

## Severe Thrombotic Complication of Eltrombopag in a Cirrhotic Patient

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### Abstract

We present a patient with hepatitis C virus (HCV) and cirrhosis who was treated with eltrombopag for idiopathic thrombocytopenic purpura and was incidentally found to have a right atrial thrombus with extension into the left internal jugular vein. Eltrombopag was discontinued and the patient was treated with thrombectomy and anticoagulation. Given the proposed use of eltrombopag in HCV-associated thrombocytopenia, we advise caution when treating cirrhotics who are at higher intrinsic risk of thrombosis.

### Introduction

The incidence of chronic idiopathic thrombocytopenic purpura (ITP) in hepatitis C virus (HCV) is estimated to be very low.<sup>1</sup> Eltrombopag, a thrombopoietin receptor agonist, is FDA approved to treat thrombocytopenia in chronic ITP and in HCV patients, so that interferon-based therapy may be initiated and maintained.<sup>2</sup>

### Case Report

A 52-year-old woman with chronic HCV and chronic ITP stable on eltrombopag presented with decompensated liver disease. She had failed to complete interferon-based therapy due to thrombocytopenia and subsequently developed cirrhosis and portal hypertension. Initial abdominal/pelvic computed tomography (CT) scan incidentally found a 2.75 x 2.46 cm right atrial thrombus. Chest CT revealed extension of the thrombus to the superior vena cava, brachiocephalic, left subclavian, and left internal jugular vein (Figure 1).

She had no prior history of thromboembolic events or identifiable thrombotic risk factors other than 3 years of intermittent eltrombopag use due to bleeding and platelet counts lower than 30,000/mm<sup>3</sup>. At eltrombopag initiation, giant platelets on peripheral blood smear consistent with ITP were noted, but no portal hypertension or hepatosplenomegaly. Her platelet count on current admission was 81,000/mm<sup>3</sup>, and this strong platelet response to eltrombopag supported an autoimmune origin over bone marrow dysfunction or sequestration.

Eltrombopag was discontinued and the patient underwent cardiothoracic surgery to remove the thrombus in the right atrium and some of its extension into the superior vena cava. Intravenous heparin therapy and warfarin was started immediately following surgery. Follow-up imaging showed improved vascular patency. Prior surveillance imaging with ultrasound revealed no evidence for hepatocellular carcinoma. The patient tested negative for anti-B2-glycoprotein and lupus anticoagulant; further hypercoagulable work-up could not be performed due to cirrhosis and anticoagulation use.

ACG Case Rep J 2016;3(2):121-123. doi:10.14309/crj.2016.20. Published online: January 20, 2016.

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**Figure 1.** Imaging of an extensive eltrombopag-induced thrombus extending from the right atria to left internal jugular vein. Chest CT demonstrated a right atrial thrombus extending into the (A) superior vena cava (arrow), brachiocephalic vein (arrowhead), and (B) left internal jugular vein (arrow).

## Discussion

Thromboembolic events are reported to occur in 2-5% of noncirrhotic patients receiving eltrombopag.<sup>3,4</sup> The safety in cirrhotic patients is less clear. An initial study in cirrhosis was discontinued due to higher rates of thrombotic events; however, a more recent study found the risk to be similar to that of noncirrhotic patients.<sup>5,6</sup> This may reflect the complex coagulation system in cirrhosis, in which antithrombin III and protein C promote coagulation simultaneously as factor VIII and von Willebrand factor deficiencies prevent coagulation; hemorrhage or thrombosis can result.<sup>7</sup> Further studies are needed to understand the mechanism behind eltrombopag's effect on this delicately balanced coagulation system. Elevation of platelet counts are one consideration, and one study showed increased thrombotic risk with platelet counts equal or greater than 200,000/mm<sup>3</sup>.<sup>5</sup>

Atrial thrombus has occurred in cirrhotic patients, usually in the setting of hepatocellular carcinoma, which likely shifts the tenuous coagulation balance toward thrombosis.<sup>8,9</sup> Our patient did not have evidence of liver nodules or masses on ultrasound or CT. We hypothesize that our patient's extensive clot with atypical location was caused by the procoagulant effects of eltrombopag. Prior to using eltrombopag in cirrhosis, the potential benefits must be weighed against the risks of thrombosis. While no evidence-based guidelines exist, it may be advisable to screen for portal vein patency with imaging prior to initiating therapy. Additionally, maintenance of platelet counts between 50,000/mm<sup>3</sup> (a count adequate for hemosta-

sis) and 150,000/mm<sup>3</sup> (a count above which there is increased thrombotic risk) is advisable according to expert consensus.

## Disclosures

Author contributions: All authors approved the final manuscript. AJ Baumann performed the literature review, drafted the manuscript, and is the article guarantor. DS Wheeler contributed to the literature review and drafting of the manuscript. G. Varadi and E. Feyssa critically revised the manuscript for important intellectual content.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Previous Presentation: This case was presented as a poster at a the American College of Physicians Regional Conference; October 2013; Philadelphia, Pennsylvania.

Received April 21, 2015; Accepted November 16, 2015

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