A CASE OF CAECAL GIST- RARE COEXISTENCE WITH ABDOMINAL TUBERCULOSIS

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Abstract :
Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal tract. The frequency of their location on the caecum is quoted with values lower than 10 of all GIST. Nearly 95 of GIST are positive for the CD 117 antigen, an epitope of KIT receptor tyrosine kinase expressed by their cell of origin, the Interstitial Cells of Cajal (ICC). Immunohistochemistry for CD117 is completely negative in approximately 5 of GISTs, though the morphological, molecular and the cytogenetic features are the same. Tuberculosis can involve any part of the gastrointestinal tract and is the sixth most frequent site of extra pulmonary involvement. The most common site of involvement of the gastrointestinal tuberculosis is the ileocecal region which can present as a palpable mass in the right lower quadrant and/or complication of obstruction.

Keyword : Tuberculosis, Gastrointestinal stromal tumour, CD117, KIT receptor, Imatinib.

CASE PRESENTATION:
A 29 year old male had presented to us with complaints of vague lower abdomen pain on and off for the past 1½ years. He has significant loss of weight and loss of appetite for 6 months duration. He did not have any history suggestive of intestinal obstruction. He denied any history of fever, trauma, night sweats or altered bowel habits. His past medical records were clean. He was not a known diabetic/ hypertensive/ asthmatic. He had no adverse social habits. He had no personal or family history of tuberculosis. On General examination, patient was moderately built & nourished. He had no anemic, icteric. There was no generalized lymphadenopathy. His vitals were stable and his Karnofsky performance index is 90. Clinical examination revealed a mass occupying the right iliac fossa and extending into the right lumbar region of size 8*6 cms, firm consistency, had restricted mobility, all borders well defined with an irregular surface.

Other system examination was found to be normal. Basic blood investigations revealed a haemoglobin of 10 gm %. ESR was slightly raised 12/22. Renal and liver function tests were normal. Urine routine and stool for occult blood were negative. Ultra sonogram of abdomen revealed a hypoechoic mass Right lumbar region 7.6*6.5 cms with distal ileal wall thickening and caecal wall thickening. There are multiple small nodes in mesentery. 

Contrast enhanced Computerized Tomography of abdomen and pelvis reported a concentric thickening of ileocecal junction, caecum and ascending colon with paraocolic tissue thickening and regional lymphadenopathy. A heterogeneous mass lesion of size 8*6 cms involving the caecum and ascending colon, liver found to be normal. No evidence of any metastatic deposits. impression: Infective / inflammatory pathology.

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Colonoscopic biopsy showed non specific colitis with no evidence of granulomatous malignancy. Chest X ray was normal, no features of active tuberculosis. Mantoux test was negative. Since malignancy could not be ruled out, patient was taken up for exploratory laparotomy.

Post operative period was uneventful. Orals started on 4 th POD and suture removal was done on 10 th POD. Patient tolerated procedure well. Histopathological examination showed following features:

Sections from thickened colonic mucosa show ulceration and extensive granulomata composed of lymphocytes, histiocytes, epitheloid langhans giant cell extending transmurally into subserosal fat. Multiple pericolic nodes show features of caseating tuberculous lymphadenitis.

Sections from grey white mass show colonic mucosa with an underlying neoplasm composed of sheets of spindle cell, with elongated nuclei, mild to moderate nuclear atypia, no. of mitosis <5/50 HPF. No areas of necrosis made out. Both resected margins are free from the tumour. The mass lesion had features of an intermediate grade Gastrointestinal Stromal Tumour.

On Immunohistochemical analysis, the GIST lesion was found to be c-KIT negative, PDGRFA positive, desmin negative and S-100 negative. Hence a final pathological diagnosis of c KIT negative GIST with coexisting tuberculosis was made. Due to intermediate grade of the lesion (absence of necrosis and mitotic rate < 5/ 50 HPF) and completeness of the resection, imatinib was not offered. The patient was also started on anti tuberculous treatment. The patient is on regular follow up and continues to remain well (follow up period- 6 months).

DISCUSSION:

Gastro intestinal stromal tumours are the most common mesenchymal tumour of the gastro intestinal tract. They account for 0.1%–3.0% of all gastrointestinal neoplasms and 5.7% of sarcomas. GISTs tend to occur in middle aged persons with a slight male predilection. The median age of onset is about 60 years. The term GIST was initially a purely descriptive term developed in 1983 by Mazur and Clark to define intra abdominal tumors that were not carcinomas and also failed to exhibit features of either smooth
muscle or nerve cells. Kindblom and colleagues suggested in 1998 that GISTs originate from stem cells that differentiate towards the interstitial cells of Cajal (ICCs), and that GISTs should be called gastrointestinal pacemaker-cell tumours. GIST can occur anywhere along the gastrointestinal tract from esophagus to anus, with the stomach being the most common site. Majority are sporadic, though familial GIST due to heritable mutations are known to exist. These are characterized by multiple tumours and hyperpigmentation. Carney’s syndrome and neurofibromatosis are associated with stromal tumours.

Clinical presentation is varied depending on the size and site of the tumour. Small tumors (< 2 cms) may be asymptomatic (20%). It can present with vague abdominal pain, dysphagia, gastro-intestinal bleed, perforation or bowel obstruction. GIST lesions can also present with hyperpigmentation. Carney’s syndrome and neurofibromatosis are associated with stromal tumours.

Features favoring benign lesions are small size (< 5 cms), low number of mitosis (< 5 per 50 HPF), low cellularity, low markers of cell proliferation and absence of mucosal invasion. Generalizations about the malignant potential of CD117 negative GISTs cannot be made, but show a correlation to mutations at codons 557/558 and mitotic rate. With prolonged follow up any GIST has the potential to behave in a malignant fashion, as nearly 50% of primary localized tumours that are resected relapse after 5 years of follow up.

The first published description of coexisting tuberculosis and carcinoma was that of Boyle who described “cavitation carcinoma” as one of the six types of tuberculosis. The association of tuberculosis and cancer has since been recorded in most organs by various authors. Carcinoma in different parts of the colon with intestinal tuberculosis has been reported by Paustian. Kaplow et al. found TB complicating neoplastic disease in only 4 out of 6472 patients with carcinoma of the colon, a prevalence of 6/10,000. Indian researchers have found a higher frequency of co-existent disease.

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Few Indian authors have proposed that the association of carcinoma and tuberculosis is coincidental; the argument being that compared to the high incidence of abdominal tuberculosis in India, the cases of coexisting tuberculosis and carcinoma are very few. This may be true in some cases particularly when the neoplasm originates at a site distant from the tubercular focus. However, to put the simultaneous occurrence of the two conditions at the same site down to mere coincidence is far too simplistic. Some diseases like ulcerative colitis, Crohn’s disease, and schistosomiasis predispose to malignancy.

Chronic inflammatory mucosal damage initiating a sequence of metaplasia and dysplasia results in neoplastic change. Evidence also suggests that pulmonary scarring of tuberculous etiology play a role in the generation of some lung cancers, usually adenocarcinomas originating in the peripheral portion of the lung. Drawing parallels it may be postulated that the ulcerative lesions of intestinal tuberculosis are precursors of carcinomas and this possibility was suggested by Japanese researchers. These carcinomas arose as a result of repeated insults by way of erosions, ulceration, and consequent regeneration.

The occurrence of GIST can also be explained with chronic inflammation arising due to tuberculosis turning on the FGF- signaling pathways, which are responsible for fibrosis and smooth muscle hypertrophy. Any mutation sustained in the precursor cells may lead on to GIST.

Treatment for resectable GIST, surgery with complete resection (wide resection or en bloc) with an intact pseudo-capsule and negative microscopic margins is mandatory. Lymphadenectomy is usually unnecessary. Treatment with adjuvant imatinib for 1 year improves relapse free survival. For unresectable GIST, targeted therapy with Imatinib (tyrosine kinase inhibitor) is given. For imatinibresistant cases, sunitinib, another tyrosine kinase inhibitor with additional anti-angiogenic activity is used. For cKIT negative tumours, sunitinib has more efficacy than imatinib.

The best treatment in cases of GIST with tuberculosis is difficult to decide as pre-operative diagnosis of such a coexisting dual pathology is virtually impossible. The primary pathology is also a matter of conjecture. Since a preoperative diagnosis is usually not possible, a case of right iliac fossa lump with evidence of tuberculosis should also be treated with a suspicion of co-existing malignancy especially in patients who fail to respond to anti-tubercular drugs.

The 5-year survival for malignant GIST varies widely and has been reported to be from 28 to 80%. Median survival of patients in whom complete surgical resection is not possible is 10–23 months. Coexistence of tuberculosis does not seem to
alter the prognosis of GIST lesions.

CONCLUSION:

In literature, the coexistence of GIST and tuberculosis have been reported in only very few instances. Whether it’s a mere pathological coexistence, or any causal relationship between the two, is yet to be firmly established. Further case reporting and long term observational studies are needed. Our unique case illustrates the need for a high index of suspicion in order to diagnose this rare condition, as this can present in patients with no particular risk factors or minimal symptoms.

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