Myelofibrosis and spinal cord ischaemia

Daniel Periard1; Michael Currat2; Salah Dine Qanadli3; Daniel Hayoz1; Peter Vollenweider2
1Department of Angiology and Medicine, Hôpital Cantonal, Fribourg, Switzerland; 2Department of Internal Medicine, Lausanne University Hospital (CHUV), Switzerland; 3Department of Radiology, Lausanne University Hospital (CHUV), Switzerland

The course of myeloproliferative syndromes (MPS) may be complicated by thrombotic episodes in the arteries, veins and capillaries (1). These thrombotic events are mainly observed with essential thrombocytosis (ET), polycythemia vera (PV) and secondary myelofibrosis (2–5), whereas they are less frequently encountered during the course of chronic idiopathic myelofibrosis (CIMF) (6, 7). Various mechanisms have been reported to trigger thrombotic events in MPS, related to platelet or leukocyte activation (8). We report here a case illustrating how CIMF may be associated with a high and long-lasting tendency to develop arterial and venous thrombosis.

A 73-year-old woman presented to our emergency department with acute bilateral lower limb paresia. Past medical history was relevant for a stroke in the territory of the left middle cerebral artery, at age 57. Chronic anemia was discovered at age 62 and bone marrow biopsy was consistent with myelofibrosis. After five years of repeated blood transfusions, the patient developed a complex pattern of immunization against erythrocyte antigens. In order to reduce blood transfusions and abdominal discomfort caused by the splenomegaly, a splenectomy was performed. Correction of the anemia occurred after splenectomy and a slight leucocytosis and thrombocytosis developed. Two weeks after the surgical intervention, she developed multiple deep venous thrombosis (splenic, portal, left internal jugular, left subclavian veins), attributed to the context of surgery, the MPS and the insertion of intravenous catheter. Hydroxyurea and vitamin K antagonist (targeting an international normalized ratio [INR] between 2.0 to 3.0) were regularly administered from age 67 to age 73. At age 73, for unknown reasons she decided to stop both treatments. Three weeks later, she presented with acute bilateral lower limb paresia.

Neurologic examination revealed an important loss of strength and sensitivitiy of the lower limbs and a decreased tone of the anal sphincter. Osteo-tendinous reflexes were present and symmetric. There was no meningeal sign. Examination of cranial nerves and upper extremities was normal.

Laboratory analysis were as follows: haemoglobin 108 g/l, leucocytes 10.1 G/l (82% neutrophils, 8% lymphocytes, 6% monocytes, 3% eosinophils) and platelets 367 G/l. Coagulation tests were normal with an INR of 1.0 and a partial prothrombin time of 22 seconds. High resolution (slice thickness of 0.625 mm) multi-detector CT scan (Lightspeed VCT, GE Medical Systems, Milwaukee, WI, USA) of the aorta showed multiple thrombosis in the descending thoracic and abdominal aorta (Fig. 1A). A thrombus was located at the origin of intercostal arteries at the level of the 7th thoracic vertebra (Fig. 1B). The ostia of both arteries were completely filled by thrombus and were not enhanced after contrast material injection. The neurologic deficit was attributed to spinal cord ischaemia, consecutive to the aortic thrombus. No aortic aneurysm favoring thrombosis could be identified. The image of aortic calcifications next to the thrombus proves the chronicity of the lesion.

Figure 1: Thrombosis in the thoracic aorta (A). A thrombus occludes the 7th intercostal arteries (B, arrows). Decrease in thrombus size (C) and recanalisation of occluded intercostal arteries (D, arrowheads).

Correspondence to:
Daniel Periard, MD
Dept. of Angiology and Medicine
Hôpital Cantonal Fribourg
Bergigny 1708 Fribourg, Switzerland
Tel.: +41 26 426 71 11; Fax: +41 26 426 72 88
E-mail: periardd@h-fr.ch

Received: September 4, 2008
Accepted after minor revision: November 26, 2008
Prepublished online: February 9, 2009

doi:10.1160/TH08-09-0570

Thromb Haemost 2009; 101: 584–585

584
bus suggested an in situ aortic thrombosis triggered by atherosclerosis rather than migration or embolism. An electrocardiogram showed regular sinus rhythm, and an echocardiography excluded an intracavitary thrombosis and a patent foramen ovale. The patient was managed by intravenous unfractioned heparin. Thrombectomy or thrombolysis were not considered, because of the risk of clot fragmentation and potential distal embolism. The outcome was favorable, with rapid improvement of the neurologic symptoms. Assisted walk was possible after five days. A computed tomography (CT) scan performed after one week of anticoagulation showed significant decrease of the aortic thrombus size (Fig. 1C) and recanalization of the intercostal arteries as demonstrated after contrast media administration (Fig. 1D).

An underlying condition for this clinical thrombophilia was searched. There was no antiphospholipid antibody (anticardiolipin, anti-β2glycoprotein, lupus anticoagulant). Plasma levels of protein C, protein S, antithrombin III were within normal range, before initiation of heparin. There were neither resistance to activated protein C nor prothrombin or factor V mutation. An occult cancer was also searched and no solid tumor was found by clinical and radiological assessment. Before discharge, heparin was relayed by long-term oral anticoagulant, and hydroxyurea was reintroduced. The patient had no neurological deficit at 12 months follow-up visit.

Discussion

The MPS are characterized by a high incidence of thrombotic as well as haemorrhagic complications during their course. Thrombosis may even precede the diagnosis of MPS (9, 10). The haematologic progenitor clonal proliferation results in abnormalities of the three lineages. The turnover of megakaryocytes and platelets is increased, resulting in thrombocytosis. Platelets show morphological and ultrastructural heterogeneity, with large size variability, modified membrane receptors and features of activation. These functional changes contribute more to the hypercoagulability than the absolute number of circulating platelets. The fibrinolytic system may also be altered in MPS, as suggested by the observation of increased levels of plasminogen activator inhibitors in patients with PV and ET and a history of thrombosis (11). The increased blood viscosity observed in PV may also contribute to thrombogenicity. Blood viscosity is mainly determined by the high haematocrit. In vivo, the axial flow of erythrocytes displaces the platelets to the vessel margin. High haematocrit reduces this space and increases platelet-platelet and platelet-endothelial interactions (12, 13). The leucocytosis was pointed out as another potential cause of thrombotic events in MPS. This is suggested by the increased levels of plasma leucocyte activation markers (14) and the increased number of circulating leucocyte-platelet aggregates observed in MPS (15). This may account for the anti-thrombotic properties of cytoreductive drugs in MPS (16). Recently, elevated plasma levels of osteoprotegerin were correlated with thrombosis and haemorrhagic complications in a cohort of 114 PV patients (17).

This case illustrates how CIMF may be associated with multiple venous and arterial thromboses. Thrombosis may affect arteries and veins of different organs and can spread out over a period of 15 years. Additional conditions such as recent surgery, intravenous catheters, anticoagulation and cytoreductive therapy withdrawal or atherosclerosis were potent triggers of thrombus formation. Resuming anticoagulation and hydroxyurea lead to a rapid regression of the thrombus and an improvement of neurologic status. This rapid improvement may be due to the localization of the thrombus, covering the ostia of the intercostal arteries that probably induced reversible spinal cord ischaemia, and the rapid clot dissolution due to its rich content in platelets, in comparison to the predominantly fibrin-containing non MPS-thrombosis. In this case, the age greater than 60 years and the recurrence of thrombotic events, two conditions recognized as risk factors for thrombosis in MPS, justify the long-term use of cytoreductive drugs (18).

References