Gastrointestinal Stromal Tumour (GIST) From an Imaging Perspective

Lt Col Vikram Khanna*, Lt Col Ritu Lakhtakia⁺, Maj Vinay Maurya[#], Lt Col BN Kapur**

MJAFI 2005; 61 : 381-384

Key Words : Gastrointestinal stromal tumour, Leiomyomas, Leiomyosarcoma

Introduction

Gastrointestinal stromal tumour (GIST) is a new term emerging from reclassification of leiomyomas and leiomyosarcomas of the gastrointestinal tract. Histopathological refinement, molecular genetics and immunophenotypic characterization has resulted in better understanding and sub classification of this disease entity [1,2,3]. Based on imaging alone it is not possible to sub classify the disease as imaging features are not specific [1]. We present two cases of GIST along with their imaging features.

Case No 1

A 37-year-old male presented with weakness, ulcer dyspepsia, anemia and melena. The patient had a palpable lump in the epigastrium and left hypochondrium. Investigations revealed anemia. Chest radiograph was normal. UGI endoscopy revealed a large polypoidal mass in the antrum and the lesser curvature of the stomach. Abdominal sonography revealed a mixed hypo-echoic mass in the mid abdomen sized 10x8x5.5cm with calcification (Fig 1). CT study revealed a 10x8.5x6cm mass with heterogenous contrast enhancement on the posterior wall and antral region of the stomach. A polypoid lesion was seen bulging into the antrum. The mass was well marginated and showed preserved perilesional fat planes. The patient underwent a partial gastrectomy with tumour removal. Histopathological examination showed a well encapsulated fleshy tumour measuring 8x9x6.5cm having areas of haemorrhage. A smaller submucosal nodule measuring 2.7x2.7x3cm was present with mucosal ulceration. Microscopic evaluation (Fig. 2) of both lesions showed a mesenchymal tumour with predominant epithelioid features containing polygonal to spindle cells in fascicles with abundant eosinophilic cytoplasm and vesicular rounded to oval nuclei. Mitoses was less than 5 per 50 HPF. Focal expression of smooth muscle antigen (SMA) was seen on immunophenotyping which excluded a leiomyosarcoma

and S-100 expression was negative.

A diagnosis of Malignant gastrointestinal stromal tumour (GIST) with epithelioid features was made. C-KIT detection by immunohistochemistry for CD-117 could not be carried out.

Case No 2

A 40 year old male presented with hiccoughs for 15 days. He had burning in the epigastrium associated with weakness over the last 6-8 months. Clinical examination revealed anaemia and a lump in the hypogastrium. The routine lab investigations, chest radiograph, Upper and lower GI endoscopy were normal. Bone marrow aspiration were normal. Lymph node biopsy of a left femoral node revealed spindle cells of muscle/neural origin. Abdominal sonography revealed multiple masses of mixed echogenicity (hypoechoic areas suggesting necrosis) in the retroperitoneum, left lumbar region and the right side of the pelvis. CT abdomen (Figs 3,4) showed poorly enhancing heterogenous masses in the

Fig. 1 : Case 1 : USG of the upper abdomen shows a well circumscribed heteroechoic mass (with few small sub cm sized hypoechoic areas) lying on the left of the aorta

*Classified Specialist (Radiodiagnosis) CT and MR Imaging, 92 Base Hospital, c/o 56 APO, ⁺Associate Professor (Pathology), Armed Forces Medical College, Pune, [#]Graded Specialist (Radiodiagnosis), 151 Base Hospital, ^{**}Classified Specialist (Medicine) and Medical Oncologist, Army Hospital (R&R), Delhi Cantt.

Fig. 2a : Case 1 : A low power view of a malignant tumour with epithelioid features showing a pushing border abutting on the muscularis propria (H & E x 4)

Fig. 2b : Case 1 : Same tumour on high power shows pleomorphic epithelioid cell pattern (H&E x 40). The inset shows focal positivity for smooth muscle antigen (DAB x 10)

Fig. 3 : Case 2 : A CECT image showing two relatively well defined heterogeneously enhancing mass lesion in the retroperitoneum (para aortic regions)

retroperitoneum, left lumbar region and pelvis along with bowel wall thickening.

The patient underwent debulking abdominal surgery with retroperitoneal mass overlying the aorta and IVC being removed and the ileal and jejunal loops were involved. The pelvic mass was associated with rectal and bladder infiltration.

Fig. 4 : Case 2 : A CECT image showing tumour involving the small bowel with eccentric wall thickening. The bowel lumen is filled with contrast and air.

Histopathological examination showed a large encapsulated mass measuring 18x11x1cm, with multiple surface and omental nodules and a grayish white cut surface with haemorrhagic areas. On microscopic examination a cellular spindle cell tumour organized in fascicles and nodules was seen arising from the muscularis propria of the small intestine. Mitotic rate was greater than 10 per 50 HPF. There was no significant necrosis. The omental nodules showed a similar histology. A diagnosis of gastrointestinal stromal tumour of high risk was made based on size and mitotic rate. Immunohistochemically the tumour showed focal neural differentiation (S-100 positively) and was SMA negative. Staining for C-KIT could not be performed.

An MRI study during follow up revealed well defined masses in the subhepatic region and a well defined mass in the pelvis on the right side with adjacent bladder and bowel involvement (Fig. 5) signifying residual/recurrent disease.

Discussion

The term “stromal tumour” was coined by Mazur and Clark in 1983 for the tumours previously classified as smooth muscle neoplasms arising from the GIT. Immunohistochemistry revealed that many of these smooth muscle neoplasms lacked immunophenotypic properties of smooth muscle differentiation. In the early 1990's there was considerable confusion regarding differentiation shown by these stromal tumours. These ranged from truly myogenic (smooth muscle antigen positive) to neural (S-100 antigen positive) while some showed bi directional differentiation and others had a null phenotype. In the later 1990's one approach was to lump all mesenchymal tumours of the GIT as GIST. The second approach was to identify a group of mesenchymal tumours with common histopathological properties that excluded true leiomyomas and schwannomas.

Currently KIT immunoreactivity, is used for GIT

Fig. 5 : Case 2 : A coronal breath hold T2WI of the abdomen gives an exquisite definition of the lesion in the pelvis and the subhepatic region. The tumour definition and the adjacent tissue involvement is excellent.

mesenchymal lesions to identify tumours differentiating towards interstitial cells of Cajal. Cajal cells are GI pacemaker cells forming the interface between autonomic nerve endings and the smooth muscle. They have immunophenotypic and ultra structural features of both smooth muscle and neuronal differentiation. The true smooth muscle and schwann cell neoplasms lack the KIT mutations and do not express the KIT protein [2,3]. The diagnosis of GIST is suspected histologically as majority of the cases have remarkably uniform appearance falling into one of the following three categories of spindle cell, epithelioid or mixed type, GIST's show consistent positivity for KIT (CD117 protein) [2,3].

It is difficult to predict behaviour or to distinguish benign from malignant. Two parameters that have gained acceptance to define risk of aggressive behaviour are tumour size and mitotic count. (Table 1).

Tumour size varies from tiny to very large. They may occur anywhere from the oesophagus to the rectum (stomach 50-60% and small intestines 20-30%). Extra GI locations include gall bladder, retroperitoneum, mesentery and omentum. Metastatic disease to the liver and peritoneum is known [1]. While reported age of presentation is 50-60 years, our cases presented in early adulthood. A male predominance is known. The common presenting symptoms include fatigue, GI bleed, palpable

Table 1

GIST- Risk of aggressive behaviour [2]

	Size	Mitotic count
Very low risk	<2cm	<5/50 HPF
Low risk	2-5cm	<5/50 HPF
Intermediate risk	<5cm	6-10/50HPF
	5-10cm	<5/50 HPF
High risk	>5cm	>5/50 HPF
	>10cm	Any mitotic rate
	Any size	>10/50HPF

mass, anaemia and malaise as in our cases. The imaging features are similar to the leiomyosarcomas [1].

On CT and MRI, this tumor appears as a heterogeneous mass with central necrosis and a large extra luminal component. Severe hemorrhage within the mass associated with hypervascular stromal tumors produces a fluid-fluid level. Calcification is occasionally demonstrated. A crescent shaped necrosis in the peripheral aspect of the extraluminal lesion is suggestive of a stromal tumour [4]. Those tumors located in the pelvis often resemble ovarian neoplasms and peritoneal carcinomatosis [1]. CT findings favouring malignant stromal tumor include size >5cm, lobulation, heterogeneity with central necrosis, mesenteric infiltration, regional lymphadenopathy and exophytic growth. Metastasis occurs by direct extension, hematogenous route or direct intraperitoneal spread. The imaging features of these tumors are similar to the leiomyomas and leiomyosarcomas [1]. MRI is useful in delineating the tumor, defining its relationships and in detecting hemorrhage and necrosis. Ill-defined margins suggest high grade lesions [5]. Multidetector CT can pick up most lesions >2cm [6]. Angiographic features of these tumors include prominent feeding and draining vessels as well as tumor staining with contrast [7,8]. Metastatic deposits are also known to reflect similar features of hypervascularity [9].

The sonographic features are echopoor with cystic/necrotic changes. These lesions are difficult to differentiate from lymphomas, metastasis and adenocarcinomas. An exophytic dumb bell shaped mass with little contact to the gut is suggestive of GIST. Lymphadenopathy is characteristically absent [10].

Surgery is the mainstay of treatment while metastatic or residual disease requires medical management. These tumors are notoriously unresponsive to chemotherapy. Treatment with STI 571 (Specific tyrosine kinase inhibitor-given in a dose of 400mg/day) results in a 60% remission rate and an 85% overall control rate [11,12].

References

- Hyun KHA, Jeong KK. The gastrointestinal tract. In: Haaga JR, Lansieri CF, Gilkeson RC eds. CT and MR Imaging of the

- Whole Body. 4th edition. Mosby, 2003: 1154-258.
2. Fletcher CDM, Berman JJ, Gorstein F, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol* 2002; 33: 459-65.
 3. Mittinen M, Wa'el el Rifai, Sobin LH. Evaluation of malignancy and prognosis of gastrointestinal stromal tumors: A review. *Hum Pathol* 2002; 33: 478-83.
 4. Rioux M, Mailloux C: Crescent shaped necrosis: A new imaging sign suggestive of stromal tumor of the small bowel. *Abdominal imaging* 1997; 22: 376-80.
 5. Hasegawa S, Smelka RC, Noone TC, et al. Gastric stromal sarcomas: Correlation of MR Imaging and histopathologica findings in nine patients. *Radiology* 1998; 208: 591-5.
 6. Nishida T, Kumano S, Sugiura T, Ikushima H et al. Multidetector CT of High Risk Patients with Occult Gastro intestinal Stromal Tumors. *AJR* 2003; 180: 185-9.
 7. Boijson E. Superior mesenteric angiography in adults. In Baum S, editor. *Abrams Angiography Vascular and Interventional Radiology*. 4th edition. Little Brown and Co. 1997: 1577.
 8. Leon DC. Retroperitoneal arteriography in adults. In Baum S, editor. *Abrams Angiography Vascular and Interventional Radiology*. 4th edition. Little Brown and Co. 1997; 1669-73.
 9. Baum S. Hepatic angiography. In Baum S, editor. *Abrams Angiography Vascular and Interventional Radiology*. 4th edition. Little Brown and Co. 1997: 1451-2.
 10. Puylaeri JBCM, Rioux M, van Oostayen JA. Appendix and small bowel. In Meire HB, Cosgrove DO, Dewbury KC, Farrant P. *Clinical Ultrasound a comprehensive text. Abdomen and General Ultra sound Vol 2*. 2nd edition. Churchill Livingstone, 2001: 862.
 11. Joensuu H, Roberts PJ, Maarit S et al: Effect of Tyrosine kinase inhibitor STI 571 in a patient with metastatic Gastrointestinal stromal tumor. *NEJM* 2001; 344: 1052-6.
 12. Blanke CD, Eisenberg BL, Henrich MC: Gastrointestinal stromal tumor: Current treatment options. *Oncology* 2001; 2(6): 485-91.