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An Enigmatic Pelvic Tumor

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Abstract: ***Gastrointestinal stromal tumors (GISTs) have been noticed as a biologically special type of tumor, distinct from previously described neural and smooth muscle tumors of the gastrointestinal tract (GIT). Extra Gastrointestinal stromal tumors (EGISTs) are tumors with immune-histological features overlapping with GISTs but found outside the GI tract in the abdomen with no contact with the gastric or intestinal wall. E-GISTs most frequently arise from the omentum, mesentery, retroperitoneum, or solid organs like the liver and the pancreas. E-GISTs originating in the pelvic cavity and not being associated with the GI tract are very uncommon. Furthermore, these E-GISTs are commonly seen in patients over 50 years of age. Imatinib hasexceptional antitumor effects through molecular inhibition and has necessitated a definite diagnosis of GIST. The crucialinterplay between the molecular genetics of GIST and the response to targeted treatment has served as a pathway for the study of targeted therapies in other solid tumors. This case report and review encapsulates our present knowledge about GIST and recent advances regarding histopathology, molecular biology, the basis for the unique targeted therapy, and present evidence-based management of these unusual tumors.***

Keywords: Extra Gastrointestinal stromal tumors, pelvic GIST, Imatinib, Review

1.Introduction

GISTs are tumors of the mesenchymal tissue of the GI tract that canarise within the whole length of the GI tract from the esophagus to the anus.[1]

After the detection of gain-of-function mutations within the c-KIT proto-oncogene in 1998, these tumors were reliably differentiated from other histopathological subtypes of mesenchymal tumors. [2, 3]

The most common location involved is the stomach (60%) followed by the small intestine (30%). Only about 10% of GISTs are localized in the esophagus, colon, rectum, omentum, and mesentery. Approximately 30% of GISTs show high-risk (malignant) behavior such as local infiltration and distant metastasis.[4, 5, 6, 7]

However, there are some GISTs that are not associated with the GI tract and are thus classified asE-GIST.8[-12] An E-GIST can arise from the retroperitoneum, or pelvic cavity. To the best of our knowledge, only 7 cases of GISTs arising from the pelvic cavity and not associated with the GI tract have been reported in the English literature.[10, 12, 13]

2.Case History

Our patient was a 52 years old male who presented to surgical OPD with complaints of difficulty in passing urine and constipation for the last 5 months. On examination, he was conscious and oriented with pulse rate and blood pressure within normal range. The abdomen was soft, non-tender, and non-distended, and there was no palpable lump and organomegaly, and no free fluid in the abdomen. On per rectal examination, the prostate was grade IV and was non-tender, firm to the hard in consistency, and smooth surface.

The serum PSA level was within normal limits. TRUS-guided prostate biopsy was done suggestive of mesenchymal neoplasm of the prostate and a soft tissue tumor diagnosis was made. He was worked up for the same with an X-ray Abdomen erect and supine, ultrasonography of the whole abdomen including the pelvis, and an MRI pelvis and lumbosacral spine. On review of his investigations, the ultrasonography of the whole abdomen revealed the prostate to be grossly enlarged with heterogenous echo texture with a volume of approximately 626cc. The patient was catheterized in view of the difficulty in passing urine and large prostate size. MRI abdomen and pelvis revealed a malignant neoplastic large well-encapsulated solid T1 and T2 hypodense mass lesion in the pelvis with an area of necrosis within causing severe mass effect on the urinary bladder, recto-sigmoid colon. The prostate gland was not well appreciated and there were multiple enlarged bilateral pelvic lymph nodes with inflammatory changes involving the left perineal muscle and medial thigh muscles. (Figure 1). The patient was planned for surgery and after all pre-operative requirements fulfillment, he was operated on 18/01/2022 with an exploratory laparotomy, and resection of the tumor was done. Intraoperatively, the mass lesion was found to be free from the adjacent rectum, colon, and bladder; however, the lesion deeply adhered to the pelvic floor. (Figure 2).

The postoperative course of the patient was uneventful. The postoperative gross specimen was an encapsulated globular mass of 14x 12 x 9 cm, tan in color with a variegated appearance and firm to hard consistency. Multiple areas of hemorrhage and necrosis were noted. (Figure 3)

Histopathological examination revealed an encapsulated high-grade spindle cell tumor with mild-moderately pleomorphic cells arranged in fascicles and interlacing bundles. Also noted were frequent mitosis and a large area of necrosis with a focal area of prominent lymphoplasmacytic infiltration. The capsule was seen to be infiltrated focally. There was no rectal, colonic, or prostatic tissue component found in the resected specimen. (Figure 4).

On IHC, the tumor cells showed diffuse immune expression for DOG 1, CD117, and CD 34 with EMA and SMA being focally positive. CK, S100, and HMB 45 were found to be negative. (Figure 5).

Based on histological and immunohistochemical features, a diagnosis of EXTRA GIST-HIGH RISK was made.

The patient was started on Imatinib therapy on follow-up. After 4 weeks of imatinib therapy, PET SCAN was done which showed evidence of a highly metabolic lesion in the liver. Thus, USG-guided FNAC from the liver lesion was taken. FNAC was suggestive of metastatic GIST. (Figure 6)

3.Discussion

GIST is a distinguished type of mesenchymal tumor that is c-kit-positive and arises from gastrointestinal pacemaker cells; also termed interstitial cells of Cajal (ICC) with ambiguous biological nature.[1] There have only been a few cases of GIST reported outside the GI tract, affecting soft tissues of the mesentery and omentum, referred to as E-GIST. Many cases of GIST in the pelvic cavity have been reported, [10-13, 14-16] most of which were originating from the small or large bowel and grew into the pelvic cavity.[10, 15-17] Colonic or rectal GISTs that extend into the pelvis cavity have also been reported in English literature.[12, 13] A rare case of GIST that arose from the ureter has also been reported.[5] However, there are only 7 cases of GISTs reported in the English literature that was not associated with the GI tract and were arising from the pelvic cavity.[10, 12] Earlier these tumors were supposed to be primary GI tract lesions with large extramural growth patterns which would sometimes result in loss of contact with the GI tract. This was attributed to the growth process of the tumor or surgery leading to the tearing and detachment of these large tumors from the gut wall.[13]

A majority of these GISTs are known to express KIT, which is a stem cell factor receptor (CD117), some express the PDGFRA gene and a very small percentage (9-15%) do not have a mutation in either gene and they are known as ‘wild type.[18]

PDGFRA and KIT both are expressed on chromosome 4q12, and both encode homologous transmembrane glycoproteins which belong to the type 3 tyrosine kinase receptor family.[19]

The immunomarkers used to differentiate GIST from other spindle cell tumors include CD117 (95%), DOG1 (98%), and CD34 (82%). The present case showed diffuse strong immunoreactivity with all these markers. Smooth muscle antigen (SMA) is found to be positive in 30% of small intestinal GISTs, however, is relatively uncommon at the stomach site. EMA is very rarely expressed in GISTs and is usually focal, as seen in the present case.[18] GISTs usually also express nestin, caldesmon, calponin, vimentin, and embryonic smooth muscle myosin.[20]

Treatment of the GISTs primarily involves surgical resection of tumors and the use of tyrosine kinase inhibitors. For resectable tumors, the only curative measure is surgical removal. It is found that these tumors do not metastasize to lymph nodes, so dissection of the lymph node is not advised.[18, 21]

For unresectable or metastatic disease, the first treatment of choice is imatinib. If the patient shows the progression of the disease even after imatinib therapy, then these patients are reassessed and can be considered for surgical therapy. The timing of the surgical intervention, however, is very crucial; the best time is when the patient has gained maximum benefit from the imatinib therapy.[21]

4.Conclusion

This case report highlights the possibilities of different and unusual signs and symptoms that can be associated with E-GIST. When a middle-aged adult having no risk factors presents with a pelvic mass, the possibility of very rare lesions such as E-GIST is almost never considered, thus E-GIST is usually not diagnosed preoperatively. A high index of clinical suspicion is required to diagnose them preoperatively. Most of the time, the diagnosis is established after surgery and histopathological examination of the specimen. Despite the lack of preoperative diagnosis, it is justified to proceed with the surgery as the longer we wait to make a preoperative diagnosis, the poorer the outcome after surgery.

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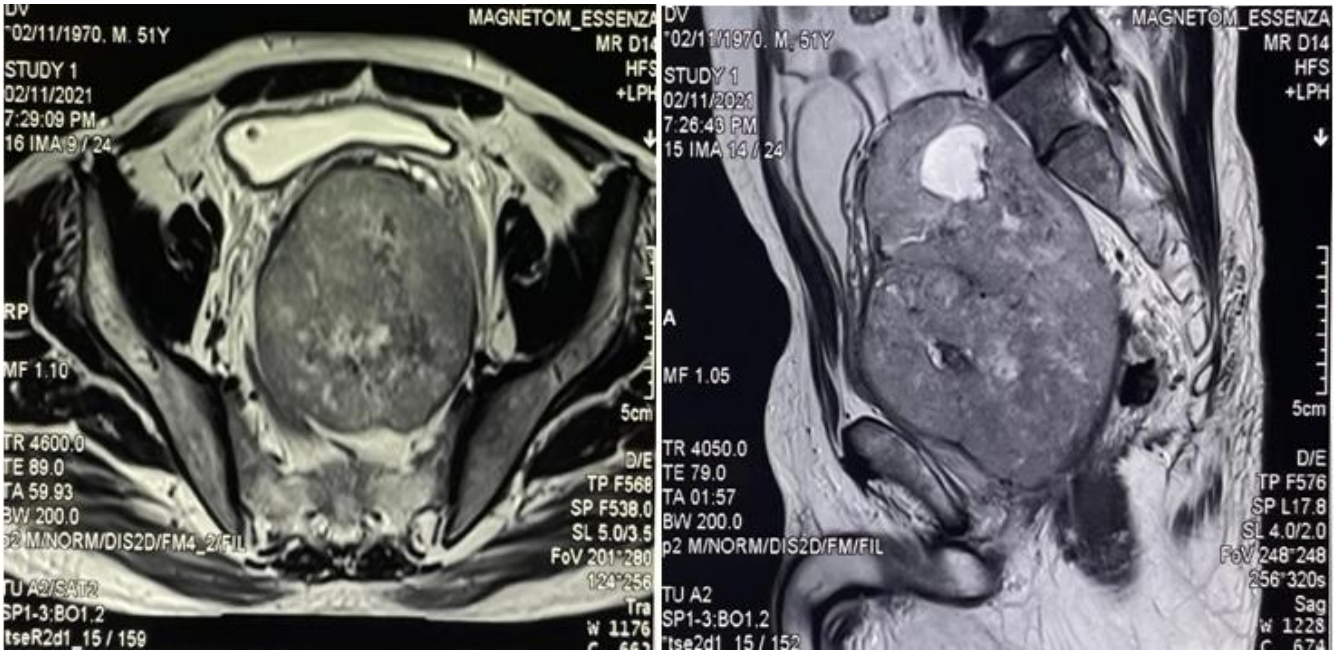

Figure 1: MRI

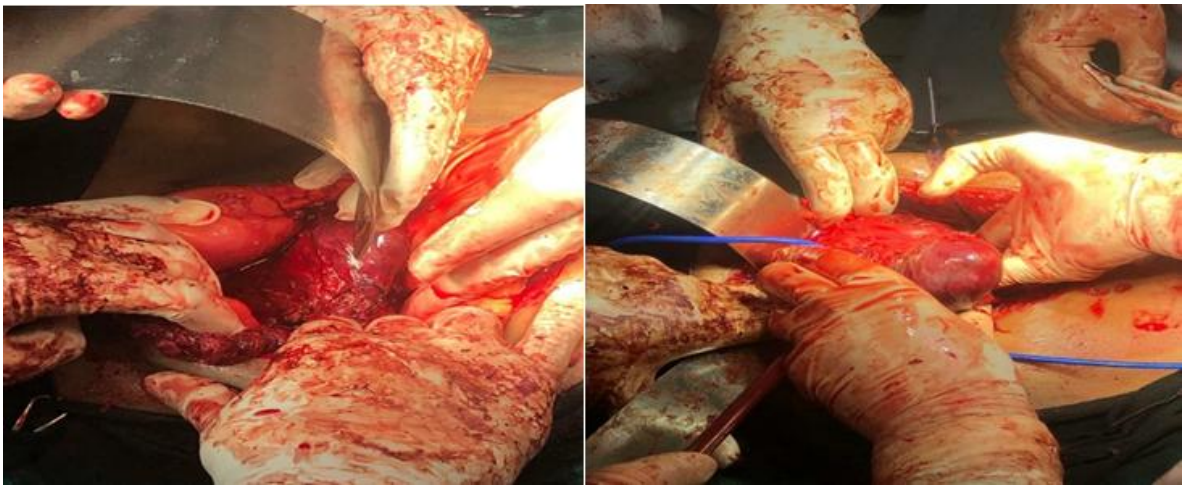

Figure 2: Intraoperative pictures showing tumor being resected and retrieved.

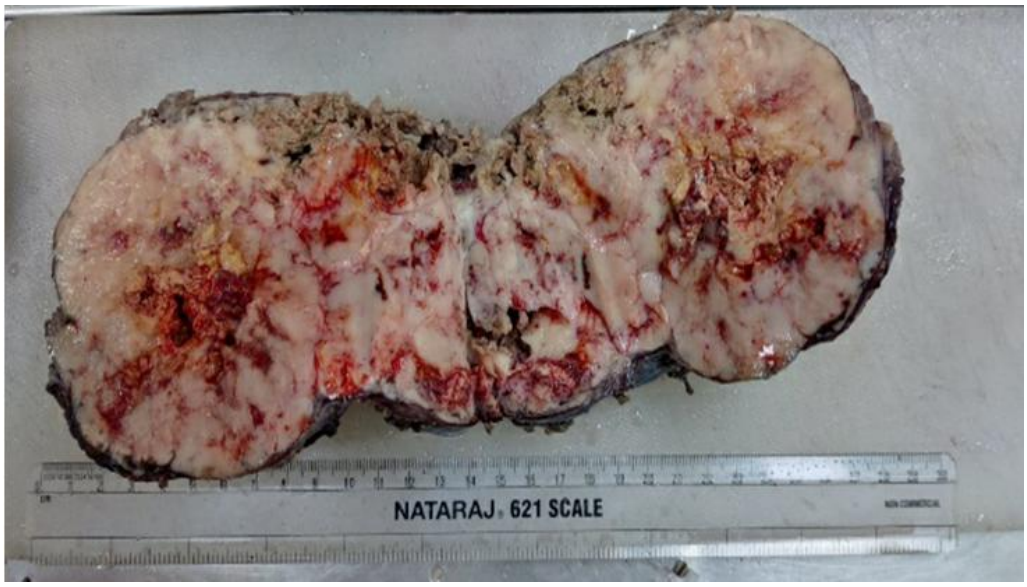

Figure 3: Cut section of Tumor with an arrow showing areas of necrosis

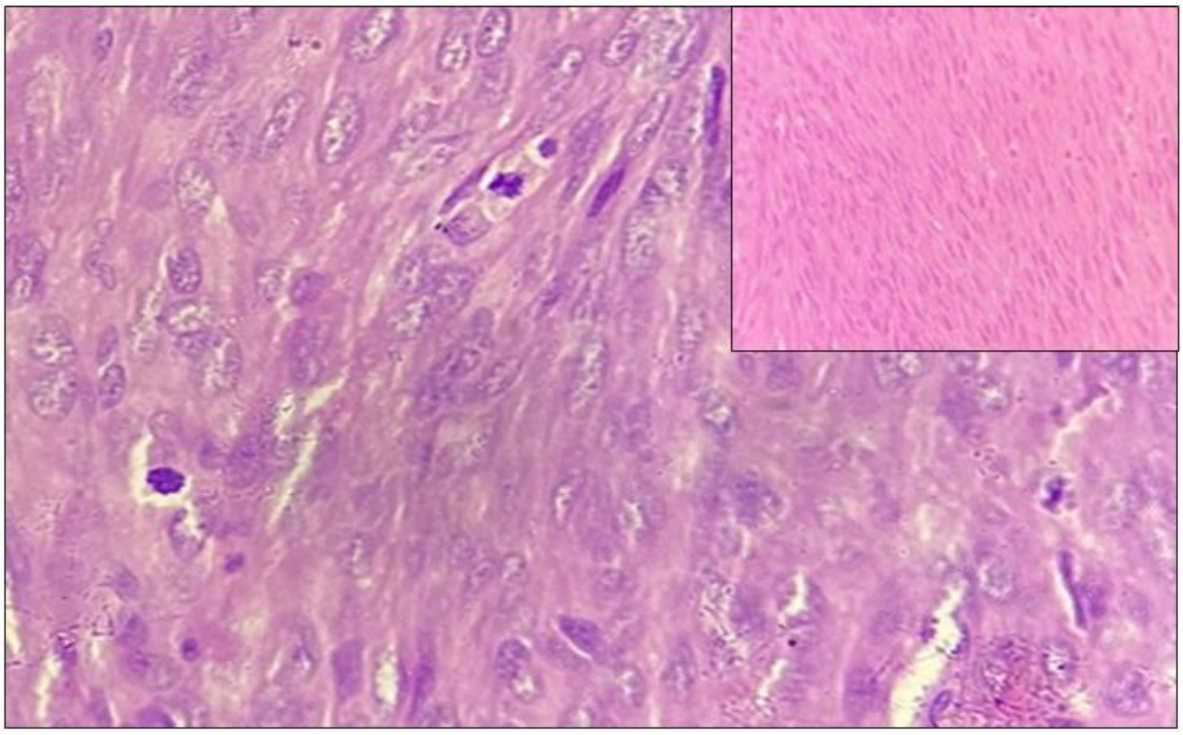

Figure 4: H & E stained section showing sheets and fascicles of spindle-shaped cells with 2 mitosis in a field; 600X

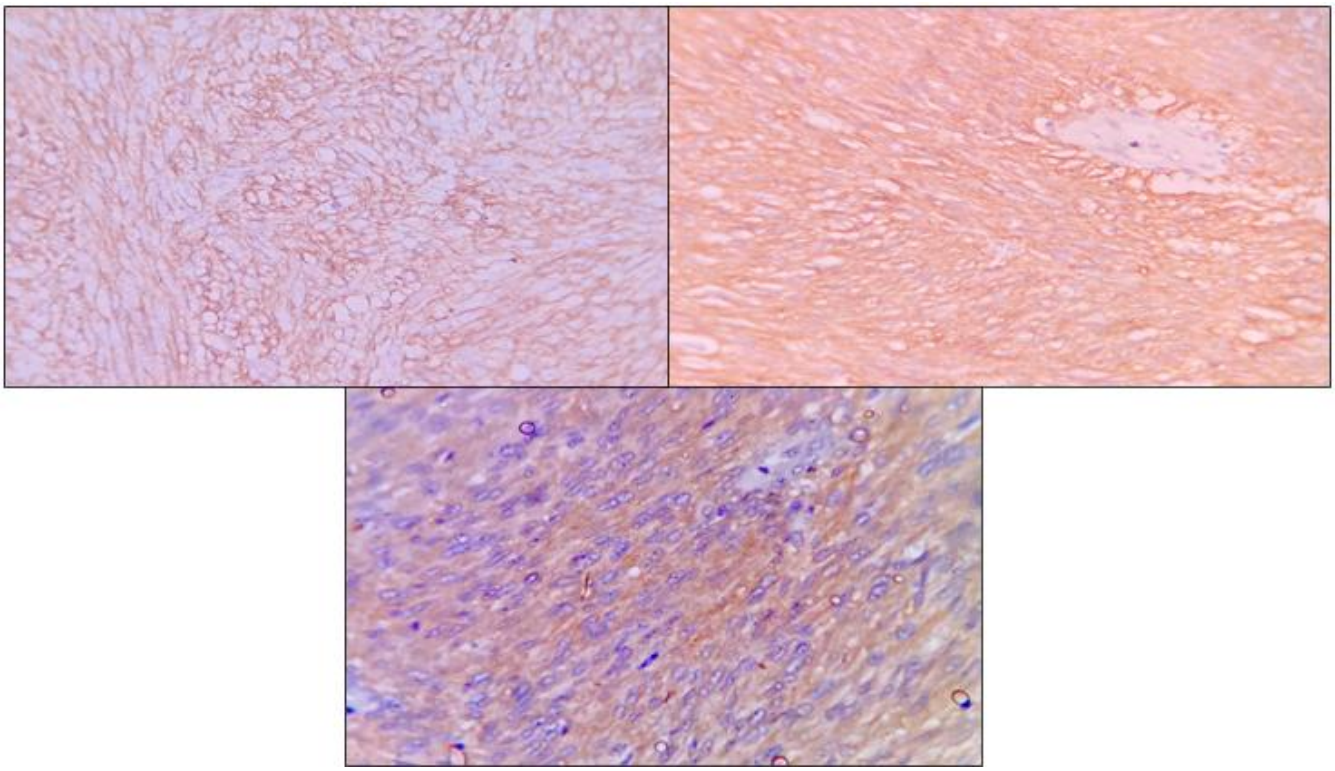

Figure 5: Diffuse membranous positivity with CD117 (a) and CD34 (b); 400X and diffuse cytoplasmic and membranous positivity with DOG1 (c); 400X

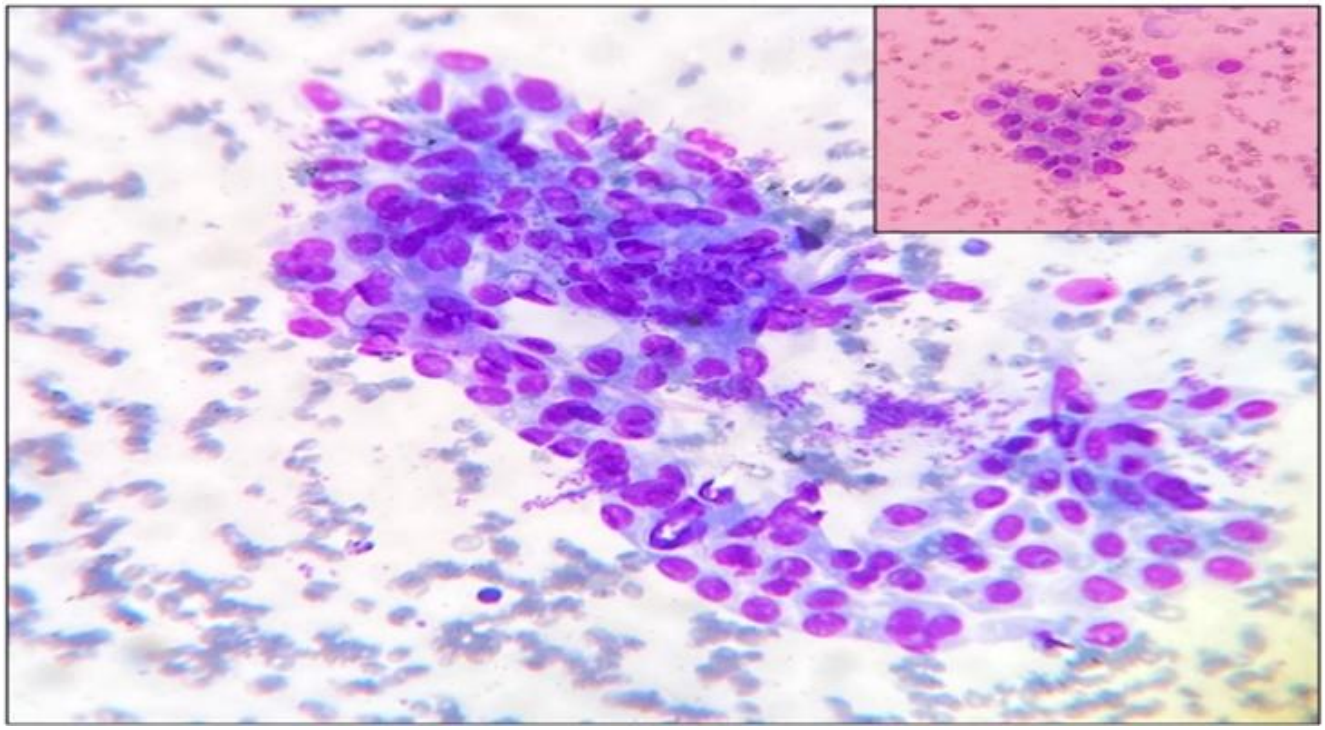

Figure 6: Liver metastasis on USG-guided, FNAC smear in form of atypical plump spindle cells showing nuclear irregularity, hyperchromatic, and moderate bluecytoplasm in a background of reactive hepatocytes (as shown in inset)