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CASE REPORT ON RARE DE-DIFFERENTIATED GIST OF STOMACH OCCURRING DENOVO

Pathology

Dr. Akshita Mehta

Dr. Pooja Murgai* *Corresponding Author

ABSTRACT

We present a rare case of de-differentiated GIST. GIST being the most common mesenchymal tumor of alimentary canal is commonly reported. However, de-defferentiation of GIST is a rare phenomenon which may occur denovo or with imatinib therapy. A 57 year old female patient presented with generalized weakness and anemia. On evaluation, a submucosal lesion on the body of stomach along the greater curvature was identified on UGI endoscopy. On CECT scan of abdomen, polypoidal intraluminal mass was seen. After sleeve gastrectomy histopathological examination showed dedifferentiated GIST, stomach which was confirmed on IHC. The patient had no prior history of Imatinib therapy/ any chemotherapy. We present this case as de-differentiated GIST occurring denovo without prior imatinib therapy is rare and not much is known about its clinical course and prognosis of such cases.

KEYWORDS

GIST, 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 [1]. Morphologically, GISTs are composed of spindle, epithelioid, or rarely pleomorphic cells and most commonly also express CD34 and DOG1 antigens by IHC.

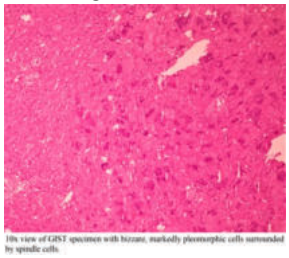
A small minority of GISTs exhibit morphological and phenotypical changes through the process of de-diferentiation.. De-differentiation can occur denovo or after prolonged therapy with tyrosine kinase inhibitor, imatinib. On IHC, de-differentiated GIST are negative for CD117.

CASE REPORT

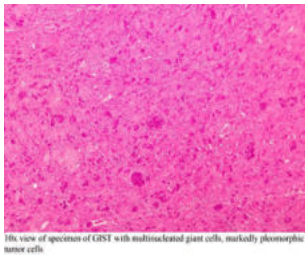
We present a case of a 57 years old female who presented to our hospital with generalized weakness which on clinical and laboratory investigations came out to be severe anemia with Hb 7.4 g/dl. During evaluation of cause of anemia, Upper GI endoscopy was done and a large submucosal lesion in body of 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.

The patient then underwent sleeve gastrectomy and we received a specimen of sleeve gastrectomy measuring 8 cm in length. On incising the sleeve, a well circumscribed and well encapsulated growth measuring 5*3*2 cms was seen in the wall of the stomach with overlying mucosa grossly unremarkable.

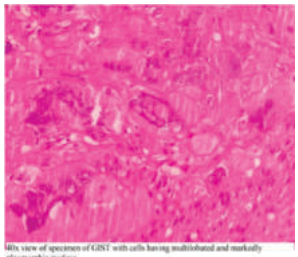
Microscopic examination of the specimen revealed intact lining epithelium with submucosa, muscularis propria and serosa infilterated by sheets, clusters, nodules of spindloid cells with marked pleomorphism, multilobed nuclei with vesicular chromatin and prominent nucleoli. Interixed with these cells were seen markedly pleomorphic multi nucleated tumor giant cells. Foci of cells with elongated nuclei and eosinophilic cytoplasm arranged in fascicles were also observed. Histopathological diagnosis of De-differentiated GIST was given and IHC was advised.



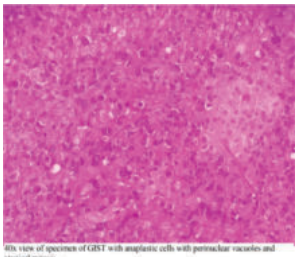
10x view of GIST specimen with bizzare, markedly pleomorphic cells surrounded by spindle cells



40x view of specimen of GIST with multinucleated giant cells, markedly pleomorphic tumor cells



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



40x view of specimen of GIST with anaplastic cells with perinuclear vacuoles and atypical mitosis

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

Neoplastic cells were immunoreactive for Desmin, SMA, Focall for h. Caldesmon.

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. De-differentiation in GIST is rare but if present may occur denovo or with prior therapy of imatinib. In our patient, there is no history of previously received chemotherapy as the tumor was identified only during evaluation of anemia.

Genetic changes that differ from conventional GIST include abrupt transformation from conventional KIT-positive tumor cells to KIT-negative cells with marked anaplasia.[4] These tumors have been termed dedifferentiated GIST.

Histologically[3] two different components arre observed in all tumors: a well-differentiated spindle cell component and an anaplastic component. The well-differentiated areas represent GIST morphology, being composed of uniform spindled to epithelioid cells, arranged in intersecting fascicles or a short storiform pattern .The dedifferentiated component is composed of anaplastic/pleomorphic phenotype, with multinucleated neoplastic giant cells, high mitotic activity (>10MF/50HPFs) and necrosis. This component shows consistent loss of CD117 and CD34 expression.

Usually there is no difference noted in the morphologic appearance of the dedifferentiated component, whether it occurred *de novo* or secondary to imatinib therapy. Similarly, in our case we saw two different components including a well differentiated spindle cell component and a dedifferentiated component which was predominant.

Based on the small number of previously reported cases, dedifferentiated tumors, especially after imatinib therapy demonstrate

resistance to the currently available TKI therapy.[5]

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