Fırat Tıp Dergisi 2011; 16(4): 206-208

Case Report

www.firattipdergisi.com

Pathological Complete Response After Imatinib Mesylate Therapy in Inoperabl Gastrointestinal Stromal Tumor: A Case Report

Baha ZENGEL[1], Ahmet ALACACIOGLU[a2], Ayse YAGCI[3], Hakan POSTACI[3], Ozgur KAVAK, Ali Galip DENECLI[1], Erhan GOKMEN

[1]*Bozyaka Research and Training Hospital, 1.General Surgery, Izmir, Turkey*

[2]*Bozyaka Research and Training Hospital, Medical Oncology, Izmir, Turkey*

[3]*Bozyaka Research and Training Hospital, Pathology, Izmir, Turkey*

[4]*Ege University Hospital, Medical Oncology, Izmir, Turkey*

ABSTRACT

Gastrointestinal stromal tumors are characterized by the expression of CD34 and c-kit (CD117) and represent the most common mesenchymal malignancy of the gastrointestinal tract. Imatinib mesylate is small molecule tyrosine kinase inhibitor that suppresses transmembrane receptor c-kit products. Clinical studies for metastatic and inoperabl GISTs have demonstrated partial response rate ranging from 40% to 69% in patients treated with imatinib mesylate. But complete response is rare. We present a 46 year old man patient with unresectable gastrointestinal stromal tumor that has histopatologically proven complete response to imatinib mesylate therapy.

Keywords: *Gastrointestinal stromal tumor, Imatinib mesylate, Patological complete response, Surgery*

ÖZET

Inoperabl Gastrointestinal Tümörde Imatinib Mesilat Tedavisi Sonrası Patolojik Tam Yanıt: Olgu Sunumu

Gastrointestinal stromal tümörler CD34 and c-kit (CD117) ekspresyonu ile karekterize olan, gastrointestinal sistemin en sık görülen mezenkimal maligniteleridir. İmatinib mesiat, transmembran reseptör c-kit ürünlerini baskılayan küçük molekül tirozin kinaz inhibitörüdür. Metastatik ve inoperabl gastarointestinal stromal tümörlerde yapılan klinik çalışmalarda imatinib mesilat tedavisi ile parsiyel yanıt oranları 40% ile 69% arasındadır. Fakat tam yanıt nadirdir. Bu yazımızda 46 yaşında anrezektabl gastrointestinal stromal tümorlü erkek hastada, imatinib mesilat tedavisi ile sağlanan patolojik tam yanıt değerlendirilmiştir.

Anahtar Kelimeler: *Gastrointestinal stromal tümor, Imatinib mesylate, Patalojik tam yanıt, Cerrahi*

Gastrointestinal stromal tumors are characterized by the expression of CD34 and c-kit (CD117) and represent the most common mesenchymal malignancy of the gastrointestinal tract (1). We present a 46 year old man patient with unresectable gastrointestinal stromal tumor that has histopatologically proven complete response to imatinib mesylate therapy.

CASE REPORT

A 46-year-old man was admitted to the hospital with epigastric pain in April 2007. Physical examination revealed a palpable epigastric mass. Laboratory results including tumor markers were within normal limits. Further evaluations including abdominal computerized tomography (CT) and gastroscopy showed a tumor located at the epigastrium infiltrating the cardia and corpus of the stomach (Figure 1). Patient underwent exploratory laparatomy for the respectability evaluation and tumor originating from corpus of the stomach was classified as inoperable (due to celiac plexus invasion), incisional biopsy was performed. Histopathological evaluation revealed a partially bounded, nodulary tumor located at submucosal area (Figure 2a). Tumor was formed from uniform and short fascicules of spindle cells. Cytoplasm was clear eosinophilic, vesicular nuclei with chromatine pattern had ovoid shape(Figure 2b). Nuclear atypia was minimal. CD 117 and CD 34 was found to be positive, actin S100 and desmin negative according to immunohistochemistry analysis (Figure 2c). Kİ67 was 2-4% positive. Final histopathological diagnosis was c-kit(CD117) positive gastrointestinal stromal tumor. Treatment with imatinib mesylate 400 mg/day initiated in May 2007. Post-therapy imaging studies including diagnostic CT and

[a] Corresponding Adress: Dr. Ahmet ALACACIOGLU, Bozyaka Research and Training Hospital, Medical Oncology, Izmir, Turkey
e-mail: dralaca2000@yahoo.com

F18-FDG PET/CT showed marked regression in tumor size and total loss of fluorodeoxyglucose uptake in tumor indicating a sustained complete metabolic response (Figure 3). Re-exploration laparatomy was performed in August 2008, the tumor was observed on the anterior of the corpus of the stomach. Complete surgical resection was performed successfully with a total gastrectomy.

After neo-adjuvant therapy with Imatinib, pathological evaluation of gastrectomy material no macroscopic tumor was identified. Serial sections showed local edema, increased vascularity and adhesions through the great curvature of the antrum. A total number of 25 sequential species were fixed by formalin and stained with H&E. Microscopic examination revealed subepithelial edema, isolated hemorrhagia and vascular ectasia. Granulation tissue associated with a foreign body reaction was detected in the area with adhesions due to previous surgery. No tumoral cells were identified.

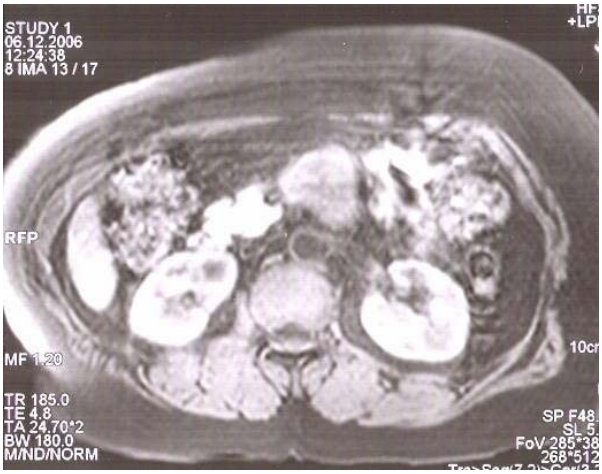

Figure 1. *CT showed a tumor located at the epigastrium infiltrating the cardia and corpus of the stomach.*

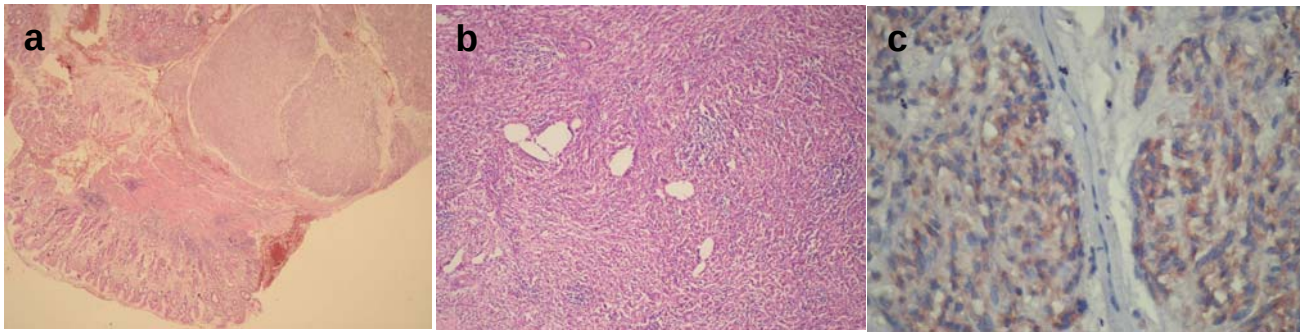

Figure 2 (a,b,c). *Histopathology of GIST*

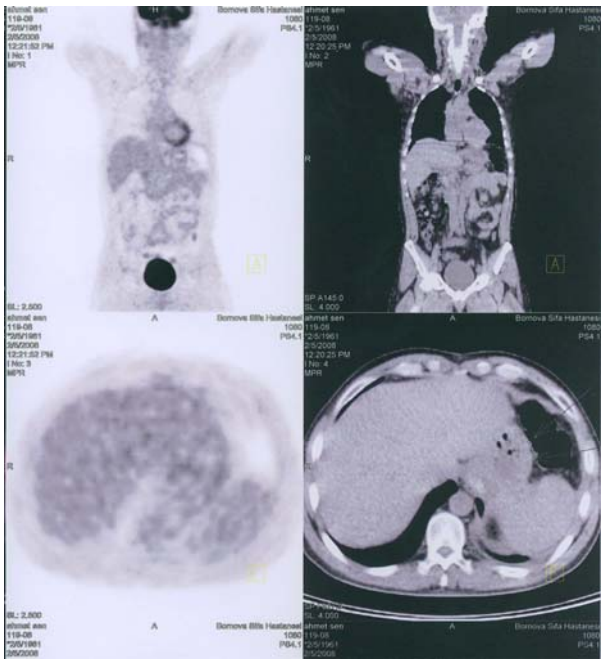

Figure 3. *F18-FDG PET/CT showed total loss of FDG uptake in tumor indicating a sustained complete metabolic response.*

DISCUSSION

Gastrointestinal stromal tumors (GISTs) represent the most common mesenchymal malignancy of the gastrointestinal tract. The incidence of GISTs was estimated to account for approximately 1% to 3% of all malignant gastrointestinal tumors (1). GISTs were initially a descriptive term developed in 1983 by Mazur and Clark to define intra-abdominal tumors excluding carcinomas (2). GISTs originate from stem cells that differentiate toward the interstitial cells of Cajal (ICCs). ICCs are the pacemaker cells of the gastrointestinal tract and act to coordinate gut peristalsis by linking the smooth muscle cells of the bowel wall with the autonomic nervous system (3). GISTs are characterized by the expression of CD34 and c-kit (CD117). Kit is the cell transmembrane receptor with a tyrosin kinase activity. There are frequent mutations of kit in GISTs. These mutations results in constitutive activation of kit signaling which leads to uncontrolled cell proliferation and resistance to apoptosis (4).

Surgical resection is the only curative treatment for non metastatic GIST. Recurrence of the disease is common and metastatic GIST is fatal. The rates of

objective antitumor response to a variety of chemotherapy agents for patients with GIST were routinely reported as 0%, at best, less than 5% (1). The median survival of metastatic disease has been reported to range between 11 and 21 months (5).

Imatinib mesylate (Glivec; Novartis Pharmaceuticals, Basel Switzerland) is small molecule tyrosine kinase inhibitor that suppresses intracelluler ABL kinase, chimeric BCR-ABL fusion oncoprotein of chronic myeloid leukemia, platelet-derived growth factor receptor and transmembrane receptor c-kit products (4, 6). Clinical studies for metastatic and unresectable GISTs have demonstrated partial response rate 40%-69% in patients treated with imatinib mesylate. But complete response is rare.

In the literature besides studies in which no complete response was obtained in GISTs using imatinib mesilate therapy there are also few cases demonstrating complete response to therapy (8, 9). In the study of Andtbacka et al a (7) total of 46 metastatic or unresectable GISTs were evaluated and following complete metabolic response proven with radiologic and metabolic imaging was detected only in 1 patient. However histopathological evidence lacks for this particular case. Similarly in the report of Chiang et al (4), although complete metabolic response was detected in 3 of 42 patients using radiologic methods and F18-FDG PET, no histopathological verification was reported. Goh et al (10) reviewed 37 unresectable and recurrent GIST cases and reported pathologic complete response in 4 patients. F18-FDG PET study was reported as stable disease in 1 and as complete metabolic response in remaining 3 patients. There are also cases reported by Salazar et al (11), Melichar et al (5) and Suzuki et al (12) in whom pathologic complete responses were reached.

Our GIST case treated with imatinib mesilate is one of the rare complete response cases verified with both CT, F18-FDG PET/CT study and pathological examination.

KAYNAKLAR

1. Demetri GD. Gastrointestinal stromal tumor. In: Cancer: Principles and practice of oncology, 8th ed, DeVita VT, Hellman S, Rosenberg SA (Eds), p 1257, Lippincott-Williams &Wilkins, Philadelphia, 2008.
2. Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol 1983; 7: 507-519.
3. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristic of the intersititial cell of Cajal. Am J Pathol 1998; 152: 1259-1269.
4. Chiang KC, Chen TW, Yeh CN, Liu FY, Lee HL, Jan YY. Advanced gastrointestinal stromal tumor patients with complete response after treatment with imatinib mesylate. World J Gastroenterol 2006; 12: 2060-2064.
5. Melichar B, Voboril Z, Nozicka J, et al. Pathological complete response in advanced gastrointestinal stromal tumor after imatinib therapy. Internal Medicine 2005; 44: 1163-1168.
6. Joensuu H, Roberts PJ, Sarlomo-Rikala M, et al. Effect of the tyrosine kinase inhibitor STI571 in a patient with a metastatic gastrointestinal stromal tumor. N Eng J Med 2001; 344: 1052-1056.
7. Andtbacka RH, Ng CS, Scaife CL, et al. Surgical resection of gastrointestinal stromal tumors after treatment with imatinib. Ann Surg Oncol 2007; 14: 14-24.
8. Gronchi A, Fiore M, Miselli F, et al. Surgery of residual disease following molecular-targeted therapy with imatinib mesylate in advanced/metastatic GIST. Ann Surg 2007; 245: 341-346.
9. Nishida T, Shirao K, Sawaki A, et al. Efficacy and safety profile of imatinib mesylate (ST1571) in Japanese patients with advanced gastrointestinal stromal tumors: a phase II study (STI571B1202). Int J Clin Oncol 2008; 13: 244-251.
10. Goh BK, Chow PK, Chuah KL, Yap WM, Wong WK. Pathologic, radiologic and PET scan response of gastrointestinal stromal tumors after neoadjuvant treatment with imatinib mesylate. Eur J Surg Oncol 2006; 32: 961-963.
11. Salazar M, Barata A, André S, et al. First report of a complete pathological response of a pelvic GIST treated with imatinib as neoadjuvant therapy.Gut. 2006; 55: 585-586.
12. Suzuki S, Sasajima K, Miyamoto M, et al. Pathologic complete response confirmed by surgical resection for liver metastases of gastrointestinal stromal tumor after treatment with imatinib mesylate. World J Gastroenterol 2008; 14: 3763-3767.

Gönderilme Tarihi: 01.12.2010