

CASE REPORT

Role of Imatinib in Achieving Euglycemic State in Patient with GIST

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Abstract

Gastrointestinal stromal tumor (GIST) are rare tumors arising from Interstitial Cells of Cajal and require immunohistochemical marker c-kit (CD 117) for diagnosis. Imatinib Mesylate is an orally administered drug which competitively inhibits tyrosine kinase associated with the KIT protein. We present a rare case report highlighting role of Imatinib Mesylate in achieving euglycemic state in patient with GIST. Imatinib Mesylate is an effective form of treatment for patients with KIT (CD 117) positive unresectable and/ or metastatic malignant GIST. Proper patient selection and adequate treatment may help in achieving euglycemic state in patient with GIST.

Key Words

Stromal, Immunohistochemical, Euglycemic, Unresectable

Introduction

Stromal tumor of the gastrointestinal tract are rare neoplasms accounting for <1% of all gastrointestinal tract malignancies. Gastrointestinal stromal tumor (GIST) are thought to arise from Interstitial Cells of Cajal (ICC) of the gastrointestinal tract (1). The immunohistochemical marker 'c-Kit' (CD117) identifies these cell and seems specific diagnostic marker currently available (2). Our case highlights dramatic improvement in clinical condition of patients with GIST on Imatininb Mesylate treatment.

Case Report

A 70 year old diabetic and hypertensive male presented to surgical outpatient department with complaint of pain in right upper abdoman for last six months and marked generalized weakness. Patient gave history of operation one year back for an abdominal mass. Computed Tomography (CT) abdomen at that time revealed mass

arising from jejunum. Exploratory laparotomy was done along with resection of a 10 x 10 cm jejunal mass (Fig 1,4,5). No evidence of metastasis in liver or lymph nodes was noted. Histopathology report of resected jejunal mass was consistent with GIST (Fig 2,3). Patient had now presented with jaundice with total serum bilirubin 3 mg/dl. Patient has raised blood sugar profile (fasting blood sugar 126 mg/dl; postprandial blood sugar 175 mg/dl). Ultrasound abdomen and CT abdomen revealed target lesions suggestive of metastasis in bilateral lobes of liver. Ultrasound guided FNAC from liver lesions revealed metastatic GIST. Treatment was started with Imatinib Mesylate 400 mg daily. Patient improved significantly within one month and his appetite increased. His liver function test results came within normal limits. CT abdomen at six months and at one year follow up period

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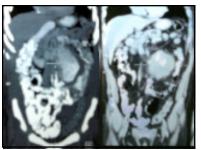


Fig. 1 CT Abdomen Showing Jejunal Mass

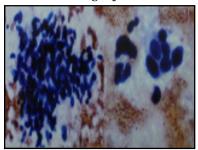


Fig. 3 FNAC from Liver Lesions Showing Metastatic GIST Lesions, 1year After Resection

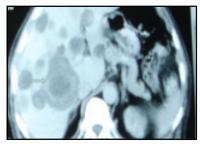


Fig. 5 CT Abdomen Showing Improvement in Radiological Findings 6 Months after Treatment with Imatinib

revealed significant improvement in radiological findings. Patient had overall good functional status at one year. Also euglycemic status was achieved without oral hypoglycemic drugs (*Graph-1*).

Discussion

GIST are rare but are nevertheless the most common mesenchymal neoplasms of the gastrointestinal tract. Mazur and Clark first introduced the term GIST in 1983 (3).

GIST are most common in stomach (60-70%) followed by the small intestine (20-30%), the colorectum (10%) and the oesophagus (1-5%) (4,5). GIST are multicentric

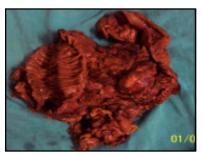


Fig.2 Image Showing Resected Jejunal Specimen

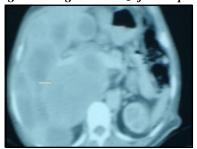
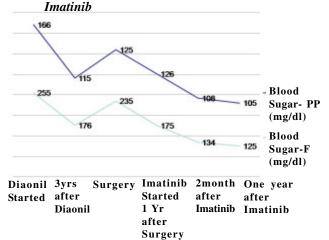


Fig. 4 CT Abdomen Showing Metastatic GIST Lesions in Liver Before Treatment with



Graph. 1 Showing Significant Improvement in Blood Sugar Levels with Imatinib Mesylate Treatment

in fewer than 5% of cases (6).Imatinib Mesylate is an orally administered competitive inhibitor of the tyrosine kinase associated with the KIT protein (stem cell factor receptor), ABL protein and platelet derived growth factor receptors. The KIT tyrosine kinase is abnormally expressed in GIST (7). Imatinib Mesylate induces a



sustained objective response in more than half of patients with an advanced unresectable or metastatic GIST (8). Overall, Imatinib Mesylate was reported to be well tolerated. The most common serious events included unspecified hemorrhage and neutropenia. Skin rash, edema and periorbital edema were the common adverse events observed (9).

Review of literature revealed only two cases for Imatinib Mesylate and diabetes control (10,11). In our case, patient presented with metastatic lesions in liver one year after operation for jejunal GIST. Patient was treated with low dose Imatinib Mesylate (400 mg daily) which was well tolerated without any side effects. Patient achieved euglycemic status without oral hypoglycemics and showed progressive improvement in radiological findings.

Conclusion

Our case highlights Imatinib Mesylate as a effective form of treatment of patients with KIT (CD 117) positive unresectable and/or metastatic malignant GIST. Patients with GIST should be diagnosed early so that they are amenable to treatment with Imatinib Mesylate. Our case is in agreement with previous studies which highlight adjunctive role of Imatinib Mesylate with other forms of treatment.

References

- Wang L, Vargas H, French SW. Cellular origin of gastrointestinal stromal tumor: a study of 27 cases. Arch Pathol Lab Med 2000; 124: 1471-75.
- Miettinen M, Lasota J. Gastrointestinal stromal tumor -Definition, clinical, histological, immunohistochemical and molecular genetic features and differential diagnosis. Virchows Arch 2001; 438(1): 1-12.
- 3. Licht J, Weissmann L, Antmann K. Gastrointestinal sarcomas. *Surg Oncol* 1988; 15: 181-88.
- Plaat BE, Hollema H, Molenoar WM, et al. Soft tissue leiomyosarcoma and malignant gastrointestinal stromal tumors: differences in clinical outcome and expression of multidrug resistance proteins. J Clin Oncol 2000; 18(18): 3211-20.
- Pidhorecky I, Cheney RT, Kraybill WG, Gibbs JF. Gastrointestinal stromal tumors: Current diagnosis, biologic behavior, and management. Ann Surg Oncol 2000; 7(9): 705-12.
- Nishida T, Hirota S. Biological and clinical review of stromal tumors in the gastrointestinal tract. *Histol Histopathol* 2000 ; 15(4): 1293-301.
- Croom KF, Perry CM. Imatinib Mesylate in the treatment of gastrointestinal stromal tumors. *Drugs* 2003; 63(5): 513-24.
- 8. Demetri GD, von Mehren M, Blanke CD, Van den Abbeele AD, *et al*. Efficacy and safety of Imatinib Mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 2002; 347(7): 472-80.
- 9. Wilson J, Connock M, Song F, Yao G, et al. Imatinib for the treatment of patients with unresectable and/or metastatic gastrointestinal stromal tumors: systemic review and economic evaluation. Health Tech Assess 2005; 9(25): 1-142.
- 10. Venri D, Franchins M, Bonora E. Imatinib and regression of type II diabetes. *N Eng J Med* 2005; 352: 1049-50.
- Breccia M, Averssa I. Improved glucose control and Imatinib in CML. Journal of Clinical Oncology 2004; 22(22): 4653-55.