

Giant small intestine gastrointestinal stromal tumor with gastrointestinal bleeding

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Abstract

Small intestine stromal tumors are relatively rare and cause subtle clinical signs and symptoms. Their diagnosis is often delayed until complications develop. Even if complications occur, an exact preoperative diagnosis may be very difficult. Surgery remains the mainstay of treatment, and other treatment modalities are limited. We present herein a patient with a giant gastrointestinal tumor who presented with gastrointestinal bleeding. Complete resection was performed despite the large tumor size (23 × 20 × 8 cm) and the patient was free of signs and symptoms during the 4-month follow-up. (*Acta gastroenterol. belg.*, 2009, 72, 458-461).

Key words : gastrointestinal stromal tumor ; small intestine ; gastrointestinal bleeding.

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract in adults (1). The clinical manifestations of GISTs of the small intestine include abdominal pain, a palpable intra-abdominal mass, vomiting, weight loss, and occult gastrointestinal bleeding. Because such symptoms can result from any of several causes, GISTs are often diagnosed after the occurrence of complications such as hemorrhage, obstruction, and perforation (2,3,4).

Case

A 30-year-old male patient was admitted to our clinic with a two-month history of loss of appetite, nausea-vomiting, epigastric pain, and weight loss of about 20 kg. His past medical history was unremarkable. On physical examination, he showed diffuse abdominal tenderness, and a partially mobile mass of approximately 15 cm was palpated on the epigastric area. The results of laboratory testing at the time of admission were as follows : Total protein : 5.4 g/dL (normal range, 6-8 g/dL), albumin : 3.1 g/dL (normal range, 3.5-5.5 g/dL), hemoglobin, 9.4 g/dL (normal range, 13.5-18 g/dL), and C-reactive protein : 156 mg/L (normal range, 0-10 mg/L). Tumor markers including CEA and CA 19-9 were in normal limits. Computed tomography scan of the abdomen revealed a solid, slightly enhanced 20 × 7 × 15 cm necrotizing mass on the proximal jejunal loops, and jejunal mesenchymal tumor was suspected (Fig. 1). Because of the patient's poor oral intake and low serum albumin

level, total parenteral nutritional support was started. Since the tumor was located on the proximal jejunal loops, upper gastrointestinal endoscopic evaluation with a colonoscope was performed and a pouch covered with necrotic walls like a diverticulum was noticed and biopsies were obtained. The patient developed melena and his hemoglobin level decreased to 5.5 g/dL. Seven units of packed erythrocytes were transfused and selective mesenteric and celiac angiography was performed, but the site of hemorrhage was not identified. Histopathological examination of the endoscopic biopsy specimens obtained from the necrotic diverticulum-like pouch revealed spindle cells with focal necrotic areas. Immunohistochemical studies revealed diffuse cytoplasmic positivity for CD 117 and no activity for CD 34, SMA or S-100 ; the tumor was reported as GIST and laparotomy was planned. On laparotomy, a giant tumoral mass filling the whole abdomen and involving particularly the serosa of the intestine originating 50 cm from the ligament of Treitz was detected and the tumor was totally excised with partial intestinal resection (Fig. 2). No residual macroscopic tumor remained. Postoperative histopathological analysis revealed a 23 × 20 × 8 cm tumor. It was serosally located and composed of spindle-shaped atypical cells with eosinophilic cytoplasm. Mitotic activity was 5-6 mitoses per 50 high power fields. The tumor invaded the small bowel submucosa and mucosa. Immunohistochemical examination revealed the same features as in the endoscopic biopsy specimens and the tumor was described as a high-grade GIST (Fig. 3). The postoperative course was uneventful and the patient was discharged on the 6th postoperative day. Because the tumor was successfully excised totally and no tumor was found on the surgical margins, follow-up without treatment was planned for this patient. The patient was free of signs and symptoms during the 4-month follow-up.

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Submission date : 22/06/2009

Acceptance date : 25/08/2009



Fig. 1. — Axial post contrast computed tomographic images show a solid, slightly enhanced $20 \times 7 \times 15$ cm necrotizing mass on the proximal jejunal loops (arrows).



Fig. 2. — A giant tumoral mass filling the whole abdomen and involving particularly the serosa. The tumor was totally excised with partial intestinal resection.

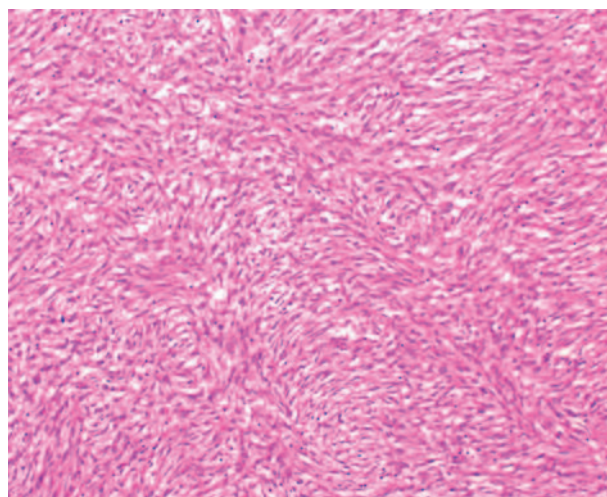


Fig. 3. — Spindle-shaped neoplastic cells with whorling pattern. Hematoxylin & eosin stain, $10\times$ magnification.

Discussion

GISTs are the most common mesenchymal tumors of the gastrointestinal tract in adults. The incidence of GISTs in all gastrointestinal tumors is 0.1%-3% (1). GISTs occur primarily in those older than 40 years (peak incidence during the 6th and 7th decades), and they are slightly more common in men (5). GISTs of the small intestine develop (in descending order of frequency) in the jejunum, ileum, and duodenum (1).

Small-sized tumors (< 2 cm) are usually asymptomatic, and are discovered incidentally (6). Crosby and

colleagues reported that the most common signs or symptoms of GISTs include abdominal pain (74%), abdominal mass (72%), gastrointestinal bleeding (44%), partial or complete small bowel obstruction (44%), weight loss (16%), and fever or abscess (14%) (1). The diagnosis of GISTs of the small intestine is often made after the occurrence of complications such as hemorrhage, obstruction, or perforation (2,3). The symptoms and signs of GISTs are not disease-specific, and metastases are already present in about half of the cases at the time of diagnosis, usually to the liver or peritoneum (3,4,7-9).

None of the diagnostic procedures, including barium examination of the gastrointestinal tract, computed tomography or angiography, can establish the correct diagnosis with 100% certainty (6,10-12). Although the main prognostic factor is the mitotic count and tumor diameter, considering the possibility of metastasis or recurrence, GISTs can be classified as low- or high-risk tumors (13-15). It should be noted that retrospective analysis of a great number of cases resulted in a new prognostic classification taking into account also the location of the tumour (16). The positivity for KIT protein (CD117 antigen) is mostly shown in the immunohistochemical examination of GISTs. In the rare cases of KIT-negative GISTs, other markers (DOG-1 and PKC θ) as well as mutations in KIT and PDGFRA genes have diagnostic impact (16). The positivity of other markers (i.e. CD34, SMA, S-100, Desmin) varies (3,7,13,17,18).

Surgical excision of the tumor is the treatment of choice for GISTs. All infiltrated tissues and the tumors should be completely resected. However, systemic lymph node dissection is not recommended by many authors (18,19). Five-year survival ranging between 48-65% is reported in complete surgical resection. Partial resection may be sufficient in cases with large tumors in whom palliation or the control of symptoms or complications such as compression of adjacent organs, hemorrhage, or pain can be achieved (7).

When symptoms or signs such as perforation, multifocal location or metastatic lesions are present, the prognosis is poor. The five-year survival is 0% in patients with metastatic tumors or multifocal tumors; whereas patients with localized or locally advanced tumors have a 46% five-year survival (6). In our patient complete resection was performed.

GISTs show poor response to conventional chemotherapy (<10%), whereas radiotherapy can be used in cases of intraperitoneal hemorrhage, when the exact location of the tumor is shown, or for analgesic purposes (7,13,19).

STI571, recently named as imatinib, has been found to be a powerful selective inhibitor of tyrosine-kinases and the receptors of platelet-derived growth factor and c-kit. Imatinib has been shown in clinical studies to be the first effective treatment for non-resectable or metastatic GISTs (7). With regard to long-term results of imatinib treatment, it becomes clear that this treatment changes the natural course of the disease; in a study comparing drug dose in patients with advanced (unresectable or metastatic) GISTs, the overall survival of these patients was 3.5 years. It should also be noted that most patients develop a clinical resistance to imatinib (21). Since our patient did not have any metastasis, complete surgical excision of the tumor was performed despite the large size and the tumor was reported as high-grade tumors in pathologic examinations.

In conclusion, there are limited treatment options in GISTs. Complete surgical resection without extensive

lymph node sampling remains the first choice for primary treatment. To the best of our knowledge, this is the largest small intestinal stromal tumor described to date in the English literature. Small intestinal GISTs cause subtle clinical signs and symptoms; their diagnosis is often delayed until complications develop. Even if complications occur, an exact preoperative diagnosis may be very difficult. GIST should be kept in mind in the differential diagnosis of patients presenting with unexplained intra-abdominal mass and/or gastrointestinal bleeding.

References

1. CROSBY J.A., CATTON C.N., DAVIS A., COUTURE J., O'SULLIVAN B., KANDEL R., SWALLOW C.J. Malignant gastrointestinal stromal tumors of the small intestine: a review of 50 cases from a prospective database. *Ann. Surg. Oncol.*, 2001, **8**: 50-9.
2. CHAO T.C., CHAO H.H., JAN Y.Y., CHEN M.F. Perforation through small bowel malignant tumors. *J. Gastrointest. Surg.*, 2005, **9**: 430-5.
3. MIETTINEN M., MAKHLOUF H., SOBIN L.H., LASOTA J. Gastrointestinal stromal tumors of the jejunum and ileum: a clinicopathologic, immunohistochemical, and molecular genetic study of 906 cases before imatinib with long-term follow-up. *Am. J. Surg. Pathol.*, 2006, **30**: 477-89.
4. MANOURAS A., PAPPAS A., KATERGIANNAKIS V., FILIS K., CHRYSIKOS J., PATTAS M., GENETZAKIS M., TSEKOURAS D., LAGOUDIANAKIS E. Gastrointestinal stromal tumors of the rectum: report of five cases. *Acta Gastroenterol. Belg.*, 2009, **72**: 257-61.
5. DE MATTEO R.P., LEWIS J.J., LEUNG D., MUDAN S.S., WOODRUFF J.M., BRENNAN M.F. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. *Ann. Surg.*, 2000, **231**: 51-8.
6. EFREMIDOU E.I., LIRATZOPOULOS N., PAPAGEORGIOU M.S., ROMANIDIS K. Perforated GIST of the small intestine as a rare cause of acute abdomen: surgical treatment and adjuvant therapy. Case report. *J. Gastrointest. Liver Dis.*, 2006, **15**: 297-9.
7. CONNOLLY E.M., GAFFNEY E., REYNOLDS J.V. Gastrointestinal stromal tumors. *Br. J. Surg.*, 2003, **90**: 1178-86.
8. UEYAMA T., GUO K.J., HASHIMOTO H., DAIMARU Y., ENJOJI M. A clinicopathologic and immunohistochemical study of gastrointestinal stromal tumors. *Cancer*, 1992, **69**: 947-55.
9. EMORY T.S., SOBIN L.H., LUKES L., LEE D.H., O'LEARY T.J. Prognosis of gastrointestinal smooth-muscle (stromal) tumors: dependence on anatomic site. *Am. J. Surg. Pathol.*, 1999, **23**: 82-7.
10. LEE C.M., CHEN H.C., LEUNG T.K., CHEN Y.Y. Gastrointestinal stromal tumor: computer tomographic features. *World J. Gastroenterol.*, 2004, **10**: 2417-8.
11. BUCHER P., VILLIGER P., EGGER J.F., BUHLER L.H., MOREL P. Management of gastrointestinal stromal tumours: from diagnosis to treatment. *Swiss. Med. Wkly.*, 2004, **134**: 145-53.
12. FANG S.H., DONG D.J., ZHANG S.Z., JIN M. Angiographic findings of gastrointestinal stromal tumor. *World J. Gastroenterol.*, 2004, **10**: 2905-7.
13. JUDSON I. Gastrointestinal stromal tumors (GIST): biology and treatment. *Ann. Oncol.*, 2002, **13**: 287-9.
14. BUCHER P., TAYLOR S., VILLIGER P., MOREL P., BRUNDLER M.A. Are there any prognostic factors for small intestinal stromal tumors? *Am. J. Surg.*, 2004, **187**: 761-6.
15. FLETCHER C.D., BERMAN J.J., CORLESS C., GORSTEIN F., LASOTA J., LONGLEY B.J., MIETTINEN M., O'LEARY T.J., REMOTTI H., RUBIN B.P., SHMOOKLER B., SOBIN L.H., WEISS S.W. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum. Pathol.*, 2002, **33**: 459-65.
16. LASOTA J., MIETTINEN M. KIT and PDGFRA mutations in gastrointestinal stromal tumors (GISTs). *Semin. Diagn. Pathol.*, 2006, **23**: 91-102.
17. HIROTA S., ISOZAKI K., MORIYAMA Y., HASHIMOTO K., NISHIDA T., ISHIGURO S., KAWANO K., HANADA M., KURATA A., TAKEDA M., MUHAMMAD TUNIO G., MATSUZAWA Y., KANAKURA Y., SHINOMURA Y., KITAMURA Y. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. *Science*, 1998, **279**: 577-80.
18. CORLESS C.L., FLETCHER J.A., HEINRICH M.C. Biology of gastrointestinal stromal tumors. *J. Clin. Oncol.*, 2004, **22**: 3813-25.

19. CHEN T.W., LIU H.D., SHYU R.Y., YU J.C., SHIH M.L., CHANG T.M., HSIEH C.B. Giant malignant gastrointestinal stromal tumors : recurrence and effects of treatment with STI-571. *World J. Gastroenterol.*, 2005, **11** : 260-3.
20. APARICIO T., BOIGE V., SABOURIN J.C., CRENN P., DUCREUX M., LE CESNE A., BONVALOT S. Prognostic factors after surgery of primary resectable gastrointestinal stromal tumors. *Eur. J. Surg. Oncol.*, 2004, **30** : 1098-103.
21. DEBIEC-RYCHTER M., SCIOT R., LE CESNE A., SCHLEMMER M., HOHENBERGER P., VAN OOSTEROM A.T., BLAY J.Y., LEYVRAZ S., STUL M., CASALI P.G., ZALCBERG J., VERWEIJ J., VAN GLABBEKE M., HAGEMEIJER A., JUDSON I ; EORTC SOFT TISSUE AND BONE SARCOMA GROUP ; ITALIAN SARCOMA GROUP ; AUSTRALASIAN GASTROINTESTINAL TRIALS GROUP. KIT mutations and dose selection for imatinib in patients with advanced gastrointestinal stromal tumours. *Eur. J. Cancer*, 2006, **42** : 1093-103.