Gastrointestinal Bleeding in Tetralogy of Fallot

Nitin Mahajan, Ashok Kondur, Luis Afonso

Abstract

This article reports an uncommon cause of gastrointestinal bleeding in a young male with uncorrected Tetralogy of Fallot (TOF). This is the first reported instance of gastrointestinal stromal tumor (GIST) causing bleeding in a patient with uncorrected TOF. A 32-year-old Caucasian male with severe developmental delay and uncorrected TOF presented with black tarry stools. On admission, the patient was hypotensive and tachycardic. He was successfully resuscitated with fluids and blood transfusion. Upper gastrointestinal endoscopy was performed and biopsy revealed GIST. It is interesting to note that the patient survived till this age without any medical or surgical treatment. This case presents GIST as a cause of gastrointestinal bleeding in uncorrected TOF. Cytogenetic analysis revealed deletion of short arm of chromosome 18. This case illustrates that tyrosine kinase inhibitor may be an acceptable alternative therapy to surgical resection.

Keywords: Fallot's Tetralogy; Gastrointestinal Stromal Neoplasms; Gastrointestinal Hemorrhages; Cytogenetic Analysis; Biological Tumor Marker; Gastrointestinal Endoscopy; Computed Tomography Scan; Protein Kinase Inhibitors.

Received: 10 March 2008
Accepted: 15 May 2008
From the Department of Internal Medicine, Wayne State University, Detroit, USA
Address correspondence and reprint requests to: Dr. Nitin Mahajan, Department of Internal Medicine, Wayne State University, University Health Center-5C, 4201 St Antoine, Detroit, MI 48201, United States of America
E-mail: nitin9696@yahoo.com

Introduction

Uncorrected Tetralogy of fallot is an uncommon entity. For unoperated patients, only 6% are alive at 30 years.[1] The data on gastrointestinal bleeding in patients with cyanotic heart disease is sparse. There have been cases reporting gastric varices secondary to splenic vein thrombosis,[2] esophageal varices secondary to anomalous right pulmonary artery[3] and early onset gastric adenocarcinoma[4] as the cause of gastrointestinal bleeding in such patients. This is the first reported instance of gastrointestinal bleeding as a consequence of gastrointestinal stromal tumors (GIST) in a patient with uncorrected TOF.

Case Presentation

A 32-year-old Caucasian male with severe developmental delay, hypothyroidism, and uncorrected Tetralogy of Fallot, presented with lethargy and black tarry stool. He had shortness of breath on exertion since childhood, which was relieved on squatting. The patient experienced 3-4 "tet spells" every year on an average that resolved with oxygen administration.

On admission, he was hypotensive (Blood Pressure-80/60 mmHg) and tachycardic (heart rate-106/minute). Physical examination revealed *microcephaly, scoliosis, and an ejection systolic murmur of 4/6 at lower left sternal border on examination. Abdominal examination revealed a palpable firm mass (8*6 cm^2) in the epigastric region.* He was initially resuscitated with fluids and packed red cells.

Two-dimensional echocardiography showed mild diastolic biventricular dysfunction, a 70mm Hg systolic gradient across right ventricular outflow tract and a large ventricular septal defect. Computed tomography of abdomen showed a smooth, well defined intramural gastric mass (8*6*2cm^3) with homogeneous attenuation straddling the posterior gastric wall. There was no evidence of any metastatic spread on computed tomography of chest, abdomen and pelvis. Upper gastrointestinal endoscopy revealed an ulcerated

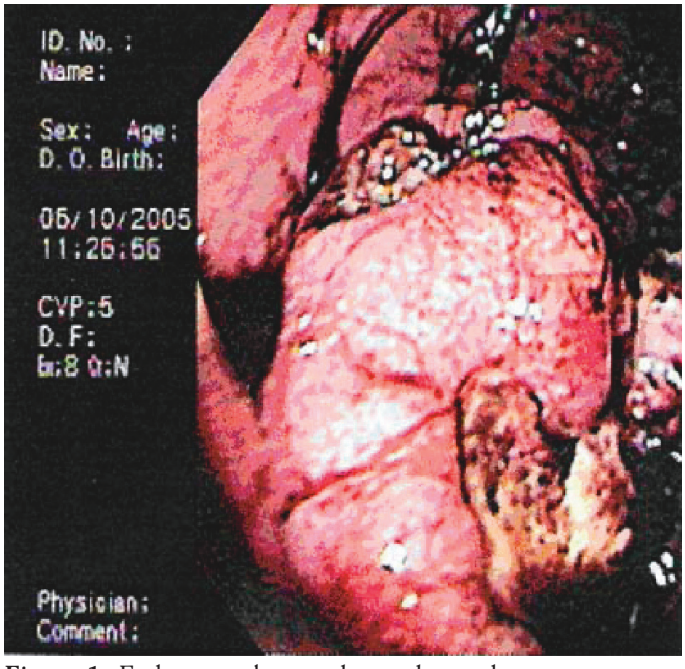

Figure 1: Endoscopy shows a large ulcerated mass on greater curvature of stomach with adjacent blood.

gastric mass (Figure 1). The gastrointestinal bleeding was self limited, and did not require any endoscopic hemostasis. The gastric mass biopsy was consistent with gastrointestinal stromal tumor (Figure 2). On immunostaining, the tumor was positive for CD-117 (C-kit) and CD-34, and negative for the smooth muscle markers actin and desmin and the neuronal marker, S-100 protein. Cytogenetic analysis revealed deletion of short arm of chromosome 18. The patient's family refused surgical resection and he was treated with imatinib mesylate (tyrosine kinase inhibitor).

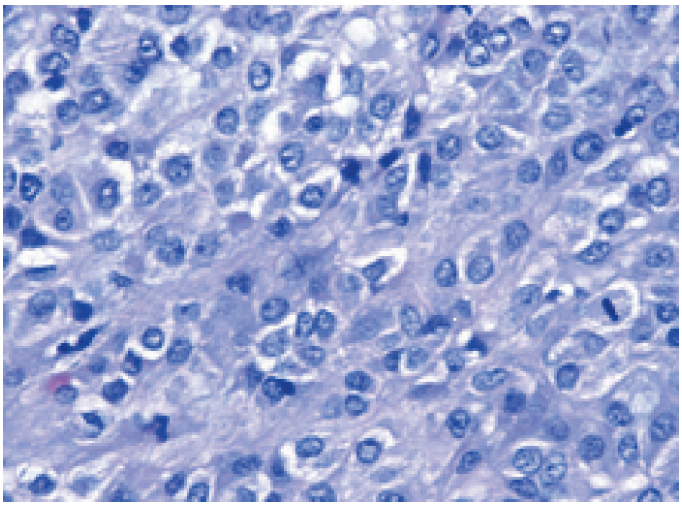

Figure 2: Shows epithelioid cells having round central nuclei within eosinophilic or clear cytoplasm.

Tetralogy of Fallot is the most common cyanotic congenital heart disease in adults and children after the age of 4 years. For unoperated patients, 11% are alive at 20 years, 6% at 30 years, and 3% at 40 years.[1]

The data on gastrointestinal bleeding in patients with cyanotic heart disease is sparse. These patients are prone to bleeding as a consequence of erythrocytosis, shortened platelet survival and clotting factor deficiencies. Prior published case-reports have reported gastric varices secondary to splenic vein thrombosis (resulting from increased blood viscosity due to polycythemia),[2] esophageal varices secondary to anomalous right pulmonary artery[3] and early onset gastric adenocarcinoma[4] as the cause of gastrointestinal bleeding in patients with TOF. This is the first reported instance of gastrointestinal bleeding as a consequence of gastrointestinal stromal tumors (GIST) in a patient with uncorrected TOF.

GISTs are rare. They constitute only 1 percent of primary gastrointestinal cancers and only a few microscopic tumors grow into masses with malignant potential. GIST is the most common subset of mesenchymal tumors specific for the alimentary tract. The interstitial cells of Cajal or more primitive progenitor mesenchymal cells are suggested as their cells of origin. The mean age of presentation is in the 6th decade. It usually presents as a solitary mass. The cellular morphology of GIST is variable and includes spindle-shaped and epithelioid cells. The cells may show juxtanuclear cytoplasmic vacuoles and nuclear palisading. Diagnostic markers include CD 34, desmin, vimentin, smooth muscle actin and CD 117. The management of these patients involves risk assessment for recurrence or metastasis. Tumors that are larger than 5cm, are lobulated, enhance heterogeneously, have mesenteric fat infiltration, ulceration, regional lymphadenopathy or an exophytic growth pattern or have >5 mitotic rate per 50 high power field are associated with a significant risk of metastasis or recurrence.[5,6] The mitotic index is the most useful histologic criterion for malignancy and prognosis. GISTs frequently metastasize to the liver, and rarely to regional lymph nodes. All GISTs ≥2 cm in size are managed with surgical resection.

This patient was managed conservatively with imatinib mesylate after the histologic confirmation of GIST. No recurrent gastrointestinal bleeds have been reported on 2 years follow-up.

Conclusion

It is also interesting to note that the patient survived till this age without any medical or surgical treatment. This case presents GIST as a cause of gastrointestinal bleeding in uncorrected TOF. It is possible that deletion of short arm of chromosome 18 is common to both TOF and GIST. This patient was managed conservatively, and continues to do well. It illustrates that tyrosine kinase inhibitor may be an acceptable alternative therapy to surgical resection.[7]

References

1. Bertranou EG, Blackstone EH, Hazelrig JB, Turner ME, Kirklin JW. Life expectancy without surgery in tetralogy of Fallot. Am J Cardiol 1978 Sep;42(3):458-466.
2. Kejariwal D, Sarkar N, Roy S, Bhattacharya M. Fallot's tetralogy presenting with variceal bleed. J Postgrad Med 2001 Jul-Sep;47(3):194-195.
3. Miller TL, Lang P, Liberthson R, Grillo HC, Israel EJ. Upper gastrointestinal hemorrhage as a late complication of congenital heart disease. J Pediatr Gastroenterol Nutr 1996 Nov;23(4):452-456.
4. Dellavecchia C, Guala A, Olivieri C, Haintink O, Cadario F, Luinetti O, et al. Early onset of gastric carcinoma and constitutional deletion of 18p. Cancer Genet Cytogenet 1999 Aug;113(1):96-99.
5. Huang HY, Li CF, Huang WW, Hu TH, Lin CN, Uen YH, et al. A modification of NIH consensus criteria to better distinguish the highly lethal subset of primary localized gastrointestinal stromal tumors: a subdivision of the original high-risk group on the basis of outcome. Surgery 2007 Jun;141(6):748-756.
6. Ghanem N, Altehoefer C, Furtwängler A, Winterer J, Schäfer O, Springer O, et al. Computed tomography in gastrointestinal stromal tumors. Eur Radiol 2003 Jul;13(7):1669-1678.
7. Katz D, Segal A, Alberton Y, Jurim O, Reissman P, Catane R, et al. Neoadjuvant imatinib for unresectable gastrointestinal stromal tumor. Anticancer Drugs 2004 Jul;15(6):599-602.