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Pathology

MALIGNANT EPITHELOID GASTROINTESTINAL STROMAL TUMOUR: A CASE REPORT

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ABSTRACT Gastrointestinal Stromal Tumours (GIST) are rare mesenchymal tumours, arising from interstitial cells of Cajal, accounting for approximately 1-3% of all gastrointestinal tumours. Epitheloid GIST previously termed as "Leiomyoblastoma" accounts for only 20% of all GIST. Molecular mechanism reveals a mutation of KIT (80-90%), PDGFRA (5%) and expresses CD-117(80-90%), CD-34(80-85%), SMA (18%), S-100(<1%)[6], Desmin(2%) and Cytokeratin(2%). DOG1 (99%) is sensitive and specific for GIST. We present a case of 55 years old female with history of melaena and pain abdomen for 1 year. MDCT reveals a mass of size 7.2x6.2 cm2 in jejunal mesentery adherent with a segment of small bowel loop. Resection of the tumour was done along with adjacent small intestine and specimen was sent for histopathological examination. Size of the tumour was 8x8x6 cm3 and on microscopy, it showed fascicular arrangement of epitheloid cells with hyperchromatic and pleomorphic nuclei with prominent nucleoli and eosinophilic cytoplasm. Mitotic rate was 2/50 hpf, hence diagnosed as Epitheloid GIST with high malignant potential (Considering location, size and mitotic rate). Diagnosis was confirmed by immunohistochemistry (CD-117+ve). Prognosis of epitheloid GIST depends on size of the tumour and mitotic rate. Targeted therapy has been developed against KIT (CD-117) mutation.

KEYWORDS : Epitheloid GIST, Interstitial cell of Cajal, Leiomyoblastoma, Immunohistochemistry

Introduction

Gastrointestinal Stromal Tumour (GIST) are rare mesenchymal tumour, arising from the Interstitial Cell of Cajal, accounting for approximately 1-3% of all gastrointestinal tumours[1]. Epitheloid GIST, previously known as "Leiomyoblastoma[2]" accounts for only 20% of all GIST[3]. Epitheloid GIST are most common at antrum. It may occur throughout the gastrointestinal tract, but common locations are stomach(60%), jejunum and ileum(30%), duodenum(5%) and colorectum(<1%)[3]. It occurs predominantly in adult age group older than 30 years, although example of childhood cases are also recorded. No sex predilection, i.e. both sexes is equally effected[4].

Case Report

A 55 years old female , who presented with history of melaena and diffuse abdominal pain for 1 year. Pain was insidious in onset and gradually progressive in nature. No family history. MDCT scan of whole abdomen (plain and contrast) revealed a mass of size approximately (7.2x6.2) cm^2 in jejunal mesentery adherent with a segment of small bowel loop. Resection of the tumour with side to side anastomosis was done under GA in State Cancer Institute and the specimen was sent for hsitopathological examination to the Department of Pathology, Gauhati Medical College and Hospital. Grossly, we received a specimen of terminal ileum measuring 28 cm long with attached tumour. Tumour was at a distance of 13 cm from one end and 5 cm from other end and it measured (8x8x5) cm^3. Tumour was friable and greyish white in colour. Mucosa appeared to be normal and no lymph node involvement noted on gross examination. On cut section, the tumour was solid with hemorrhagic areas. Grossly the tumour involved the muscle layer. 14 lymph node were dissected out, 7 from the level of the tumour, 4 from below the level of the tumour and 3 from above the level of the tumour, largest one measuring (0.8x0.4x0.4) cm^3. On cut section of the largest node, it was greyish white. Microscopically, multiple sections from the tumour show fascicular arrangement of epitheloid cells with pleomorphic and hyperchromatic nuclei and eosinophilic cytoplasm. Multinucleated cells were also seen. Overlying mucosa was normal. Mitotic rate was 2/50 HPF. Both the cut margin was free from tumour. 14 out of 14 lymph nodes dissected out show features of reactive node. Differential diagnosis was given as:

1. Epitheloid GIST,
2. Epitheloid Leiomyosarcoma

Immunohistochemistry was done for CD117, which came out to be positive and for desmin, which was negative, thus ruling out the possibility of Epitheloid Leiomyosarcoma. So combining the histopathological and immunohistochemistry report, tumour was diagnosed as Epitheloid Gastrointestinal Stromal Tumour with malignant potential. Epitheloid cytomorphology in the small intestinal GIST is usually associated with a high mitotic rate and malignant behaviour. Such tumours in the ileum have 24% metastatic rate (A study by Miettinen et al)[5]. The current consensus is to treat all GIST as malignant one as because of its potential for malignant behavior. It is to be noted that recurrence and survival rate also depends on location (small bowel GIST has worse prognosis) and type of (Epitheloid variety has worse prognosis) of GIST, hence they require long term follow up. Our patient was followed up and no post-operative complications developed till date.

Gross And Histological Appearance

Fig A: Gross appearance of the tumour with attached part of small bowel.

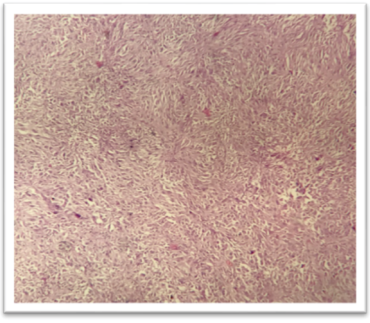

Fig B: 10x view: Shows the epitheloid cells in fascicular arrangement in low power view.

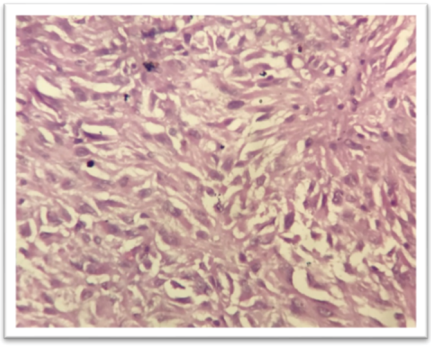

Fig C: 40x view: Shows the epitheloid cell in high power view. Cells have pleomorphic and hyperchromatic nuclei and eosinophilic cytoplasm.

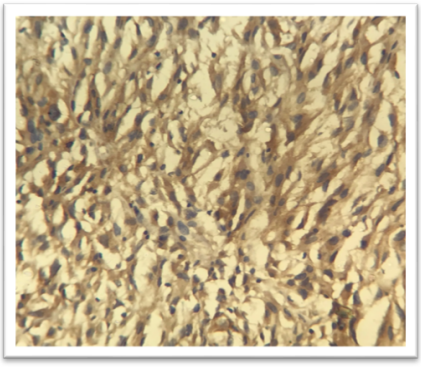

Fig D: 40x view: Tumour shows diffuse positivity with CD117 (KIT).

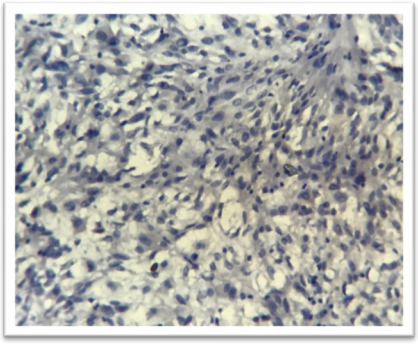

Fig E: 40x view: Tumour shows negative staining with Desmin.

Discussion

Gastrointestinal stromal tumour(GIST) has 3 subtypes-
1. Spindle cell type (70%)
2. Epitheloid cell type (20%)
3. Mixed cell type (10%)[3]

Patients generally present with nonspecific symptoms such as abdominal pain, bloating, melaena, and fatigue secondary to anaemia or obstruction. Molecular mechanism reveals a mutation in the KIT(95%) and PDGFR(5%).Strong and diffuse immunoreactivity for KIT(CD117) in 80-90% cases, CD34 in 80-85% cases, SMA in 18% cases. Some tumour also shows positivity for Desmin (5%), S-100(<1%) [6], Cytokeratin 8 and 18, h-caldesmon and PKC-theta, vimentin, NSE, synaptophysin etc[3]. A few tumours show no detectable mutation, called "Wild type"[6]. DOG-1(99%) and ANO1 are sensitive and specific markers[7]. Recognized predisposing conditions contribute to only a minority of cases and include NF1[8] and two others syndrome, Carney triad (Gastric GIST, extradrenal paraganglioma, pulmonary chondroma)[9] and Carney-Stratakis syndrome (GIST with paraganglioma) associated with SDH mutation and they usually show epitheloid variety of GIST[10]. Familial GIST is associated with younger age of presentation and early metastasis. Differential diagnosis are Epitheloid Leiomyosarcoma, Epitheloid schwannoma, Epitheloid Melanoma involving the GIT, which can be differentiated by using KIT, CD-34, SMA, Desmin, S-100 etc[3]. Treatment is done by surgical resection of the tumour since the tumour shows low responses to chemotherapy and radiotherapy. Imatinib Mesylate and Sumatinib Malate are competetive inhibitors of ATP binding site of KIT and PDGFR that are used in first and second line treatment of GIST. Other second generation drugs are Sorafenib, Dasatinib, Nilotinib[11]. Treatment related changes are-

1. Hypocellular and prominent stromal changes in the form of sclerosis, calcification, myxoid degeneration, necrosis
2. In some cases, phenotype changes from spindle cell to epitheloid cell type
3. Loss of KIT immunoexpression[12].

Conclusion

Prognosis predominantly depends on size and mitotic rate. Location and type of tumour also influences the prognosis, all of them require extensive follow up. Early diagnosis and treatment is crucial for favorable outcome. Combination of histopathology and immunohistochemistry is mandatory for treatment.

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