

**Recurrence of Gastrointestinal Stromal Tumor- A Cytological Diagnosis**Shukla Saumya<sup>1</sup>, Awasthi Punit Namrata<sup>2</sup>, Anand Nidhi<sup>3</sup>, Husain Nuzhat<sup>4</sup>, Kori Channabasappa<sup>5</sup>,Kumar Vijay<sup>6</sup>, Vijay Varun<sup>7</sup>, Malhotra Preet Kiran<sup>8</sup><sup>1, 2, 3</sup>MD (Pathology), Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh<sup>4</sup>MD (Pathology), FICP, IFCAP, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh.<sup>5, 6</sup>MS (General Surgery) Mch(Surgical Oncology), King George's Medical University, Lucknow, Uttar Pradesh<sup>7</sup>D. Orth, DNB Orth(Casualty Medical Officer), King George's Medical University, Lucknow, Uttar Pradesh<sup>8</sup>MD (Pathology), DNB, PDCC (Renal Pathology) Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh**\*Corresponding author**

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**Abstract:** Gastrointestinal stromal tumors (GISTs) neoplasms develop from pleuripotent stem cells that are programmed to differentiate into interstitial cells of Cajal and smooth muscle cells. A 47 year old male who was operated previously for malignant GIST of the small bowel presented with massive ascites. Cytologic examination of the ascitic fluid showed three-dimensional clusters of atypical spindle to epithelioid cells with indistinct cell borders, scant to moderate amount of cytoplasm and large oval to round hyperchromatic nuclei. Based on the cytologic morphology and clinicopathologic co-relation a diagnosis of malignant peritonitis due to metastasis from malignant GIST was made. The cytologic diagnosis is difficult as these lesions mimic other common tumors which include adenocarcinoma, smooth muscle tumours and schwannomas. Demonstration of CD117 or DOG1 antigen can clinch the diagnosis. The identification of GIST is essential for focused management, since GIST is the first model for targeted therapy in oncology.**Keywords:** Malignant gastrointestinal stromal tumor, ascitis.

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**INTRODUCTION**

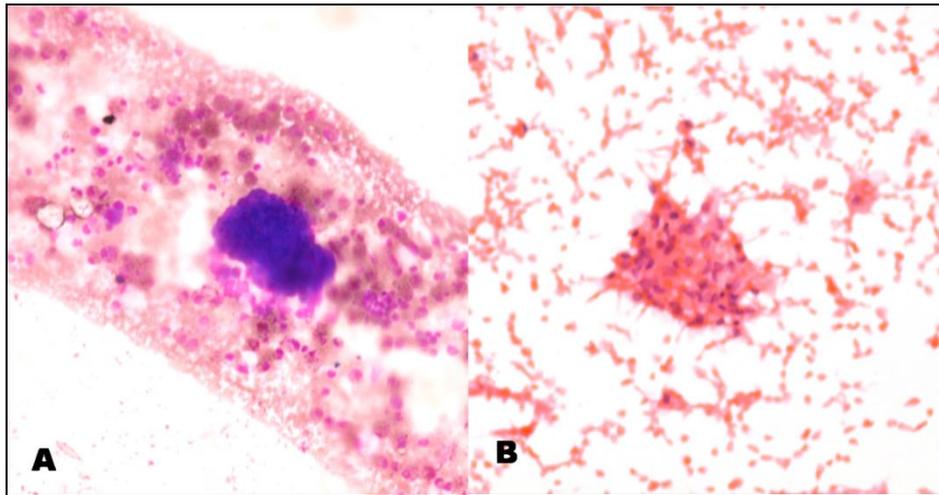
Gastrointestinal stromal tumors (GISTs) constitute a heterogeneous group of neoplasms arising anywhere in the gastrointestinal tract, from esophagus to the rectum [1]. GISTs are uncommon; they represent the most frequent mesenchymal neoplasms of the gastrointestinal tract accounting for 0.1-3% of all gastrointestinal neoplasms. Miettinen et al used the term "GIST" to designate a group of mesenchymal tumors with myogenic or neurogenic differentiation. In 1998, Kindblom et al reported that GISTs develop from pleuripotent stem cells that are programmed to differentiate into interstitial cells of Cajal (ICCs) and smooth muscle cells. GISTs have been documented in all parts of the gastrointestinal tract. A great majority of them occur in the stomach (60-70%) and small intestine (25-35%), with rare occurrence in the colon and rectum (5%), esophagus (<2%) and appendix [2-4]. Peritoneal metastases from GIST are rare and scant case reports are available [2,5]. The cytologic diagnosis of GIST is difficult as the spindle cell morphology of the cells mimics many other common tumors [5,6].

**CASE REPORT**

A 47 year old male patient presented with massive ascites. Computed tomography (CT) scan

revealed ill defined lobulated intra peritoneal soft tissue lesion with massive ascites and mesenteric lymphadenopathy. The patient had been operated 14 months back for malignant Gastro-intestinal stromal tumour (GIST) of the small bowel. About 1 liter of hemorrhagic ascitic fluid was received for cytologic examination. The fluid was centrifuged and sediment smears were prepared. The smears were stained with Leishman's stain and Hematoxylin and Eosin as per the standard protocol.

Cytologic examination of the ascitic fluid showed three-dimensional clusters of atypical elongated spindle shaped cells. The spindle cells had a high nucleo-cytoplasmic ratio with indistinct cell borders and scant to moderate amount of lightly stained cytoplasm. The nuclei were large oval to round hyperchromatic with coarse chromatin and few prominent nucleoli. Few mitotic figures and cytoplasmic vacuoles were also evident. The background was hemorrhagic with reactive mesothelial cells and foamy macrophages. (Figure 1) Based on the cytologic morphology and clinicopathologic co-relation a diagnosis of malignant peritonitis due to metastasis from malignant GIST was made.



**Fig-1: A: Three-dimensional clusters of atypical elongated spindle shaped cells on a heamorrhagic background (Leishman stain x 200) , (B) The spindle cells with indistinct cell borders, scant to moderate amount of lightly stained cytoplasm and large oval to round hyperchromatic nuclei (H & E x 200)**

## DISCUSSION

GISTs are frankly malignant in 10-30% of cases and cause mortality in 2% cases [2]. The criteria to predict the behavior of the tumor can only be well defined on histopathologic examination. The important criteria include the tumor size, necrosis and the mitotic rate. A mitotic rate of 5 per 50 HPF of size more than 5cm is indicative of malignancy [4,7]. GISTs are seen in the gastrointestinal tract but rarely also occur in the omentum and mesentery (extraintestinal GIST). Mesentery and omentum lack interstitial cells of Cajal, which confirms GIST's origin from multipotent mesenchymal cells. GIST has no age preference for gender; its peak incidence is between 40-70 years [2]. The histomorphology of GISTs varies from cellular spindle cell tumors to epithelioid and pleomorphic ones, and morphology differs somewhat by site.[3] Immunohistochemically GISTs are positive for KIT (CD117) or DOG 1 antigen, nestin (90-100%) and CD34 (70%). Smooth muscle actin (20-30%) and heavy caldesmon (80%) are often expressed, whereas desmin is usually absent [1-4,8]. GIST cells acquire an epithelioid appearance in ascitic fluid and certain diagnostic problems arise in differentiating GIST from other epithelioid and non-epithelioid neoplasms [2,6,9]. In ascitic fluid GISTs morphologically resemble adenocarcinomas. The most confusing findings are related to cells in a nested pattern and presence of intracytoplasmic vacuoles. The immunoreactivity for Vimentin suggests the mesenchymal nature of the cells and PAS demonstrating the lack of mucin within the cytoplasmic vacuoles supports the diagnosis of GIST [2].

Mesotheliomas may display PAS-negative, or rarely PAS positive, intracytoplasmic vacuoles, but in contrast to GIST, pancytokeratin positivity is a characteristic of mesotheliomas [2].

Amelanotic melanomas with its large nuclei and prominent nucleoli might be confused with GIST; weak CD117 positivity of its cells has also been reported, as well as Vimentin positivity. However, melanoma cells grow as single elements and are S-100 positive whereas GIST cells are seen in three-dimensional clusters and are usually S-100 negative [2].

Leiomyomas and leiomyosarcomas are the gastrointestinal tract tumors that are most frequently confused with GISTs. In these cases, cytologic samples are often moderately cellular with inconspicuous mitotic features. Smooth muscle differentiation (SMA-positivity, desmin positivity) is typical of these tumors, but they show nonreactivity for hematopoietic stem cell marker (CD34) and absent or only weak immunoreactivity for CD117 [2,6]. Schwannomas typically stain positive for CD34 and S100, but negative for CD117 [2,6].

The specific identification of GIST has become more important after the availability of KIT selective tyrosine kinase inhibitor Imatinib mesylate in the treatment of unresectable or metastatic cases. The identification of GIST is essential for focused management, since GIST is the first model for targeted therapy in oncology [2-4,10].

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