. Tumour rupture and spread are related to worsening of the illness, tumour recurrences and a short survival and these should be prevented during surgery [10].

It has been proved that Imatinib mesylate and Sunitinib maleate are very effective for metastatic GISTs. The reported recurrence rates

of 17–21% and 5-year survival rates of 48–70%, even in patients with resectable GISTs, calls for the need for an adjuvant treatment. Currently, the main indications for adjuvant Imatinib treatment are unresectable or metastatic diseases [3].

In conclusion, as the diagnostic tools and methods have improved, with the help of immunohistochemical analyses, GISTs can be diagnosed more easily. Thus, major surgical resections can be prevented and the patients can be cured with minimally invasive procedures. In all the GIST cases (benign or malignant), long-term follow-up is essential.

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