

Gastrointestinal Stromal Tumor: A Cytologist's Perspective

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Abstract

Introduction: Gastro-intestinal stromal tumors are mesenchymal tumors they have a unique immunophenotype, expressing c-KIT (CD117), DOG-1 and CD34 in most cases. Most commonly occurring in small intestine and stomach.

Case report: We report a case of EUS guided FNA from gastric mass in a 60 year old patient. Cytology showed cellular smears with palisade of tumor cells and blunt end spindle cells.

Discussion: GIST is very difficult to differentiate from other benign tumors i.e. leiomyoma and schwannoma. EUS guided FNA can be a very useful tool in approaching deep seated intra-abdominal lesion with ease. It also helps in diagnosis and treatment of the disease in a better way.

Keywords: GIST; Endoscopic ultrasound guided; Stromal tumors; Cytology; Fine needle aspiration

Abbreviations: CD: Cluster of Differentiation; DOG-1: Discovered on GIST 1; EGIST: Extra-Gastrointestinal Stromal Tumor; EUS: Endoscopic Ultrasound; FNAC: Fine Needle Aspiration Cytology; GIST: Gastrointestinal Stromal Tumor; ICC: Immunocytochemistry; IHC: Immunohistochemistry

Introduction

Gastrointestinal stromal tumors (GIST) are mesenchymal tumors arising in the gastrointestinal tract and occasionally elsewhere in the abdomen. They constitute approximately 1% of gastrointestinal malignancies [1]. Traditionally the majority of these tumors were thought to be derived from smooth muscle cells. However, they do not express markers of smooth muscle differentiation, such as desmin. Instead, they have a unique immunophenotype, expressing c-KIT (CD117), DOG-1 and CD34 in most cases [2]. The introduction of a new targeted treatment for GIST in the form of imatinib mesylate (STI-571, Gleevec), a receptor tyrosine kinase inhibitor, has further validated this entity [3]. An accurate pre-operative cytological diagnosis GIST is therefore important to help the clinician in deciding the treatment plan. Moreover, with the advent of endoscopic ultrasound guided fine needle aspiration (EUS guided FNA), cytological material from these tumors can be obtained from almost anywhere in the gastrointestinal tract and it is thus important for the cytologist to be aware of the spectrum of cytological features of GIST. Our case highlights the classical features of GIST on cytology.

Case Report

A 60 year old, male patient presented with complaints of a lump in the epigastric region with pain since 3 months. The pain was insidious in onset, gradually progressive, extending from the epigastric region to

left hypochondrium. He was a chronic alcoholic with dysphagia on and off. There were no other complaints.

On examination a firm to hard lump, not moving with respiration, was arising in the peritoneal cavity, with a dull note on percussion and measuring approximately 20 × 20 cm. USG abdomen showed evidence of an ill-defined large heterogeneous lesion of size 20 × 16 × 15 cm in the epigastric region with solid and cystic areas and mild vascularity on Colour Doppler. CECT showed a large heterogeneously enhancing intra peritoneal mass lesion with broad base along the greater curvature of stomach with extent and local mass effect (Figure 1).

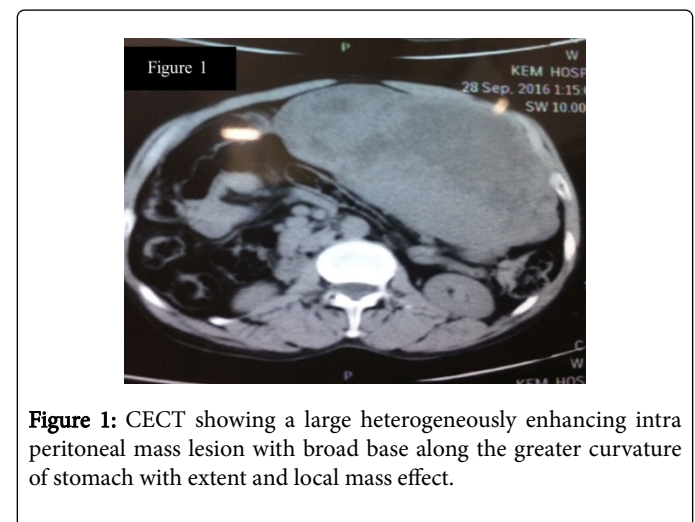


Figure 1: CECT showing a large heterogeneously enhancing intra peritoneal mass lesion with broad base along the greater curvature of stomach with extent and local mass effect.

EUS guided FNAC was done from the mass in the greater curvature of stomach. Smears were stained with routine H&E stain and Geimsa stain. Smears were cellular with tumor cells in clusters and singly scattered cells as well as bare nuclei (Figure 2a).

The cells were uniform, spindle shaped with blunt ended nuclei and fine, uniform chromatin. Characteristic streaming and palisading of tumor cells was seen at many places (Figure 2b and 2c). The cytoplasm was delicate, wispy, fibrillary and elongate cytoplasmic processes were seen at many places (Figure 2d).

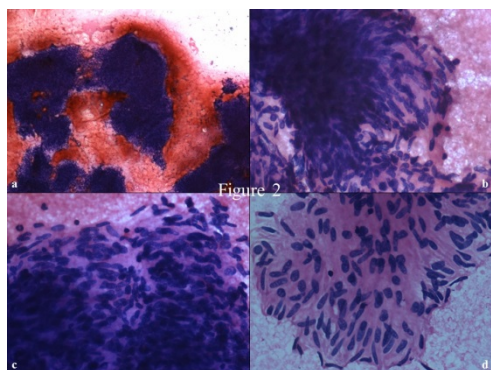


Figure 2: (a) Smears are cellular with tumor cells in clusters and singly scattered; (b and c) Characteristic streaming and palisading of tumor cells was seen at many places; (d) Smears show uniform spindle shaped cells with blunt ended nuclei and fine, uniform chromatin, cytoplasm is delicate, wispy, fibrillary and elongate cytoplasmic processes seen. (H&E 10X, 40X).

No necrosis or mitotic activity was noted. Few inflammatory cells comprised of plasma cells, neutrophils and lymphocytes were scattered in the background. Taking into account the clinical, radiologic and EUS guided FNAC features; an impression of spindle cell tumor, possibly GIST was given.

Following this the patient underwent gastrectomy and the histopathology report was in concordance with cytology findings and reported as GIST (Figure 3). IHC showed diffuse cKit (CD117) positivity in the tumor.

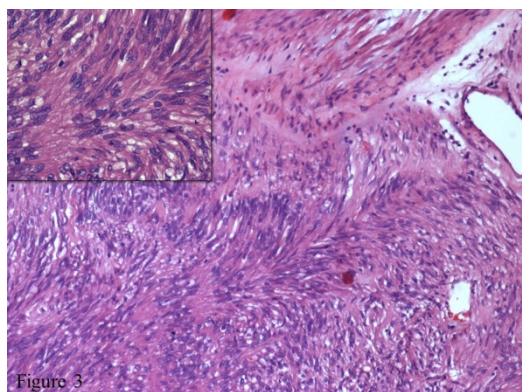


Figure 3: Histopathology showing features of GIST (H&E, 10X, 40X).

Discussion

Gastrointestinal stromal tumors are the most common mesenchymal tumors of the gastrointestinal tract. The name "GIST"

was proposed in 1983, but the cell of origin remained unclear until 1998 when interstitial cells of Cajal or their precursors were reported as the cells of origin. Majority of the GIST occur in the stomach (60% to 70%) and small intestine (25% to 35%) with rare occurrence in colon and rectum (5%), esophagus (2%) and appendix [3]. Though primary GISTs are described in the omentum, mesentery or retro-peritoneum, most GISTs in these sites are metastases from stomach or intestine [2,4].

The cytological studies on GIST in literature are not comparable as many of the earlier published cytologic studies have combined GIST into a group of neoplasms encompassing leiomyoma, schwannoma, leiomyosarcoma, and an epithelioid leiomyoblastoma [2,5]. However recently, few authors have established EUS-FNAC as a reliable method for diagnosing GIST and EGIST before surgical procedure [3,6].

In general, GISTs can be divided into epithelioid and spindled types. The smears obtained from FNA of these tumours are variably cellular. The spindled varieties have both single cells and 3-dimensional clusters of bipolar, spindled cells, arranged in fascicles. The nuclei in these fascicular bundles are elongated and irregular, with blunt ends and finely granular chromatin. They appear to have a streaming arrangement. The cytoplasm has a delicate, wispy texture. Because of indistinct cell borders, the groups of cells appear to form a syncytium. Fibrillary, metachromatic matrix is commonly seen within these bundles of spindled cells. The cellularity of epithelioid GISTs is also variable, and the cells are found in cohesive clusters on the smears prepared from the FNA. As in the spindled variety, the nuclear chromatin is finely granular, though the nuclear borders are rounded instead of being elongated. Some of the rounded, polygonal cells can be found singly in the background [2,3].

Finding mitoses in cytologic samples is often a difficult task because the tissue fragments come out in thick chunks, often too thick to be able to visualize anything in the midst of the fragment. Furthermore, just as in tissue sections necrosis and nuclear pleomorphism are often absent from even the most malignant of GISTs making it impossible to rely on this finding that is useful in other types of malignancies. In this way, it is rather impossible to accurately give a risk stratification based on cytologic material alone [2].

The important differential diagnosis of GIST without significant nuclear pleomorphism includes leiomyoma's and schwannoma. This is clinically important as the GIST have potential malignant behavior while the latter two pursue a benign course [3]. Several studies have tried to look at reliable indicators to differentiate GIST from Leiomyoma and although this distinction is difficult, the anatomic site (stomach), moderate to marked cellularity of the clusters, presence of isolated single cells and wispy cytoplasm with nuclear palisading favour GIST over leiomyoma. However, owing to significant morphologic overlap a definite diagnosis of GIST on FNAC is only possible with adjuncts such as immunocytochemistry (c-KIT, DOG-1, CD 34) on smears or cell block [7]. The need of the hour therefore is onsite evaluation of EUS FNA and collection of additional material for cell block and ICC in all cases of spindle celled gastrointestinal tumors.

Conclusion

EUS-FNAC can be being utilized to render diagnosis in palpable and deep seated masses, a cytopathologist needs to keep in mind the possibility of GIST and collect appropriate material when encountering cellular tumors with tight clusters of slender spindle cells.

Declarations

Ethical clearance: Permission for publication of this case was obtained by Institutional Ethics Committee, Seth GSMC & KEMH, Mumbai.

Consent to participate: Written informed consent to participate was obtained.

Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials: All the data regarding the findings are available within the manuscript.

Competing interests: The authors declare that they have no competing interests.

Author's Contributions

TS carried out concepts and design, literature search, participated in clinical study, data acquisition, data analysis and manuscript preparation will stand as guarantor also. KK carried out concepts and design, literature search, manuscript review. PS participated in clinical study, data acquisition and manuscript review. PG carried out literature search, clinical study and data acquisition. All the authors read and approved the final manuscript.

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