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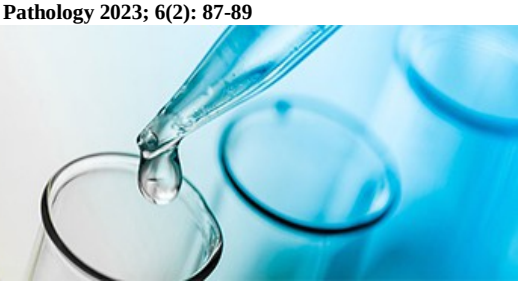

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**Rajinder Singh**
Assistant Professor, Department of Pathology, Military Hospital, Jammu, Jammu and Kashmir, India

**Yasmin Muhammed**
Associate Professor, Department of Pathology, Military Hospital, Jammu, Jammu and Kashmir, India

**Ajay Shanker Sharma**
Associate Professor, Department of Pathology, Military Hospital, Jammu, Jammu and Kashmir, India

**Jasbir Singh**
Associate Professor, Department of Pathology, Military Hospital, Jammu, Jammu and Kashmir, India

**Corresponding Author:**
**Rajinder Singh**
Assistant Professor, Department of Pathology, Military Hospital, Jammu, Jammu and Kashmir, India

# Gastrointestinal stromal tumour-sclerosing epithelioid a rare variant: A case report

**Rajinder Singh, Yasmin Muhammed, Ajay Shanker Sharma and Jasbir Singh**

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**Abstract**
Gastrointestinal stromal tumours are the most common mesenchymal neoplasms of the gastrointestinal tract. They should be differentiated from other types of mesenchymal tumours. GISTs harbour specific activating mutations in the KIT or platelet-derived growth factor receptor a (PDGFRA) receptor tyrosine kinases, which makes them responsive to pharmacologic inhibitors. The advances in the identification of GISTs, by its molecular and immunohistochemical basis, have led to a better understanding of the rare gastrointestinal tract tumours with predictable behaviour and outcome, replacing the older terminologies like leiomyoma, schwannoma or leiomyosarcoma. This report presents a case of 64 yr. old male recently operated on for a rare sclerosing epithelioid variant of the gastrointestinal tumour.

**Keywords:** Gastrointestinal stromal tumours, Immunohistochemistry, Pathological features

## Introduction
Gastrointestinal stromal tumours (GISTs), although the most common mesenchymal neoplasms of the gastrointestinal tract, are rare, accounting for approximately 1% to 3% of all gastrointestinal tumours. The term GIST was coined in 1983 by Mazur and Clarke for a distinct set of mesenchymal tumours of the GI tract that have no ultrastructural or immunohistochemical features characteristic of smooth muscle differentiation.
The cell of origin of these tumours is a pluripotent mesenchymal stem cell that differentiates into interstitial cells of Cajal, as demonstrated by Kindblom and associates in 1998. These cells of the GI tract, also known as "pacemaker cells", are responsible for initiating and co-coordinating GI motility. The most critical development that distinguished GIST as a unique clinical entity was done in 1998 by Hirota and colleagues, who discovered c- kit proto-oncogene gain-of-function mutations in these tumours.
GIST is believed to result from activating mutations of proto-oncogenes c-KIT or platelet-derived growth factor receptor alpha polypeptide. These mutations increase tyrosine kinase receptor activity, resulting in the uncontrolled proliferation of stem cells that differentiate into intestinal cells of Cajal. Most GISTs occur in a sporadic and isolated form but can be features of multiple neoplastic syndromes [1-3].

## Case Report
A 64 years old male with a known case of hypertension reported to the Physician for a routine examination; he was advised routine clinical investigations along with USG abdomen. USG Abdomen revealed a well-defined mass measuring 4.1 x 4.0 x 4.3 cm in the lesser sac, likely of pancreatic origin. After which, CECT Abdomen was done, which revealed the possibility of GIST likely in the gastrohepatic ligament/arising from the lesser curvature of the stomach. USG Guided- FNAC of SOL Lesser sac stomach was also done, which shows puci-cellular smears reveal clusters of round to spindle cells in the background of peripheral blood and fatty elements. After that, the patient underwent tumour excision with sleeve gastrectomy under general anaesthesia. There was no infiltration of the mass into the surrounding structures nor any evidence of metastases or lymphadenopathy. The tissue was excised and sent to the Department of Pathology for histopathological examination.

**Gross Examination:** The specimen received was sleeve gastrectomy with a tumour measuring 5.2 x 4.0 x 3.5 cm with attached stomach tissue measuring 1.0 x 2.5 x 1.0 cm (Figure 1 & Figure 2).

**Fig 1:** Sleeve gastrectomy

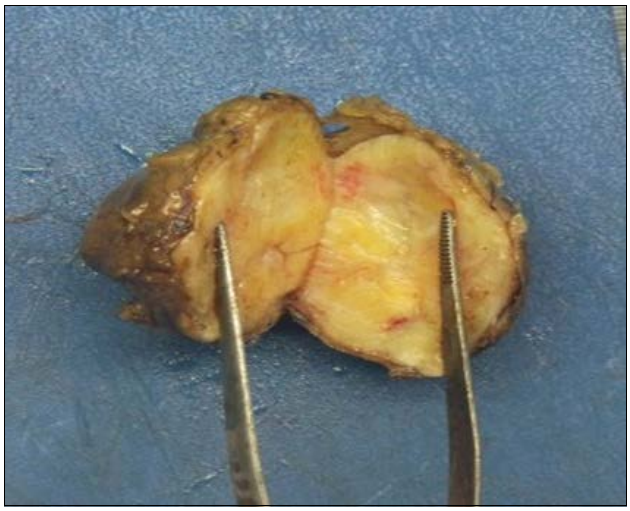

**Fig 2:** Stomach tissue

**H & E Microscopic Finding:** Show a neoplasm within the stomach wall. The cells are composed of predominantly epithelioid to spindle cells with mild nuclear atypia and extensively hyalinized stroma. Mitotic count is low (1-2/50 HPF). No necrosis was seen (figure 3).

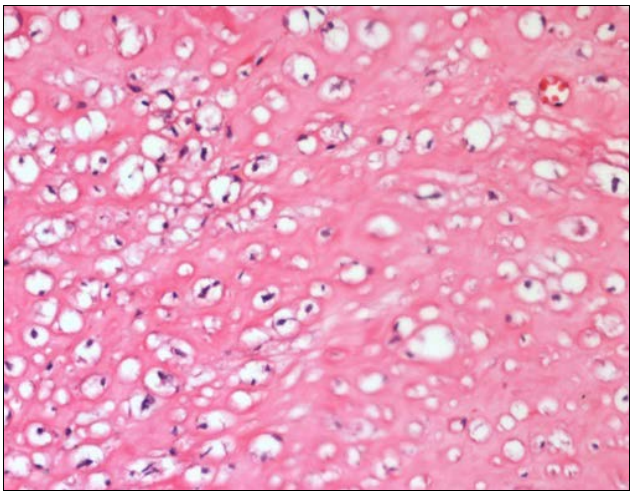

**Fig 3:** H & E microscopic finding

**Immunohistochemistry:** Tumor cells are positive for CD117, DOG1 AND CD34.

| MARKERS (CLONES) | RESULT | IMAGES |
|---|---|---|
| CD117 (Polyclonal) | POSITIVE | |
| DOG 1 (DOG1.1) | POSITIVE | |
| CD34 (QBEND-10) | FOCAL POSITIVE | |
| CK (AE1/ AE3) | NEGATIVE | |
| Ki67 (MIB-1) | 2% | |
| S100 (EP 32) | NEGATIVE | |

**Fig 4:** Immunohistochemistry

## Discussion

Gastrointestinal stromal tumours have been reported in all age groups, predominance in adults older than 50. There is a slight male predilection, but no association with geographic location or ethnicity have been reported. Although GISTs can occur throughout the gastrointestinal tract, the locations most common are the stomach (60%), jejunum and ileum (30%), colorectum (5%), and duodenum (5%). Clinical presentation of GISTs is generally incidental radiological finding when a patient is investigated for nonspecific symptoms such as abdominal pain, bloating, fatigue secondary to anaemia, obstruction, upper or lower GI bleeding or melena, primarily if the tumour is located within the tubular gut. However, it can also be presented as an emergent idiopathic spontaneous intra-abdominal haemorrhage or, in some cases, may be present with a palpable abdominal lump [3-6].

**Pathologic Features of GISTs:** These are primarily well-circumscribed lesions arising within the stomach or intestine wall. They exhibit a typical tan-white, fleshy cut surface with foci of cystic degeneration, haemorrhage, or necrosis. Large tumours may present with ulceration of the overlying mucosa. Microscopically, most GISTs demonstrate three main histologic subtypes: spindle cell type (most common), epithelioid type, and mixed spindle and epithelioid type. GISTs are generally characterized by a uniform, monotonous appearance with minimal mitotic activity or cytologic atypia. Nuclear pleomorphism is occasionally evident in a GIST and, when present, often admixed with more conventional cytologic features.

Spindle cell GISTs comprise cells arranged in short fascicles and whorls, accounting for nearly 70% of all cases. Epithelioid GISTs account for approximately 20% of cases (as is our case) and are characterized by rounded cells arranged in nests or sheets, with Vesicular nuclei and variably eosinophilic to clear cytoplasm. Combining both epithelioid and spindle cells GISTs account for approximately 10% of the cases [5, 7].

**Immunohistochemistry of GISTs:** Gastrointestinal stromal tumours are generally CD117 - positive and C-KIT or PDGFRA mutation-driven mesenchymal tumours of the gastrointestinal tract, probably originating in interstitial cells of Cajal or related precursors. CD117 is the best diagnostic marker for GISTs, but 5-10% are negative. C-KIT's high sensitivity and specificity are helpful markers in differentiating GIST from other mesenchymal tumours of the gastrointestinal tract. Solid and diffuse immunoreactivity for C-KIT (CD117) is seen in our case. Another standard marker expressed in nearly 80% of gastric GISTs, 50% of small intestinal GISTs, and 95% of GISTs arising in the oesophagus and rectum but not as sensitive or specific for GIST is CD34. In our case, the tumour is positive for CD34. Variable and weak immunopositivity is also seen with other markers, such as h-caldesmon, S100, desmin, and cytokeratins 8 and 18. Focal desmin staining is commonly seen in epithelioid GISTs arising in the stomach.

To improve the diagnostic accuracy for C-KIT-negative GISTs, several newer markers discovered on gene expression arrays have been studied. A calcium-activated chloride channel composed of 8 transmembrane domains is one such marker discovered on GIST 1 (DOG1) and was highly expressed in GIST. Recent studies have demonstrated that the overall sensitivity of DOG1 staining in GIST ranges from 75% to 100%, depending on the type of antibody used. The antibodies used are DOG1.1 (Stanford *et al*.) and clone K9 DOG1 (Novocastra antibodies, Leica Microsystems, Wetzlar, Germany). The antibody clone K9 DOG1 appears more sensitive in detecting KIT-positive and KIT-negative tumours. As seen in KIT, the newer DOG1 monoclonal antibodies do not highlight mast cells. The interstitial cells of Cajal (ICC) serve as an internal positive control for evaluating DOG1 expression immunohistochemically [7-11].

## Conclusion

Awareness of GIST as a distinct GI tract lesion is paramount in managing these rare and often aggressive tumours. Recent advances in diagnosis and immunohistochemistry have led to a detailed understanding of the molecular pathogenesis of gastrointestinal stromal tumours. It is now known that GISTs have C-KIT or PDGFRA mutations and respond to specific small-molecule tyrosine kinase C-KIT inhibitors with promising clinical results. With all these advancements, there is increased hope of providing alternative therapeutic modalities to reduce recurrence and prolong survival in patients diagnosed with GIST. A successful outcome requires a multidisciplinary approach, postoperative targeted molecular therapy in intermediate and high-risk patients, and continued surveillance.

## Conflict of Interest

Not available

## Financial Support

Not available

## References

1. Strickland L, Letson GD, Muro-Cacho CA. Gastrointestinal Stromal Tumors, Cancer Control, 8.
2. Van der Zwan SM, DeMatteo RP. Gastrointestinal stromal tumor: 5 years later. Cancer. 2005 Nov 1;104(9):1781-8.
3. Sorour MA, Kassem MI, Ghazal AEHA, El-Riwini MT, Abu Nasr A. Gastrointestinal stromal tumors (GIST) related emergencies. International Journal of Surgery. 2014 Apr;12(4):269-80.
4. Lau S, Tam KF, Kam CK, Lui CY, Siu CW, Lam HS, *et al*. Imaging of gastrointestinal stromal tumour (GIST). Clin Radiol. 2004 Jun;59(6):487-98.
5. Connolly EM, Gaffney E, Reynolds J V. Gastrointestinal stromal tumours. British Journal of Surgery. 2003 Sep 22;90(10):1178-86.
6. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: Recent advances in understanding of their biology. Hum Pathol. 1999 Oct;30(10):1213-20.
7. Parab TM, DeRogatis MJ, Boaz AM, Grasso SA, Issack PS, Duarte DA, *et al*. Gastrointestinal stromal tumors: a comprehensive review. J Gastrointest Oncol. 2019 Feb;10(1):144-54.
8. Corless CL, Schroeder A, Griffith D, Town A, McGreevey L, Harrell P, *et al*. PDGFRA mutations in gastrointestinal stromal tumors: Frequency, spectrum and *in vitro* sensitivity to imatinib. Journal of Clinical Oncology. 2005;23(23):5357-64.
9. Miettinen M, Lasota J. Gastrointestinal stromal tumors - Definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Vol. 438, Virchows Archiv. 2001. p. 1-12.
10. Eikki H, Oensuu J, Oberts EJR, Aarit M, Arlomo R Ikala S, Ndersson ECA, *et al*. Brief Report 1052. [Internet], N Engl J Med; c2001. p. 344. Available from: www.nejm.org
11. Tryggvason G, Gíslason HG, Magnússon MK, Jónasson JG. Gastrointestinal stromal tumors in Iceland, 1990-2003: The Icelandic GIST study, a population-based incidence and pathologic risk stratification study. Int J Cancer. 2005 Nov 1;117(2):289-93.

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