Acute stent thrombosis in a patient with giant cell arteritis

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A 70-year-old man presented with a non-ST elevation myocardial infarction attributable to a 99% occlusion of his mid-left anterior descending artery and concomitant symptoms suggestive of giant cell arteritis. He underwent bare metal stenting, with an excellent angiographic result, and was placed on dual antiplatelet therapy, as well as oral prednisone 30 mg twice daily, while awaiting confirmatory temporal artery biopsy. Unfortunately, 70 h after percutaneous coronary intervention, he developed acute stent thrombosis. Platelet aggregometry demonstrated that he was responsive to acetylsalicylic acid, but marginally responsive to clopidogrel. Over the next 30 days, he had a marked clinical improvement, with an improvement in platelet response to clopidogrel that paralleled the clinical resolution of his vasculitis. The present case reports the first incidence of acute stent thrombosis associated with giant cell arteritis, and suggests that the proinflammatory milieu of acute inflammatory arthritides may warrant prolonged, aggressive antiplatelet therapy in the setting of an acute coronary syndrome.

Key Words: *Clopidogrel resistance; Giant cell arteritis; Stent thrombosis*

Acute stent thrombosis (AST) is a rare complication of percutaneous coronary intervention (PCI). Predisposing factors associated with AST include patient characteristics, the nature of the clinical presentation, findings at angiography and platelet response to antiplatelet agents. It is in the latter circumstance that inflammatory rheumatological disorders can present unique management issues during PCI. We report the first known case of AST associated with platelet hyper-reactivity as a result of acute giant cell arteritis (GCA).

CASE PRESENTATION

A 70-year-old man with hypertension and dyslipidemia presented to our hospital with a non-ST elevation myocardial infarction (peak troponin 5 µg/L; normal less than 0.1 µg/L). He had no previous history of cardiac or rheumatological diseases. He was initiated on medical therapy including acetylsalicylic acid (325 mg daily), clopidogrel (300 mg load followed by 75 mg daily) and intravenous unfractionated heparin. Coronary angiography the day following admission demonstrated a culprit critical 99% stenosis of the mid-left anterior descending (LAD) artery. He subsequently underwent uncomplicated stenting with a BiodivYsio 3 mm × 15 mm bare metal stent (Abbott Laboratories, USA). During the procedure, the patient received unfractionated heparin (50 units/kg) and intravenous eptifibatide (180 µg/kg periprocedural intravenous loading dose and 18 h infusion at 2 µg/kg/h).

Postprocedure, the patient related a history of temporal headaches and intermittent jaw pain for three months' duration. Examination revealed minor right-sided temporal tenderness, but no evidence of proximal weakness. Investigations revealed anemia of chronic disease and an active inflammatory state, with erythrocyte sedimentation rate (ESR) greater than 100 mm/h (normal values less than 10 mm/h) and C-reactive protein (CRP) 191 mg/L (normal values less than 6 mg/L).

Une thrombose aiguë de l'endoprothèse chez un patient atteint de la maladie de Horton

Un homme de 70 ans s'est présenté en raison d'un infarctus du myocarde sans élévation du segment ST attribuable à une occlusion à 99 % de la moitié de la branche antérieure de l'artère coronaire gauche et à des symptômes concomitants évocateurs d'une maladie de Horton. Il s'est fait installer une endoprothèse à métal nu, a obtenu d'excellents résultats angiographiques et a entrepris un double traitement antiplaquettaire accompagné de 30 mg de prednisone deux fois par jour, tout en attendant une biopsie de confirmation de l'artère temporale. Malheureusement, 70 heures après l'intervention coronaire percutanée, il a développé une thrombose aiguë de l'endoprothèse. L'aggrégométrie plaquettaire a démontré qu'il répondait à l'acide acétylsalicylique, mais peu au clopidogrel. Au cours des 30 jours suivants, son état clinique s'est considérablement amélioré, avec une meilleure réponse plaquettaire au clopidogrel parallèle à la résolution clinique de la vasculite. Le présent cas relate la première incidence de thrombose aiguë de l'endoprothèse associée à une maladie de Horton et laisse supposer que le milieu pro-inflammatoire de l'arthrite inflammatoire aiguë peut justifier une thérapie antiplaquettaire énergique et prolongée en présence d'un syndrome coronarien aigu.

A tentative diagnosis of GCA was entertained and he was started empirically on oral prednisone 30 mg twice daily.

Unfortunately, while awaiting confirmatory temporal artery biopsy, the patient experienced an episode of acute chest pain associated with anterior ST elevation 70 h post-PCI. Emergent coronary angiography revealed a thrombotic occlusion of the recently implanted LAD artery stent (Figure 1). He underwent successful repeat balloon angioplasty and stenting after receiving additional heparin and eptifibatide, both of which were continued for an additional 48 h.

Bedside platelet aggregometry using the Ultegra Rapid Platelet Function Analyzer (Accumetrics, USA) was performed four days after his AST to assess acetylsalicylic acid and clopidogrel responsiveness. The manufacturer defines acetylsalicylic acid resistance as greater than 550 aspirin reaction units, and clopidogrel response as a percentage of platelet inhibition (Product Monograph, August 17, 2005). The assay demonstrated adequate responsiveness to acetylsalicylic acid, with a measured value of 429 aspirin reaction units, but borderline responsiveness to clopidogrel, with only 27% platelet inhibition. As a result, the patient's clopidogrel dose was increased to 75 mg twice daily.

Temporal artery biopsy performed one week after admission confirmed the diagnosis of GCA. Throughout his stay in hospital, the patient continued to improve clinically without further chest pain. The ESR and CRP both decreased significantly (56 mm/h and 9.6 mg/L, respectively, at discharge). He was discharged home 11 days after admission on acetylsalicylic acid 325 mg daily and clopidogrel 75 mg twice daily for two weeks, followed by 75 mg daily.

One month after discharge, his GCA was under biochemical and clinical control on a tapering course of prednisone. Repeat ESR and CRP assays were significantly lower, at 14 mm/h and 1.6 mg/L, respectively.

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Figure 1 Angiogram on presentation demonstrating 90% tubular stenosis of the left anterior descending (LAD) artery before (A) and after (B) angioplasty with stenting. Repeat angiogram 70 h postintervention demonstrating acute stent thrombosis (arrows) of the proximal LAD artery stent before (C) and after (D) angioplasty

Platelet aggregometry revealed improved responsiveness to clopidogrel, with 46% platelet inhibition. This corresponded to a 170% increase in platelet inhibition with improved control of the GCA.

DISCUSSION

AST is a well-documented but relatively rare complication of PCI, with an approximate incidence of 0.5% for both bare metal and drug-eluting stents. Predisposing factors include patient characteristics (chronic kidney disease, diabetes, left ventricular dysfunction), presentation (unstable angina, or myocardial infarction within one week), lesion location (involvement of the LAD or circumflex arteries), findings at angiography (type 'C' morphology, bifurcation lesions, angiographic filling defect or total occlusion), complications of the procedure itself (failed balloon angioplasty, stent malapposition, abrupt stent closure during procedure, residual proximal or distal dissection) and stent-related factors (length greater than 20 mm to 25 mm, diameter less than 3 mm, or more than three stents implanted) (1). Recently, platelet receptor polymorphisms and nonresponse to antiplatelet therapy have also been implicated as potential causes of AST (2).

We have reported the first case of AST associated with acute GCA. GCA is a medium and large vessel granulomatous vasculitis present in up to 17.8 per 100,000 people over the age of 50 years. It most often manifests as temporal arteritis with jaw claudication, visual symptoms, polymyalgia rheumatica and/or transient ischemic attacks. GCA may also present as inflammatory large vessel vasculitis affecting the ascending aorta and its proximal branches, resulting in complications such as stroke, aortic aneurysm, insufficiency and/or dissection, and peripheral arterial thrombosis.

Previous studies have suggested that atherosclerosis, and particularly acute coronary syndromes (ACS), is an inflammatory disorder. This inflammatory state may be worsened by a concomitant disorder such as GCA, due to its propensity to increase production of fibrinogen

and acute phase reactants. Moreover, the granulomata of GCA may directly liberate cytokines such as interleukin-6, an important inflammatory marker in atherosclerosis and ACS (3).

GCA has been shown to demonstrate the greatest platelet hyperactivity of all the inflammatory arthritides, with elevated surface activation and platelet aggregation found in up to 75% of patients (4). This accentuated platelet response, combined with the potential for reactive thrombocytosis, may contribute to the increased risk of cardiovascular events observed among patients with GCA.

Because our patient lacked most of the traditional risk factors for AST, we believe that the significant proinflammatory milieu of his acute GCA provided a substrate for AST. Our hypothesis is supported by the observed low response to clopidogrel that improved with successful treatment of his GCA, and the associated reduction in his proinflammatory state. This effect cannot be attributed to prednisone therapy alone (5). As a result, it may be postulated that ACS, in the context of concomitant inflammatory conditions, may be associated with decreased platelet responsiveness to standard antiplatelet regimens. Such patients may require more aggressive short-term antiplatelet therapy if an invasive strategy is used to treat ACS, to prevent subsequent acute and subacute complications.

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