

## CASE REPORT

# Imatinib-induced gastric antral vascular ectasia in a patient with chronic myeloid leukemia

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We have received word of another patient, an 80-year-old woman, with CML on imatinib who has been diagnosed with GAVE.

## Introduction

Gastrointestinal intolerance defines well-known adverse effects of imatinib, most commonly nausea, vomiting, and/or diarrhea. Gastric antral vascular ectasia (GAVE) has been reported very rarely in imatinib-treated gastrointestinal stromal tumor (GIST) and scleroderma patients treated with imatinib for pulmonary hypertension. We report here a case of GAVE in a chronic myeloid leukemia (CML) patient after treatment with imatinib. To our knowledge, this is the first report in imatinib-treated CML.

Tyrosine kinase inhibitors, first-in-class imatinib mesylate, have revolutionized the treatment of CML. Imatinib has been approved worldwide for more than a decade for the therapy of CML, Philadelphia chromosome (Ph)-positive acute lymphoblastic leukemia, myelodysplastic/myeloproliferative neoplasm associated with PDGFR gene rearrangement, aggressive systemic mastocytosis with D816V mutation, hypereosinophilic syndrome, and chronic eosinophilic leukemia as well as unresectable KIT-positive

## Key Clinical Message

Gastric antral vascular ectasia (GAVE) has been reported very rarely in imatinib-treated gastrointestinal stromal tumor (GIST) and scleroderma/pulmonary hypertension patients. We present the first report of a case of GAVE in a chronic myeloid leukemia (CML) patient after treatment with imatinib. This diagnosis should be considered in CML patients with upper gastrointestinal symptoms and anemia.

## Keywords

GAVE, Gastric antral vascular ectasia, chronic myeloid leukemia, imatinib.

GIST. Side effects of imatinib are well described and manageable [1, 2].

Experimental non-hematological uses of imatinib include the treatment of pulmonary hypertension. Imatinib reduces smooth muscle hypertrophy and hyperplasia of the pulmonary vasculature in a variety of disease processes, including portopulmonary hypertension [3]. Imatinib's potential to slow pulmonary fibrosis has been tested in systemic sclerosis patients [4].

Imatinib is usually well tolerated but occasionally very significant side effects can be seen. GAVE is an extremely rare adverse reaction, the mechanism of which remains unclear. That has been reported in imatinib therapy of a GIST patient [5] as well as patients undergoing imatinib therapy for systemic sclerosis[6].

## Case Presentation

In February 2002, this 57-year-old woman presented with leukocytosis. Work-up confirmed the diagnosis of chronic

phase Ph-positive CML in May 2002, and imatinib therapy (400 mg once daily) was initiated. After 18-month treatment, she achieved complete molecular response (CMR, now confirmed MR4.5, IS 0.0032%).

In December 2006, her hemoglobin (Hb) dropped to 96 g/L, and her mean corpuscular volume (MCV) was 97.4 femtoliter. Blood work revealed deficiencies in iron and Vitamin B12. She underwent work-up for a source of bleeding. Upper GI endoscopy revealed GAVE, treated with local cauterization. She was treated with iron supplement, B12, and a proton pump inhibitor.

Despite treatment, she had several intermittent recurrent incidents of active GI bleeding, requiring cauterization and blood transfusion. With the thought of etiology of the GAVE, imatinib was stopped in February 2012. She has since had no active GI bleeding, no further local therapy, and no requirement for transfusion. Her Hb improved to 122 g/L, MCV was normal, and she remains with undetectable bcr-abl now 19 months after stopping imatinib and with no other therapy initiated.

## Discussion

GAVE is a rare but significant cause of GI bleeding. It is usually associated with such systemic illnesses as cirrhosis, autoimmune disorders, and chronic kidney diseases [7]. Our patient developed imatinib-induced GAVE – to our knowledge, the first reported case in a CML patient.

GAVE can present as mild anemia due to chronic blood loss, or in the more severe form, as acute GI bleeding, requiring blood transfusion [7]. Imatinib's mechanism of inducing GAVE in CML patients is not clear. In GIST patients, the known complication of GI bleeding is attributed to imatinib-induced tumor necrosis [2].

Imatinib-induced GAVE has been reported in one GIST patient [5]. Eight months after imatinib therapy (400 mg/day) was initiated, the patient developed severe anemia, with Hb of 59 g/L suggesting acute and severe GI bleeding. Esophagogastroduodenoscopy (EGD) revealed GAVE. Imatinib was withheld, and the patient was started on a proton pump inhibitor. One month later, EGD showed significant improvement in the stomach's erythema with resolution of GAVE, indicating that it was likely imatinib-induced, although an alternate unknown etiology that responded to the PPI could not be ruled out. The patient was not rechallenged.

GAVE was also reported during a 1-year, Phase I/IIa, open-label pilot study of imatinib for a non-malignant condition [6]. Twenty systemic sclerosis patients with associated interstitial lung disease were treated with imatinib (up to 600 mg/day). Three patients suffered

marked anemia, fatigue, muscle weakness, and GAVE. In this instance, GAVE cannot confidently be attributed to imatinib, as the condition may be associated with autoimmune disease.

In the case we report here, GAVE did not resolve despite PPI therapy and local cauterization over several years, until imatinib was stopped, suggesting with a little more confidence that it was involved in the etiology.

## Conclusion

Imatinib-induced GAVE is a rare but significant cause of GI blood loss and anemia, which may be acute or chronic. Although our patient was treated several times endoscopically, which is the treatment of choice [7], she continued to have low Hb and GI bleeding until imatinib was stopped. This confirms a direct cause-and-effect relationship between imatinib and GAVE.

## Conflict of Interest

None declared.

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