

# Coronary Dissection in a Patient with Essential Thrombocytosis

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## ABSTRACT

A 50-year-old man was admitted to the hospital with left shoulder and arm discomfort. He had no recent history of change in his energy level, limitations to activity, exertional chest pain, or shortness of breath. He had cardiac risk factors, including a strong family history of premature coronary artery disease and dyslipidemia. He had a syncopal episode in 2003 with a positive troponin I, but had a negative cardiac workup, including cardiac catheterization that showed luminal irregularities and no significant coronary artery disease. An echocardiogram was performed to rule out potential cardiac causes for shoulder pain and showed regional wall motion abnormalities. Follow-up cardiac catheterization revealed left anterior descending artery proximal and mid dissection and a long area of dissection in the first diagonal branch. Laboratory evaluation showed significant platelet elevation and positive *JAK2* study. Ultrasound of the abdomen revealed moderate splenomegaly. The enlarged spleen, positive *JAK2* study, and persistently elevated platelet count confirmed the diagnosis of essential thrombocythemia. Essential thrombocythemia can predispose individuals to vascular dysfunction and damage, which may contribute to coronary artery dissection. With this case, we propose that essential thrombocythemia should be excluded in the presence of coronary dissection and thrombocytosis.

## INTRODUCTION

Coronary dissection is a rare, potentially fatal condition that usually affects women.<sup>1</sup> The etiology of spontaneous coronary dissection (SCD) is unknown, but reports suggest a potential association with certain myeloproliferative disorders, such as polycythemia vera.<sup>2</sup> We report a case of coronary dissection of the left anterior descending artery and first diagonal branch in a male patient with essential thrombocythemia. This is the first report demonstrating an association between essential thrombocythemia and SCD. The patient was treated conservatively and continues to be asymptomatic.

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## CASE PRESENTATION

A 50-year-old man was admitted to the hospital with left shoulder and arm discomfort in 2013. The discomfort was not associated with any chest pain or shortness of breath. The pain was worse in the elbow area, and he had tenderness to palpation in the posterior shoulder. The pain showed no sign of improvement over a period of 3 days, and the patient was admitted to rule out acute coronary syndrome. He had no recent history of change in his energy level, limitations to activity, exertional chest pain, or shortness of breath.

The patient had cardiac risk factors, including a strong family history of premature coronary artery disease and dyslipidemia. No other familial risk factors for

acute coronary syndrome were noted. He did not smoke and denied any history of hypertension or diabetes. The patient had no history of drug abuse and reported medications included only naproxen, multivitamin, omeprazole, and *Lactobacillus* supplements. Of note, he had a syncopal episode in 2003 with a positive troponin I, but had a negative cardiac workup, including cardiac catheterization that showed luminal irregularities and no significant coronary artery disease.

Upon admission, the patient's troponin I was negative. An electrocardiogram revealed poor anterior R-wave progression. An echocardiogram showed mildly decreased global left ventricular systolic function with an ejection fraction of 40% with akinetic apex and hypokinetic apical septal, apical lateral, apical anterior, and apical inferior segments. Baseline regional wall motion abnormalities indicated cardiac catheterization rather than stress echocardiogram.

Cardiac catheterization showed a normal left main artery, but the left anterior descending artery had ostial and very complex proximal and mid dissection with the appearance of multiple lumens (Figure). A large first diagonal branch also had a long area of dissection. The circumflex artery was free of significant

disease. The dominant right coronary artery provided collaterals to the distal left anterior descending. No significant lesions were noted in the right coronary artery. Left ventriculography revealed apical akinesia with low normal to mildly decreased overall left ventricular function. Left ventricular end-diastolic pressure was 15 mmHg.

Cardiothoracic surgery was consulted to evaluate for coronary artery bypass graft surgery. However, it was felt that the angiographic findings were chronic, and that the patient would not benefit from bypass grafting. Therefore, he was treated medically with a betablocker, clopidogrel bisulfate, nitrates, and aspirin.

Laboratory results showed elevated hemoglobin (18.2 g/dL, normal 12.9–17.3 g/dL), hematocrit (52.4%, normal 38–51%), white blood cell count (WBC) (11,000/ $\mu$ L, normal 4,100–10,900/ $\mu$ L), and platelets (581,000/ $\mu$ L, normal 175,000–450,000/ $\mu$ L). Platelet levels increased further, reaching 696,000/ $\mu$ L 2 days later. Previous laboratory results from 2003 showed a hemoglobin of 17.3 g/dL, hematocrit of 48.8%, WBC of 10,300/ $\mu$ L, and platelets of 681,000/ $\mu$ L. Lipoprotein(a) was normal at <3 mg/dL. LDL cholesterol was normal at 81 mg/dL, HDL was low at 31 mg/dL (normal 35–80 mg/dL), and total cholesterol was 137 mg/dL. Other common causes for SCD, such as Marfan's syndrome, were ruled out by genetic testing.

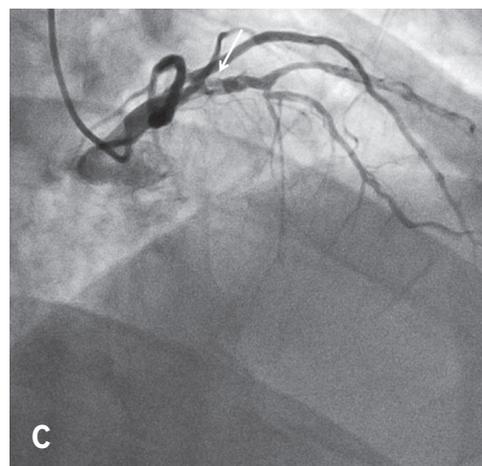
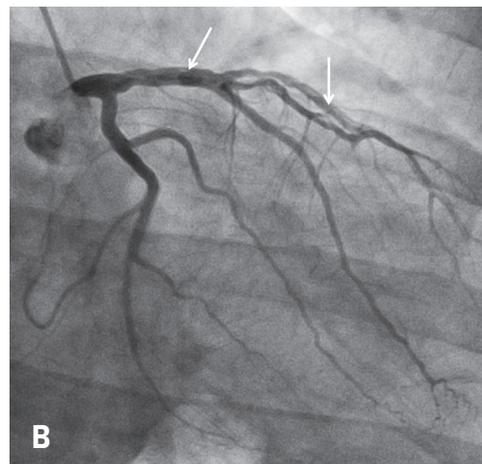
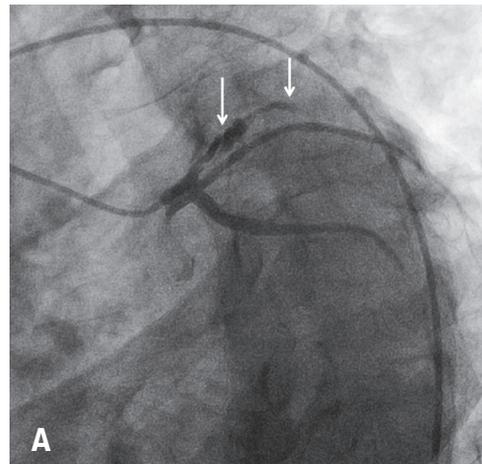
Further workup for thrombocytosis came back negative by polymerase chain reaction for *BCR-ABL* mutation, ruling out chronic myeloid leukemia, and positive for *JAK2* mutation. The patient also had a normal erythropoietin level at 4 mU/mL (normal 4–24 mU/mL). Ultrasound of the abdomen revealed moderate splenomegaly with slightly increased size since 2003. Platelet count 5 days later was persistently elevated at 482,000/ $\mu$ L.

The enlarged spleen, positive *JAK2* study, and persistently elevated platelet count confirmed the diagnosis of essential thrombocythemia. The patient was continued on aspirin and began hydroxyurea to lower platelet count. Following administration of hydroxyurea, the patient's platelet count came down to 458,000/ $\mu$ L in 6 months and to within the normal range at 348,000/ $\mu$ L in the following 6 months. The patient continues to be followed by hematology for monitoring of platelet counts.

## DISCUSSION

The pathogenesis of SCD remains controversial. It traditionally has been associated with young, predominantly female patients without cardiovascular risk factors, especially in the peripartum period.<sup>1</sup> SCD also has been associated with connective tissue disease, vasculopathies, and chronic inflammatory processes.<sup>3</sup> SCD is a rare cause of myocardial infarction, accounting for less than 1% of cases,<sup>4</sup> and lack of available data makes optimal treatment unclear.<sup>1</sup> In the context of acute coronary syndrome, management depends on the location, accessibility and extent of dissection, and the patient's clinical status.<sup>1</sup> Conservative treatment

Figure. Cardiac Catheterization



Shows a normal left main artery, but (A) left anterior descending artery with ostial and (B) very complex proximal and mid dissection and the (C) appearance of multiple lumens.

is preferred when SCD involves small vessels,<sup>1,4</sup> and percutaneous angioplasty or coronary bypass surgery is recommended in multivessel lesions, proximal lesions, or in patients with persistent ischemia, as they generally have the worst prognosis.

Essential thrombocythemia is a myeloproliferative disorder characterized by a high platelet count, originating from a pluripotent stem cell and is more commonly found in females, with an average age at diagnosis of 50 to 60 years.<sup>1</sup> Previous reports in the literature describe asymptomatic, chronic cases of SCD as well as an association with polycythemia.<sup>2,5</sup> Others have reported an association between essential thrombocythemia and internal carotid artery dissection and coronary occlusion,<sup>6,7</sup> but no association between SCD and essential thrombocythemia has been previously reported.

Myeloproliferative disorders are categorized broadly into 2 groups, including classic and atypical myeloproliferative neoplasias. For a complete discussion of these disorders, please see the World Health Organization (WHO) classification system described in 2009 by Tefferi and colleagues.<sup>8</sup> The group of classic myeloproliferative disorders includes polycythemia vera, essential thrombocythemia, primary myelofibrosis, and chronic myelogenous leukemia, all of which are associated with hypercoagulability. The incidence of thrombosis in patients with myeloproliferative neoplasms is significantly elevated with a higher incidence of arterial, rather than venous, thrombosis. Strokes are also frequent, followed by myocardial infarction, and peripheral arterial occlusion. Approximately 50% of patients with essential thrombocythemia are asymptomatic, while the other 50% have vasomotor, thrombotic, or hemorrhagic symptoms. Typical essential thrombocythemia is a Philadelphia *BCR-ABL* mutation-negative (Ph1-), chronic myeloproliferative disorder with a good prognosis for overall survival.<sup>9</sup>

The Polycythemia Vera Study Group (PVSG) originally defined diagnostic criteria for essential thrombocythemia in the 1980s, including a platelet count >600,000/ $\mu$ L, megakaryocytic hyperplasia on bone marrow aspiration and biopsy, absence of the Philadelphia chromosome, absence of infection, inflammation, or other causes for reactive thrombocytosis, normal red blood cell mass or a hemoglobin concentration of <13 g/dL, and the presence of stainable iron in a bone marrow aspiration or  $\leq 1$  g/dL increase in hemoglobin concentration after a 1-month trial of oral iron therapy.<sup>10</sup> Notably, the PVSG criteria did not include histopathological data. In 2001, the WHO developed a classification for chronic myeloproliferative disorders, incorporating clinical, laboratory, and morphologic data.<sup>11</sup> These classifications were further updated in 2008 with availability of additional genetic data.<sup>8</sup> The original PVSG criteria proposed a sustained platelet count of >600,000/ $\mu$ L, but the WHO lowered the threshold to 450,000/ $\mu$ L since the 95th percentile for normal platelet count, adjusted for gender and race, is below

400,000/ $\mu$ L and the PVSG criteria were thought to potentially compromise the detection of early phase essential thrombocythemia. The demonstration of *JAK2* mutation is present in 50% to 55% of patients with essential thrombocythemia, and demonstration of this marker or another clonal in its absence is included in the WHO criteria. Since the *JAK2* mutation is absent in approximately half of essential thrombocythemia patients, bone marrow biopsy is still required for diagnosis according to WHO criteria. Importantly, the *JAK2* mutation is absent in patients with reactive thrombocytosis.<sup>8,9</sup>

There is no consensus as to which set of criteria should be followed for diagnosis of essential thrombocythemia and some hematologists continue to use the PVSG criteria. Ultimately, the diagnosis of essential thrombocythemia is made by sustained platelet elevations of 450,000/ $\mu$ L without signs of reactive thrombocytosis and the presence of the *JAK2* mutation, or in its absence, a bone marrow exam excluding the presence of other myeloproliferative disorders, such as polycythemia vera, primary myelofibrosis, or chronic myeloid leukemia.

The management of thrombocytosis in patients with myeloproliferative neoplasms currently entails the use of antiplatelet and cytoreductive therapies. In a randomized trial, aspirin was found to reduce the risk of thrombosis in patients with polycythemia, but it did not reduce mortality.<sup>9</sup> Cytoreductive therapies, such as hydroxyurea, phlebotomy, and interferon- $\alpha$ , are considered for patients at high risk for thrombosis or bleeding, including those older than 60 years of age, those with a history of major thrombosis or hemorrhage, and those with platelet counts greater than 1.5 million/ $\mu$ L. Hydroxyurea effectively reduces elevated cell counts, spleen size, and thrombotic risk.<sup>9</sup> In the case presented here, the patient was treated conservatively with aspirin and hydroxyurea, and continues to be asymptomatic.

## CONCLUSION

Essential thrombocythemia can predispose individuals to vascular dysfunction and damage, which may contribute to coronary artery dissection. With this case, we propose that essential thrombocythemia should be excluded in the presence of coronary dissection and thrombocytosis.

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## REFERENCES

1. Vanzetto G, Berger-Coz E, Barone-Rochette G, et al. Prevalence, therapeutic management and medium-term prognosis of spontaneous coronary artery dissection: results from a database of 11,605 patients. *Eur J Cardiothorac Surg.* 2009;35:250-254.

2. Kay IP, Williams MJ. Spontaneous coronary artery dissection: long stenting in a patient with polycythemia vera. *Int J Cardiovasc Intervent*. 1999;2:191-193.
3. McCann AB, Whitbourn RJ. Spontaneous coronary artery dissection: a review of the etiology and available treatment options. *Heart Vessels*. 2009;24:463-465.
4. Shamloo BK, Chintala RS, Nasur A, Ghazvini M, Shariat P, Diggs JA, Singh SN. Spontaneous coronary artery dissection: aggressive vs. conservative therapy. *J Invasive Cardiol*. 2010;22:222-228.
5. Ghosh N, Chow CM, Korley V, Chisholm R. An unusual case of chronic coronary artery dissection: did cisplatin play a role? *Can J Cardiol*. 2008;24:795-797.
6. D'Ambrosio D, Della-Morte D, Garguilo G, et al. Intrapetrous internal carotid artery dissection and essential thrombocythemia: what relationship? A case report. *Cases J*. 2008;1:354.
7. Nanavanti A, Patel N, Burke J. Thrombocytosis and coronary occlusion. *JACC Cardiovasc Interv*. 2012;5:e18-19.
8. Tefferi A, Thiele J, Vardiman JW. The 2008 World Health Organization classification system for myeloproliferative neoplasms: order out of chaos. *Cancer*. 2009;115:3842-3847.
9. Michiels JJ, Berneman Z, Van Bockstaele D, van der Planken M, De Reeve H, Schroyens W. Clinical and laboratory features, pathology of platelet-mediated thrombosis and bleed complications and the molecular etiology of essential thrombocythemia and polycythemia vera: therapeutic implications. *Semin Thromb Hemost*. 2006;32:174-207.
10. Murphy S, Iland H, Rosenthal D, Laszlo J. Essential thrombocythemia: an interim report from the Polycythemia Vera Study Group. *Semin Hematol*. 1986;23:177-182.
11. Thiele J, Kvasnicka HM. Chronic myeloproliferative disorders. The new WHO classification. [Article in German] *Pathologe*. 2001;22:429-443.

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