Development of multiple myeloma in a patient with gastrointestinal stromal tumor treated with imatinib mesylate: A case report

D Tzilves, A Gatopoulou, K Zervas, E Katodritou, F Patakiouta, A Tarpagos, I Katsos

D Tzilves, A Gatopoulou, A Tarpagos, I Katsos, Department of Gastroenterology, Theagenio Cancer Hospital, 2 Al. Simeonidi 54007, Thessaloniki, Greece

K Zervas, E Katodritou, Department of Hematology, Theagenio Cancer Hospital, 2 Al. Simeonidi 54007, Thessaloniki, Greece

F Patakiouta, Department of Pathology, Theagenio Cancer Hospital, 2 Al. Simeonidi 54007, Thessaloniki, Greece

Correspondence to: Dr. Anthia Gatopoulou, Theagenio Cancer Hospital, 2, Al. Simeonidi 54007, Thessaloniki, Greece. gatop@otenet.gr

Telephone: +30-2310-898412

Fax: +30-2310-898408

Received: 2007-02-01

Accepted: 2007-03-08

Abstract

Gastrointestinal stromal tumors (GISTs) are rare tumors, which represent approximately 1% of the neoplasms of the gastrointestinal tract. These tumors rarely give extra-abdominal metastases. However, their clinical outcome is potentially adverse. In some rare cases, co-existence of GISTs with other malignancies has been reported. Here we present a case of a 74-year old male with GIST, which was managed by surgical resection. Fourteen months later, the patient presented with liver metastases and imatinib mesylate was administered. During treatment, the patient reported skeletal pain and plane X-rays revealed osteolytic bone lesions. Further investigation revealed the presence of multiple myeloma. To the best of our knowledge, this is the first report of the co-existence of multiple myeloma (MM) with GIST.

© 2007 The WJG Press. All rights reserved.

Key words: Gastrointestinal stromal tumor; Multiple myeloma; Imatinib mesylate

Tzilves D, Gatopoulou A, Zervas K, Katodritou E, Patakiouta F, Tarpagos A, Katsos I. Development of multiple myeloma in a patient with gastrointestinal stromal tumor treated with imatinib mesylate: A case report. *World J Gastroenterol* 2007; 13(13): 2011-2013

<http://www.wjgnet.com/1007-9327/13/2011.asp>

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) represent

rare neoplasms of the gastrointestinal tract, which are characterized by a specific histological and immunohistochemical pattern. These neoplasms have been recently defined as a discrete molecular and pathological entity. The management of GIST has not been clearly established^[1].

In some rare cases coexistence of GIST with other malignancies has been reported^[2-6]. Here we describe a case of a 74-year old male with GIST who developed multiple myeloma (MM) during the course of GIST treatment. To the best of our knowledge, the co-existence of GIST and multiple myeloma has not been reported so far.

CASE REPORT

A 74-year old male was presented complaining of dyspepsia. Clinical examination revealed a palpable epigastric mass, with no other abnormal clinical findings. Computed tomography of the abdomen showed a 15 cm × 16 cm solid mass in the right side of abdomen, deriving from the gastric wall. A submucosal non-metastatic tumor was suspected (Figure 1A). Endoscopy showed normal mucosa of the gastrointestinal tract. Laboratory tests were normal. During the surgery, a 5 cm × 11 cm mass of the posterior wall of the gastric antrum protruding from the inner muscularis propria to the mucosa was found. The mass was completely resected and the histological examination demonstrated whirling sheets of spindle cells which were stained positively for CD 117 (c-kit) and CD34, mitotic index > 10/50 HPF, while smooth muscle actin (SMA) and vimentin were focally positive, and keratine, desmin, S-100 protein were negative. This specific immunophenotype characterized GIST. No further therapy was applied. Physical examination, laboratory tests and computed tomography were performed when the patient was followed up at 3-month intervals.

Fourteen months after resection, a CT scan of the abdomen showed liver metastases (Figure 1B) and imatinib mesylate at a dose of 400 mg once daily, as the appropriate second line therapy, was administered. After one month of treatment, the patient reported persistent skeletal pain, especially on the thorax, accompanied with weakness and fatigue. X-ray bone survey showed lytic lesions. Laboratory examination revealed normocytic, normochromic anemia (Hb: 10.6 gr/dL), hypercalcemia (Ca: 11.7 mg/dL) and abnormal ESR (140 mm/h). Serum protein electrophoresis and immunofixation showed an

Figure 1 Computed tomography of abdominal mss (A), liver metastases (B), and progression of liver metastases (C).

IgA κ monoclonal protein. Bence-Jones proteinuria was also detected. Bone marrow aspiration and biopsy showed a 90% plasma cell infiltration confirming the diagnosis of multiple myeloma. The patient was treated with melphalan and prednisone. Imatinib therapy was also continued. The patient did not respond sufficiently to either anti-myeloma or GIST therapy (Figure 1C). Eighteen months after GIST resection and six months after multiple myeloma diagnosis, the patient deteriorated rapidly and died.

DISCUSSION

GISTs are rare tumors of the gastrointestinal tract, with an annual incidence of 10 to 15 cases per million in Caucasian populations. These tumors often give rise to numerous intra-abdominal metastases located on the peritoneal, omental, mesenteric, and other serosal surfaces as well as liver metastases, whereas extraabdominal metastases are rare^[7,8]. The current treatment for localized disease is surgical resection whereas therapy with imatinib mesylate can be applied in non-operable and /or metastatic tumor^[1].

GIST co-existing with adenocarcinoma has rarely been reported^[2-6,9,10]. In one study, significantly more synchronous or metachronous gastrointestinal neoplasms were found in GIST patients compared to malignancies occurring in the normal Hungarian population^[11]. Furthermore, cases of synchronously occurring GIST and mucosa associated lymphoid tissue as well as GIST and

carcinoid tumors of the stomach have been described in the literature^[12,13]. Janovisk *et al*^[14] recently reported a case of coexistence of hepatocellular carcinoma and GIST. Andea *et al*^[15] reported a case of multiple gastric stromal tumors with coexistence of gastric submucosa lipoma and carcinoid.

Co-existence of MM and GIST has never been reported. The present case raises the question of whether this is incidental or the two malignancies have any biological relevance. The role of treatment with imatinib mesylate in the development of myeloma could not be supported as the duration of treatment was short although Garipidou *et al*^[16] reported the development of MM in a patient with chronic myeloid leukemia treated with imatinib mesylate.

Concerning the biological action of imatinib mesylate on MM, it has been shown that this drug inhibits proliferation of MM cells *in vitro* by arresting cell-cycle progression^[17]. Furthermore, it has been shown that it may inhibit the proliferation of MM cells resistant to dexamethasone or melphalan and may have an additive effect when combined with dexamethasone^[17]. It was also demonstrated that imatinib exhibits a small stimulatory effect on the proliferation of MM cells through activation of the Erk1/2 mitogen-activated protein kinases route^[17]. However, in the present case, imatinib mesylate did not exhibit any therapeutic action on MM.

In conclusion, this is the first case of GIST co-

existing with multiple myeloma. Although the existence of a second malignancy in a patient with GIST is very uncommon, such a possibility should not be ignored. Long-term observation of GIST patients may prove a causal relationship between GIST and other malignancies.

REFERENCES

- 1 **Blay JY**, Bonvalot S, Casali P, Choi H, Debiec-Richter M, Dei Tos AP, Emile JF, Gronchi A, Hogendoorn PC, Joensuu H, Le Cesne A, McClure J, Maurel J, Nupponen N, Ray-Coquard I, Reichardt P, Sciot R, Stroobants S, van Glabbeke M, van Oosterom A, Demetri GD. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20-21 March 2004, under the auspices of ESMO. *Ann Oncol* 2005; **16**: 566-578
- 2 **Bircan S**, Candir O, Aydin S, Başpınar S, Bülbül M, Kapucuoglu N, Karahan N, Ciriş M. Synchronous primary adenocarcinoma and gastrointestinal stromal tumor in the stomach: a report of two cases. *Turk J Gastroenterol* 2004; **15**: 187-191
- 3 **Moschos J**, Tzilves D, Paikos D, Tagarakis G, Pilpilidis I, Antonopoulos Z, Kadis S, Katsos I, Tarpagos A. Large mesenteric gastrointestinal stromal tumor in a patient with familial adenomatous polyposis syndrome. *Wien Klin Wochenschr* 2006; **118**: 355-357
- 4 **Rauf F**, Ahmad Z, Muzzafar S, Hussaini AS. Synchronous occurrence of gastrointestinal stromal tumor and gastric adenocarcinoma: a case report. *J Pak Med Assoc* 2006; **56**: 184-186
- 5 **Melis M**, Choi EA, Anders R, Christiansen P, Fichera A. Synchronous colorectal adenocarcinoma and gastrointestinal stromal tumor (GIST). *Int J Colorectal Dis* 2007; **22**: 109-114
- 6 **Al-Brahim N**, Radhi J, Gately J. Synchronous epithelioid stromal tumour and lipoma in the stomach. *Can J Gastroenterol* 2003; **17**: 374-375
- 7 **Tran T**, Davila JA, El-Serag HB. The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1,458 cases from 1992 to 2000. *Am J Gastroenterol* 2005; **100**: 162-168
- 8 **Joensuu H**. Gastrointestinal stromal tumor (GIST). *Ann Oncol* 2006; **17** Suppl 10: x280-x286
- 9 **Lin YL**, Tzeng JE, Wei CK, Lin CW. Small gastrointestinal stromal tumor concomitant with early gastric cancer: a case report. *World J Gastroenterol* 2006; **12**: 815-817
- 10 **Liu SW**, Chen GH, Hsieh PP. Collision tumor of the stomach: a case report of mixed gastrointestinal stromal tumor and adenocarcinoma. *J Clin Gastroenterol* 2002; **35**: 332-334
- 11 **Kalmár K**, Tornóczy T, Póto L, Illényi L, Kalmár Nagy K, Kassai M, Kelemen D, Horváth OP. Gastrointestinal stromal tumours in a single institute: is there an association to other gastrointestinal malignancies? *Magy Seb* 2004; **57**: 251-256
- 12 **Kaffes A**, Hughes L, Hollinshead J, Katelaris P. Synchronous primary adenocarcinoma, mucosa-associated lymphoid tissue lymphoma and a stromal tumor in a *Helicobacter pylori*-infected stomach. *J Gastroenterol Hepatol* 2002; **17**: 1033-1036
- 13 **Buragas M**, Kidd M, Modlin IM, Cha C. Multiple gastrointestinal stromal tumors and synchronous ileal carcinoids. *Nat Clin Pract Oncol* 2005; **2**: 166-170; quiz 1 p following 170
- 14 **Jaworski R**, Jastrzebski T, Swierblewski M, Drucis K, Kobierska-Gulida G. Coexistence of hepatocellular carcinoma and gastrointestinal stromal tumor: a case report. *World J Gastroenterol* 2006; **12**: 665-667
- 15 **Andea AA**, Lucas C, Cheng JD, Adsay NV. Synchronous occurrence of epithelial and stromal tumors in the stomach. *Arch Pathol Lab Med* 2001; **125**: 318-319
- 16 **Garipidou V**, Vakalopoulou S, Tziomalos K. Development of multiple myeloma in a patient with chronic myeloid leukemia after treatment with imatinib mesylate. *Oncologist* 2005; **10**: 457-458
- 17 **Pandiella A**, Carvajal-Vergara X, Tabera S, Mateo G, Gutiérrez N, San Miguel JF. Imatinib mesylate (STI571) inhibits multiple myeloma cell proliferation and potentiates the effect of common antimyeloma agents. *Br J Haematol* 2003; **123**: 858-868

S- Editor Wang J L- Editor Wang XL E- Editor Ma WH