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Pathology

COMPARATIVE CASE REPORT OF 2 MORPHOLOGICALLY DISTINCT TYPE OF GIST STOMACH.

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ABSTRACT We present a comparative analysis of 2 cases one of mixed GIST and other of a case of de-differentiated GIST. GIST being the most common mesenchymal tumor of alimentary canal is commonly reported. Here, we compare the morphological features of two types of GIST. One patient is a 49 years old male with abdominal discomfort and pain and mass in body of stomach. Other patient a 57 years old female who presented with generalized weakness and anemia. Both of them were histologically GIST one mixed type and other de-differentiated type.

KEYWORDS : GIST. Mixed and De-differentiated

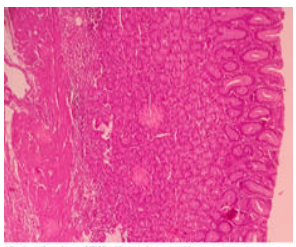
INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the alimentary tract.[1] GISTs are believed to arise from the interstitial cells of Cajal. Over 80% express CD117 (c-Kit) by immunohistochemistry (IHC)[2]. Genetic alteration attributed to formation of GISTs include activating mutations in KIT, or platelet derived growth factor receptor alpha (PDGFRA). These genetic alterations result in activation of tyrosine kinases [3]. Morphologically, GISTs are composed of spindle, epithelioid, both or rarely pleomorphic cells and most commonly also express CD117, CD34 and DOG1 antigens by IHC.

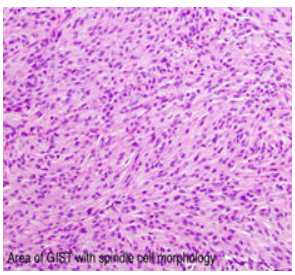
De-differentiation refers to morphological and phenotypical change which can occur denovo or after prolonged therapy with tyrosine kinase inhibitor, imatinib. On IHC, de-differentiated GIST are negative for CD117.

CASE REPORT

We present two cases. First case is a 49 years old male with abdominal discomfort and pain. On USG a well defined solid mass measuring 2.5 cm was mass seen in stomach. On UGI endoscopy a noduler mass was seen in the body of stomach. Patient underwent sleeve gastrectomy and sample was sent for histopathology. We received a sleeve measuring 3 cm in length and attached nodular mass mesauring 2.5x2x2 cm. On microscopic examination mucosa was intact and unremarkable and submucosa revealed mixture of spindled to plump elongated cells with eccentric nucleus arranged in fascicles. No mitoses was seen. IHC revealed positivity for CD117, DOG1 and Ki-67 index <5%.

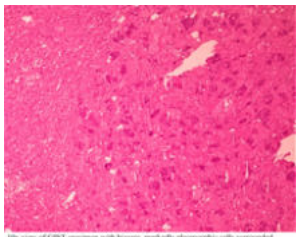


10x view of specimen of GIST with normal mucosa without any tumor infiltration.

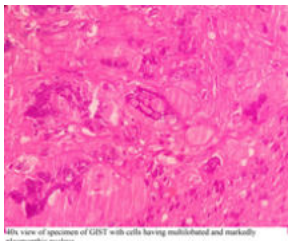


Area of GIST with spindle cell morphology

Other patient is a 57 years old female who presented with generalized weakness and anemia. On clinical and laboratory investigations severe anemia with Hb 7.4 g/dl was noted. During evaluation for cause of anemia, Upper GI endoscopy was done and a large submucosal lesion in body of the stomach along the greater curvature was seen. On CECT abdomen a polypoidal intraluminal hetrogenously enhancing mass measuring 4.1*5.2 cm was seen in the fundus of stomach and radiological impression of GIST was made. Microscopic examination of the specimen revealed intact lining epithelium with submucosa, muscularis propria and serosa infilterated by sheets, clusters, nodules of spindloid cells with marked pleomorphism, multilobed nuclei with vesicular chromatin and prominent nucleoli. Intermixed with these cells were seen markedly pleomorphic multi nucleated tumor giant cells. Foci of cells of spindled GIST were also seen. Histopathological diagnosis of De-differentiated GIST was given and IHC was advised.



10x view of GIST specimen with bizzare, markedly pleomorphic cells surrounded by spindle cells.



40x view of specimen of GIST with cells having multilobated and markedly pleomorphic nucleus.

On IHC, DOG1 was non immunoreactive; CD117/ c-KIT was focally positive in spindle cells and non-immunoreactive in the de-differentiated area.

Pleomorphic cells were immunoreactive for Desmin, SMA.70-80% cells showed Ki-67 positivity.

On IHC impression of High Grade pleomorphic tumor favoring de-differentiated GIST was given.

DISCUSSION

GIST is the most common mesenchymal tumor of alimentary canal. Arises from interstitial cells of cajal. Can occur in any part of GIT. Morphologically can be composed entirely of spindled cells: Spindle type or plump endothelial cells: Endothelial type or mixed type comprised of both types of cells. De-differentiation is a rare phenomenon and can occur with imatinib therapy or very rarely denovo as in our case. No morphological variation seen in both types of de-differentiated GIST.

Genetic changes occuring in conventional GIST is KIT and PDGFRA mutation that differ from de-differentiated GIST which lack KIT mutation and positivity on IHC.[5] Based on the small number of previously reported cases, dedifferentiated tumors, especially after imatinib therapy demonstrateresistance to the currently available TKI therapy.[6]

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