

Idiopathic Thrombocytopenic Purpura in Patients with Ischaemic Heart Disease - A Therapeutic Challenge

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Abstract:

Idiopathic thrombocytopenic purpura (ITP) and myocardial infarction (MI) in an individual patient is a rare combination. MI mandates thrombolytic and antiplatelet therapy which increases the risk of bleeding in ITP. So far, no guideline deals with

management protocol for ischaemic heart disease (IHD) in ITP patients. Here, we describe 2 cases of IHD who developed ITP while on antiplatelet therapy.

Key Words: Idiopathic Thrombocytopenic Purpura, Coronary Artery Disease, Thrombocytopenia.

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Introduction:

Idiopathic thrombocytopenia purpura (ITP), also called immune thrombocytopenic purpura, is an autoimmune disorder with a low platelet count and mucocutaneous bleeding. Autoantibody-mediated platelet destruction, as well as, impaired platelet production both contribute to the pathophysiology of ITP. Quantitative as well as qualitative deficiency in platelet function leads to a bleeding tendency. On the other hand, ITP tends to increase the risk of cardiovascular diseases (CVD) e.g., IHD, stroke, transient ischemic attack and heart failure.¹ ITP may even lead to a prothrombotic state which may be related to endothelial damage caused by antigenic mimicry between platelets and

endothelial cells² or, related to administration of intravenous immunoglobulin (IVIg) for the treatment of ITP³. Occurrence of acute coronary syndrome⁴⁻⁶, deep vein thrombosis and pulmonary embolism^{7,8}, and ischaemic stroke⁹⁻¹¹ has been described in association with ITP. Thrombolytic and antiplatelet therapy, the integral part of standard management of these patients, certainly increases the risk of bleeding in the context of already compromised platelet function. So far, no consensus exists regarding the optimal revascularization strategy and antiplatelet treatment policy in patients with ACS or stable coronary artery disease who have simultaneous ITP. Here, we present 2 cases of old MI who developed ITP while on antiplatelet drugs.

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Case 1

A 71-year-old hypertensive man was on aspirin along with standard treatment for stable coronary artery disease with the history of postero-infero-lateral MI 1 year back. He was allergic to clopidogrel. During routine follow up, his serial platelet counts were 115,000 and 45,000/mm³ over 4 weeks. However, he had no obvious bleeding manifestations, and there was no bony tenderness, lymphadenopathy or organomegaly. Also, he did not have fever recently and take any new drug. He was referred to a haematologist. Bone marrow examination was suggestive of ITP. Platelet count further dropped to 10,000/mm³, however, no obvious bleeding occurred. Aspirin was withheld for fear of bleeding,

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oral methyl prednisolone followed by azathioprine was given. Platelet count rose to 55,000/mm³ but the general condition of the patient deteriorated and he developed significant adverse effects characterized by mouth ulceration, glucose intolerance and hepatitis. Methyl prednisolone and azathioprine were stopped, the patient improved rapidly, and the platelet count remained between 30,000 and 60,000/mm³. Aspirin was reintroduced with close clinical and haematological monitoring. The platelet count remained unchanged, no bleeding encountered, and the patient remained stable.

Case 2

A 65-year-old diabetic man with history of inferior MI was on clopidogrel along with other medications. He refused any invasive procedures. During routine follow up, his platelet count was 65,000/mm³, however, he did not have any bleeding manifestations. His hemoglobin was 12.6 g/dL, erythrocyte sedimentation rate (ESR) 20 mm in first hour, serum creatinine 1.03 mg/dL, and SGPT 35 units/L. Bone marrow examination by a haematologist revealed features suggestive of ITP. Clopidogrel was continued while the patient was on close clinical and haematological monitoring. There was no bleeding manifestations, and he was doing well in 9-month follow up.

Discussion:

Simultaneous occurrence of IHD and ITP is rare because of the physiological role of platelets in coagulation. Nevertheless, acute MI has been reported in even severely thrombocytopenic patients.¹² On the other hand, ITP developing in otherwise stable coronary artery disease (CAD) patients, as is the issue in the 2 cases presented here, has not been reported adequately. Presence of thrombocytopenia of ITP poses serious management problems in ACS, as well as, in stable CAD patients in which a good balance between the prevention of thrombosis and haemorrhagic risk demands.

Patients with acute ST-elevation MI and ITP have successfully been managed with thrombolytic therapy with limited experience.¹³ Coronary revascularization either by percutaneous coronary intervention (PCI) or by coronary artery bypass graft (CABG) surgery seems to be safe and feasible, having a good early outcome and a low complication rate.¹⁴ Historically, CABG was preferred to PCI in ITP patients with CAD because majority of the coronary artery lesions can be dealt with in a more predictable way and antiplatelet therapy can be managed with greater flexibility with CABG in comparison to PCI.¹⁵ In fact, despite low platelet count, CABG has successfully been carried out with some increase in bleeding risk compared to CABG in the general

population.¹⁶⁻⁹ On the other hand, available data suggest that PCI, including primary PCI, can be safe and feasible in carefully selected patients.^{16, 20-6} Li-Sha et al. reported a 75-year-old patient with ITP who underwent 3 separate coronary interventions for recurrent ACS and in-stent restenosis, including PCI and cutting-balloon angioplasty and using unfractionated heparin, dual antiplatelet therapy and platelet transfusion.²¹ They also analyzed the reported 18 cases of ITP who underwent PCI between 1999 and 2013; pre-procedural platelet count ranged from 3 × 10⁹/L to 322 × 10⁹/L (mean 78.5 ± 81.5 × 10⁹/L). Glycoprotein IIb/IIIa inhibitors were administered during 4 PCI procedures, clopidogrel before and during PCI in 9, ticlopidine in 1, aspirin in 9, and no antiplatelet drug before and during PCI in 5. One instance (5.6 %) of major bleeding²⁷ and 6 minor bleeding were observed. Ten patients (55.6 %) were discharged on double antiplatelet therapy, 3 on single antiplatelet drug, while 3 patients did not receive any antiplatelet agent. Performance of PCI in a patient with ITP requires sufficient inhibition of platelet function to prevent stent thrombosis, but not enough to cause bleeding. For this reason, most expert opinions recommended bare-metal stent (BMS) as opposed to drug-eluting stent (DES) to minimize the duration of dual antiplatelet therapy in case bleeding occurs.¹⁴ However, DES has also been implanted successfully.¹⁶ Platelet transfusion and IVIG have been used in some cases of ITP to reduce the risk of bleeding during coronary revascularization. IVIG may paradoxically induce thromboembolic events including myocardial infarction.²⁸⁻³⁰ Since severe bleeding is uncommon when the platelet count is above 30,000/mm³, treatment is usually initiated when the count falls below 30,000/mm³.³¹

Antiplatelet therapy in the setting of ITP and IHD should be used with great caution. Dual antiplatelet drugs e.g., combination of aspirin and clopidogrel, when indispensable, should be used generally only for short time, with special attention to the indication, platelet count, and bleeding risk. In both the cases presented here, mostly single antiplatelet drug was used, in the first case only aspirin because of suspected clopidogrel intolerance, and in the second case only clopidogrel because of gastrointestinal intolerance. Aspirin can be safely continued after CABG and PCI unless clinical bleeding occurs, or until the platelet count falls to 10,000–20,000/mm³.³² This may probably be applicable to those otherwise stable CAD patients with ITP who did not have any revascularization strategy, as are the cases presented here.

Actually, in ITP, in contrast to the more common findings of petechiae and purpura, severe haemorrhage, such as intracranial haemorrhage, overt gastrointestinal bleeding,

and haematuria, is uncommon. This was illustrated in a systematic review of prospective clinical studies, which included 5336 adults with ITP³³; the incidence of intracranial haemorrhage was 1.4%, while that of other severe bleeding was 9.6%. In a population-based study that included 3771 patients with ITP, the risk of severe bleeding at disease onset was <1%³⁴. Predictors of severe bleeding include the degree of thrombocytopenia (from <10,000 to <20,000/mm³), previous minor bleeding, and chronic ITP (i.e., diagnosis >12 months prior).³³

Take-home message:

Combination of ITP and IHD including ACS, though rare, does occur. Presence of thrombocytopenia in ITP is not protective to ACS.

Despite increased risk of haemorrhage, major bleeding rarely occurs until platelet count falls below 20,000 to 10,000/mm³.

No established protocol exists for management of IHD in the setting of ITP, or ITP in case of chronic IHD. Treatment should be individualized.

Safety of thrombolytic therapy is limited by inadequate experience.

Growing evidence favours coronary revascularization including PCI and CABG.

BMS may be preferable to DES. Periprocedural anticoagulants and antiplatelets may be used, certainly with careful monitoring. Platelet transfusion is rarely needed.

For maintenance therapy, single antiplatelet drug, preferably aspirin, can usually be safely given or continued as long as platelet count is approximately more than 30,000/mm³, or there is evidence of bleeding.

Antiplatelet drugs should be withdrawn when platelet count falls below 10,000/mm³, or there is active major bleeding, and treatment should probably be started to raise platelet count.

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