Published in final edited form as:
Leuk Res. 2009 April ; 33(4): 573–574. doi:10.1016/j.leukres.2008.06.016.

Early renal arterial stent thrombosis associated with the JAK2 V617F mutation

Piotr Tabaczewski[1], **Suhasini Nadesan**[2], and **Seah H Lim**[2]

1 *Department of Internal Medicine, Texas Tech University Health Sciences Center in Amarillo*

2 *Texas Oncology Cancer Center, Amarillo*

Myeloproliferative diseases (MPD) are a recognized risk factor for thrombotic events. Patients with MPD can sometimes present with thrombotic complications even prior to the diagnosis or manifestation of any clinical features of MPD, although the exact incidence of such a mode of presentation of MPD remains unclear, since it had been difficult to make a diagnosis of early or occult MPD without the use of *in vitro* bone marrow colony assays not commonly available in the routine laboratory. The recent identification of an association between the JAK2 V617F mutation and MPD enables the convenient early diagnosis in these patients using a molecular approach. JAK2 V617F is a gain-of-function mutation that results in a constitutive activation of the JAK-STAT signaling pathway and leads to the expansion of the affected hematopoietic precursor cells, with skewing towards the erythroid lineage. JAK2 V617F mutation has been found in more than 90% of patients with polycythemia rubra vera but with a lesser frequency in the other MPD. Recently, a strong association has been found between JAK2 V617F mutation and idiopathic Budd-Chiari syndrome or splanchnic thrombosis. A study that involved 139 cases of non-cirrhotic splanchnic vein thrombosis identified the JAK2 V617F mutation in 27 (21%) of these patients, 14 of whom had overt MDS, 3 developed MDS during follow up (median 41 months) and 11 were still disease free at the time of reporting (1). Similar studies have been carried out in other common thrombotic diseases but no correlation was found between JAK2 V617F mutation and deep venous thrombosis, pulmonary embolus, stroke or early myocardial infarction (2). It has, therefore, been proposed that the JAK2 V617F mutation should be tested in patients with non-cirrhotic Budd-Chiari syndrome and thrombosis of the splanchnic circulation, even in the absence of any clinical features of MPD. The routine use of this test for other forms of thromboembolic diseases, however, remains debatable.

Although the association between splanchnic thrombosis and early MPD is well recognized, the occurrence of arterial stent thrombosis in patients with occult MPD has not previously been reported. We report in this paper the first case of a patient with an occult MPD unmasked by a bilateral early renal arterial stent thrombosis. The diagnosis of an occult MPD was made possible molecularly by the detection of the JAK2 V617F mutation.

A 72 years old lady with a history of hypertension and renal impairment was found to have a bilateral renal artery stenosis by CT scan. Her right renal artery was 80–85% and her left renal artery 85–90% stenosed. She underwent a percutaneous bilateral renal arterial angioplasty with insertion of the Dynalink nitinol 6-Fr stents. The success of the procedure was confirmed by

Correspondence to: Seah H Lim, MD, PhD, FRCP (Lond.), FRCPath., Texas Oncology Cancer Center, 1000 Coulter Drive, Amarillo 79106, Texas, Tel. No. 1-806-358 8654, Fax No. 1-806-356 9303, Email: E-mail: seah.lim@usoncology.com.

a repeat CT scan that showed 100% patency of the stents. The procedure also resulted in an improved renal function. Ten days after the procedure, the patient presented with abdominal and loin pain. Repeat CT scan showed total occlusion of the renal arterial stents by thrombus and the development of renal infarction. The unfortunate and unusual early adverse thrombotic event triggered the investigations for a thrombophilic tendency. A careful examination did not reveal any established genetic risk factors. She did not have any family history of thromboembolic disease. The genetic workup was unremarkable, without any evidence for Factor V Leiden mutation, Prothrombin gene mutation or methyltetrahydrofolate reductase gene mutation. Her serum homocysteine level was not elevated. Serum Protein C, Protein S and antithrombin III were all within limits. Her only risk factor for thromboembolic disease was a history of smoking half a pack of cigarette per day. Antiphospholipid antibody screening was also negative. She had six previous pregnancies without any thromboembolic complications. Her peripheral blood was checked for the JAK2 V617F mutation by PCR because she had a mild leukocytosis. The white cell count of 11 was associated with a normal hemoglobin and platelet count, although her white cell count was normal just before insertion of the renal arterial stents. She was found to be strongly positive for the JAK2 V617F mutation by qualitative PCR on two separate occasions. With further follow-up 3 months, her leukocytosis has resolved spontaneously and she has continued to have a normal complete blood count without developing any clinical features of MPD.

Early thrombosis of the arterial stents (<30 days after the procedure) is observed with both bare metal as well as drug-eluting stents and it occurs at the same frequency of 0.7% for both types of stents (3). It is an uncommon but serious complication of interventional angioplasty. The risk of early stent thrombosis is correlated with the local hemodynamic conditions (4), thrombophilia associated with malignancies (5), hypersensitivity drug reaction in drug eluting stents (6), smoking and younger age (7). The in-stent thrombus is triggered by pro-thrombotic local conditions and facilitated by the local pro-inflammatory reactions that result in platelets aggregation (8). Changes in the practice of interventional cardiology and radiology have led to the increasing use of stents for patients with arterial diseases. It is, therefore, anticipated that the number of cases of arterial stent thrombosis will increase in the next few years.

The case presented here raises an important point. Occult MPD may be a previously unrecognized predisposing factor for arterial stent thrombosis. With the availability of molecular approach to the diagnosis of MPD, it may now be possible to carry out a perspective study to determine the exact impact of occult MPD on this rare complication of interventional cardiology and radiology. Early identification of an occult MPD in these patients may suggest that a more aggressive antithrombotic approach is needed in these patients following the stenting procedure.

Acknowledgments

We acknowledge that there is no financial support for or conflict of interest in this work.

References

1. De Stefano V, Fiorini A, Rossi E, Za T, Farina G, Chiusolo P, Sica S, Leone G. Incidence of the Jak2 V617F mutation among patients with splenchnic or cerebral venous thrombosis and without overt chronic myeloproliferative disorders. J Thromb Haemost 2007;5:708–714. [PubMed: 17263783]
2. Pardinani A, Lasho TL, Schwager S, Finke C, Hussein K, Pruthi RK, Tefferi A. JAK2V617F prevalence and allele burden in non-splanchnic venous thrombosis in the absence of overt myeloproliferative disorder. Leukemia 2007;21:1828–1829. [PubMed: 17460706]
3. Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schomig A, Pfisterer ME, Stone GW, Leon MB, de Lezo JS, Gay J, Park S-J, Sabate M, Suttorp MJ, Kelback H, Spaulding C, Menichelli M, Vermeersch P, Dirksen M, Cervinka P, Petronio AS, Nordmann AJ, Diem P, Meier B, Zwahlen M,

Reichenbach S, Trelle S, Windecker S, Juni P. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet 2007;370:937–948. [PubMed: 17869634]

4. Moussa I, Di Mario C, Reimers B, Akiyama T, Tobis J, Colombo A. Subacute stent thrombosis in the era of intravascular ultrasound-guided coronary stenting without anticoagulation: Frequency, predictors and clinical outcome. J Am Coll Cardiol 1997;29:6–12. [PubMed: 8996288]
5. Hobson AR, McKenzie DB, Kunadian V, Purcell I, Zaman A, Dawkins KD, Curzen N. Malignancy: An unrecognized risk factor for coronary stent thrombosis? J Invasive Cardiol 2008;20:E120–123. [PubMed: 18398242]
6. Nebeker JR, Virmani R, Bennett CL, Hoffman JM, Samore MH, Alvarez J, Davidson CJ, McKoy JM, Raish DW, Whisenant BK, Yarnold PR, Belknap SM, West P, Gage JE, Morse RE, Gligoric G, Davidosn L, Feldman MD. Hypersensitivity cases associated with drug-eluting coronary stents. J Am Coll Cardiol 2006;47:175–181. [PubMed: 16386683]
7. Suarez A, Perez-Vizcayno MJ, Moreno R, Escaned J, Banuelos C, Jimenez P, Bernardo E, Angiolillo DJ, Hernandez R, Macaya C. Intravascular ultrasound findings during episodes of drug-eluting stent thrombosis. J Am Coll Cardiol 2008;50:2095–2097. [PubMed: 18021881]
8. Wexberg P, Jordanova N, Strehblow C, Syeda B, Meyer B, Charvat S, Zorn G, Scheinig D, Wojta J, Huber K, Glogar D, Gyongyosi M. Time course of prothrombotic and proinflammatory substance release after intracoronary stent implantation. Thromb Haemost 2008;99:739–748. [PubMed: 18392332]