Case Report

Mesenteric infarction due to iatrogenic polycythemia

Katrina Skoog, Marie Carmelle-Elie, Kevin Ferguson

University of Florida School of Medicine, Gainesville, FL, USA

Corresponding Author: *Katrina Skoog, Email: katrinaskoog@ufl.edu*

BACKGROUND: Polycythemia vera is defined as a chronic myeloproliferative disorder characterized by increased red blood cell count. There have been no reports on mesenteric thrombosis resulting from iatrogenic polycythemia.

METHODS: We present a patient with a history of non-small cell lung cancer undergoing maintenance oral chemotherapy on tarceva and adjunctive use of procrit. The patient presented to our emergency department with an acute abdomen and was found to have ischemic bowel from unmonitored procrit, which lead to hyperviscosity of blood and mesenteric infarction.

RESULTS: The patient remained intubated with ventilator support. He refused a tracheostomy. He continued on feeding through the J port of the nasojejunal tube. His white cell count, and hematocrit and creatinine levels remained normal. Procrit use and chemotherapy were not restarted. He was transferred to a subacute nursing facility for further treatment.

CONCLUSIONS: Procrit and other erythropoiesis stimulating drugs can cause significant morbidity and mortality with an increased risk of cardiovascular events, gastrointestinal bleeding, thromboembolism and stroke. This case report suggests that without closely monitoring hematocrit levels, epoetin may also be associated with an increased risk of mesenteric infarction.

KEY WORDS: Mesenteric infarction; Iatrogenic polycythemia

World J Emerg Med 2013;4(3):232–234
DOI: 10.5847/ wjem.j.issn.1920–8642.2013.03.014

INTRODUCTION

Polycythemia vera is defined as a chronic myeloproliferative disorder characterized by increased red blood cell count. Secondary polycythemia is caused by adaptation to high altitude, chronic pulmonary disease and iatrogenic causes such as the use of erythropoiesis-stimulating agents. Polycythemia vera should be suspected in patients with elevated hematocrit levels >55%, splenomegaly, or portal venous thrombosis.[1]

Symptoms are related to hyperviscosity, sludging of blood flow, and venous and arterial thromboses. The resultant hyperviscosity of blood impairs microcirculation, and hence predisposes patients to thrombosis. The literature showed that the thrombotic complications from polycythemia vera related to a myeloproliferative disorder are different from those related to iatrogenic polycythemia from erythropoiesis-stimulating agents such as procrit. Both types of polycythemia cause thrombotic complications including cerebrovascular events, myocardial infarctions, deep vein thrombosis, and pulmonary emboli. However, the only reports of portal, splenic or mesenteric vein or arterial thrombosis were from polycythemia vera.[2] There have been no reports on mesenteric thrombosis resulting from iatrogenic polycythemia. This report is the first case of mesenteric infarction due to iatrogenic polycythemia in the literature.[3–13]

CASE REPORT

A 50-year-old man with a history of stage IV non-small cell lung cancer undergoing maintenance oral chemotherapy on tarceva and adjunctive use of procrit (epoetin alfa) 10 000 units subcutaneously MWF presented to our Emergency Department with respiratory distress, coffee ground emesis and an acute surgical abdomen. The patient was diagnosed with non-small cell lung cancer 7 months ago and had completed 11-week treatment with paclitaxel/carboplatin four months

ago. He was transferred to our hospital from an outside facility together with records of routine complete blood counts. His CBC was checked on December 5, 2011 and H/H at that time was 19/58.6, and it trended up to 23/66 on December 11, 2011. The patient denied a history of any hematologic diagnosis. He reported erythema of the bilateral upper extremities and hands. He denied a history of gastrointestinal bleeding, peptic ulcer disease, alcohol use, or heavy non-steroidal anti-inflammatory use. On arrival to the Emergency Department, the initial vital signs of the patient were: temperature 37 degrees celsius, pulse 140 beats per minute, respiratory rate 28, oxygen saturation 98% on 2 liters nasal cannula, and blood pressure 80/55 mmHg. His airway was patent with clear bilateral breath sounds. On cardiac examination, the patient had a fast heart rate with a regular rhythm. His abdomen was firm, diffusely tender with peritoneal signs. His rectal examination revealed bright red blood per rectum. His upper extremities were erythematous. He vomited a large amount of dark, coffee ground emesis which was tested hem-occult positive.

Initial I-stat chem 8 revealed a hemoglobin level that was "unable to calculate" and a hematocrit level >75%. One hour later CBC revealed WBC 10.5, RBC 7.48, HGB/HCT 24.0/77.9, PLT 184, and bandemia 22%. Basic metabolic panel was normal except for a bicarbonate level of 13. Initial lactate level was 6.77. Repeat CBC revealed HGB/HCT 23.5/70.5, and PLT 55. The repeat lactate level one hour after the initial was 9.5. ABG revealed a metabolic acidosis with pH 7.29, pCO_2 18, HCO_3 9. Further review of his records revealed that the hemoglobin/hematocrit level had been on the rise in the past several weeks, with no intervention and continued use of procrit. A CBC drawn before one week revealed a hemoglobin/hematocrit level of 19/58.6.

CT scan revealed diffuse dilatation of the esophagus, stomach, small bowel and large bowel (Figures 1 and 2). General surgery was simultaneously consulted for the acute abdomen. Hematology was also considered, and suspected iatrogenic rise in H/H was secondary to the unmonitored use of procrit. Surgical consultation was also recommended for bowel ischemia due to hyperviscosity from the elevated hematocrit level and/or venous thrombosis. The patient was taken to the operation room emergently for suspicion of ischemic gut because of elevated lactate levels with an acute abdomen. Exploratory laparotomy showed that he had a significant amount of necrotic bowel from the sigmoid to the ileum. The operation included an enterectomy and subtotal colectomy. The operative team also suspected the source to be secondary to hyperviscosity and/or mesenteric thrombosis. He was taken to the ICU post-operatively.

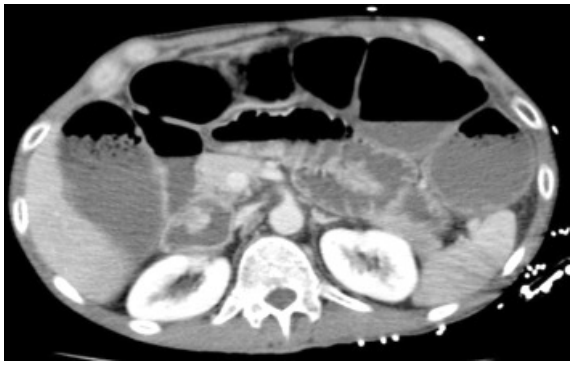

Figure 1. Upper abdomen with diffuse dilatation of the esophagus, stomach and small bowel.

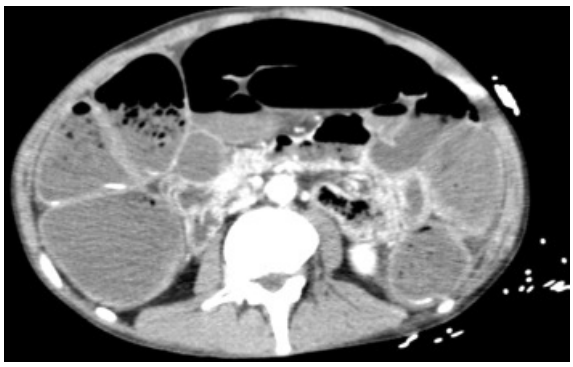

Figure 2. Lower abdomen with diffuse dilatation of the large bowel.

He was initially weaned from the ventilator and extubated 3 days later, but had to be re-intubated for respiratory distress after suspected aspiration. He remained intubated with ventilator support. He refused a tracheostomy. He received continuously feeding through the J port of the nasojejunal tube. His white cell count, and hematocrit and creatinine levels remained normal. Procrit use and chemotherapy were not restarted. He was transferred to a subacute nursing facility for further treatment.

DISCUSSION

To our knowledge, there have been no reports on the occurrence of mesenteric ischemia due to iatrogenic polycythemia after the use of procrit. We searched Pub Med, CINAHL, Cochrane Central, MEDLINE, and Web of Science databases (key words: erythropoietin, procrit, mesenteric ischemia), and the public website of the US Food and Drug Administration. The possible adverse effects of erythropoiesis stimulators such as procrit are well known to induce thromboembolism if not closely monitored. Several studies have shown the link between epoetin use and thromboembolism. A prospective,

randomized, placebo-controlled trial with 1 460 patients found that as compared with placebo, epoetin alfa was associated with a significant increase in the incidence of thrombotic events (hazard ratio, 1.41; 95% *CI*, 1.06 to 1.86).[3] A meta-analysis review showed the results of trials evaluating ESAs (erythrocyte stimulating agents) for the treatment of anemia in the oncology setting. This review analyzed 51 clinical trials with 13 611 patients and concluded that erythropoiesis-stimulating agent administration to patients with cancer is associated with increased risks of venous thromboembolism (VTE) and mortality. The group found a 1.57-fold increase of VTE risk.[4] However, neither of these studies found mesenteric thrombosis as a potential thrombotic complication, as we found in our patient.

An updated systematic review of 57 trials and 9 353 cancer patients from articles, abstracts, and reports published in the Cochrane Library, MEDLINE and EMBASE between 1985 and 2005 on the effects of epoetin alfa for prophylaxis or treatment of anemia in cancer patients with or without concurrent antineoplastic therapy found that treatment with epoetin increased the risk of thrombo-embolic events (*RR*=1.67, 95% *CI*=1.35 to 2.06; 35 trials and 6 769 patients). A meta-analysis found that of 6 769 patients in 35 trials, thrombo-embolic events (such as transient ischemic attacks, stroke, pulmonary emboli, deep vein thrombosis, and myocardial infarction) were observed in 229 of the 3 728 patients treated with epoetin or darbepoetin. Within this, the relative risk of a thrombo-embolic event was increased by 67% in the treated group compared with the control group (*RR*=1.67, 95% *CI*=1.35 to 2.06).[5] However, similar to the aforementioned articles, there were no findings of mesenteric thrombosis as a thrombotic complication of erythropoiesis-stimulating drugs.[3–13]

Subsequent to this review, in 2007 the FDA issued a public health advisory entailing that patients taking erythropoiesis stimulating agents had a higher chance of death and an increased number of thromboses, strokes, and myocardial infarctions when erythropoiesis stimulating agents were given to maintain hemoglobin levels of more than 12 g/Dl.[6] Our patient had a hemoglobin value ranging from 19–24, therefore placing him at a higher risk of thrombo-embolic complications.

In conclusion, procrit and other erythropoiesis stimulating drugs, while intended for the treatment of anemia due to the effect of concomitantly administered chemotherapy, can cause significant morbidity and mortality with an increased risk of cardiovascular events, gastrointestinal bleeding, thromboembolism and stroke. This case report suggests that without closely monitoring hematocrit levels, epoetin may also be associated with an increased risk of mesenteric infarction.

Funding: None.

Ethical approval: The present study was approved by the Ethical Committee of University of Florida School of Medicine, Gainesville, FL, USA.

Conflicts of interest: The authors have no competing interests relevant to the present study.

Contributors: Skoog K proposed and wrote the paper. All authors contributed to editing the final manuscript for content and style.

REFERENCES

1 Berlin NI. Diagnosis and classification of the polycythemias. Semin Hematol 1975; 12: 339–351.
2 Chait Y, Condat B, Cazals-Hatem D, Rufat P, Atmani S, Chaoui D, et al. Relevance of the criteria commonly used to diagnose myeloproliferative disorder in patients with splanchnic vein thrombosis. Br J Haematol 2005; 129: 553–560.
3 Corwin HL, Gettinger A, Fabian TC, May A, Pearl RG, Heard S, et al. Efficacy and safety of epoetin alfa in critically ill patients. N Engl J Med 2007; 357: 965–976.
4 Bennett CL, Silver SM, Djulbegovic B, Samaras AT, Blau CA, Gleason KJ, et al. Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia. JAMA 2008; 299: 914–924.
5 Bohlius J, Wilson J, Seidenfeld J, Piper M, Schwarzer G, Sandercock J, et al. Recombinant human erythropoietins and cancer patients: Updated meta-analysis of 57 studies including 9353 patients. J Natl Cancer Inst 2006; 98: 708–714.
6 Richard K. FDA: Public Health Advisory: erythropoiesis-stimulating agents (ESAs). March 2007.
7 Hershman DL, Buono DL, Malin J, McBride R, Tsai WY, Neugut AI. Patterns of use and risks associated with erythropoiesis-stimulating agents among medicare patients with cancer. J Natl Cancer Inst 2009; 101: 1633–1641.
8 Dicato M. Venous thromboembolic events and erythropoiesis-stimulating agents: an update. Oncologist 2008; 13: S11–15.
9 Juneja V, Keegan P, Gootenberg JE, Rothmann MD, Shen YL, Lee KY, et al. Continuing reassessment of the risks of erythropoiesis-stimulating agents in patients with cancer. Clin Cancer Res 2008; 14: 3242–3247.
10 Favaloro EJ, Lippi G, Franchini M. Coagulopathies and thrombosis: usual and unusual causes and associations, part III. Semin Thromb Hemost 2010; 36: 1–5. Epub 2010 Apr 13.
11 Melosky BL. Erythropoiesis-stimulating agents: benefits and risks in supportive care of cancer. Curr Oncol 2008; 15: S10–15.
12 Kang J, Gong P, Ren YB, Gao DN, Ding QL. Effect of β-sodium aescinate on hypoxia-inducible factor-1α expression in rat brain cortex after cardiopulmonary resuscitation. World J Emerg Med 2013; 4: 63–68.
13 Wright JR, Ung YC, Julian JA, Pritchard KI, Whelan TJ, Smith C, et al. Randomized, double-blind, placebo-controlled trial of erythropoietin in non-small-cell lung cancer with disease-related anemia. J Clin Oncol 2007; 25: 1027–1032. Epub 2007 Feb 20.

Received January 20, 2013
Accepted after revision June 1, 2013