Learning Point for Clinicians

- The intrinsic low risk of spontaneous brain haemorrhage in factor XI (FXI) deficiency may be significantly enhanced by concomitant factors, particularly hypertension and vascular abnormalities, which therefore need careful search and treatment.
- Silent FXI deficiency should be considered in young patients with typical hypertensive haemorrhage when aPTT is abnormally prolonged.

A 36-year-old Pakistan man presented with a sudden loss of consciousness. Brain computed tomography (CT) scan demonstrated a wide cerebellar haemorrhage, without fracture of the occipital bone. Cerebral angiography showed no evidence of aneurism or arteriovenous malformations, but a focal stenosis of basilar artery, immediately after the origin of anterior–inferior cerebellar arteries (Figure 1). These findings were confirmed by CT angiography, which identified a 60–70% stenosis of the intermediate tract of basilar artery, attributable to fibromuscular dysplasia.

The medical history of the patient was significant for arterial hypertension, inadequately treated with angiotensin-converting enzyme (ACE) inhibitors.

Neurological examination revealed right-cerebellar syndrome with mild right-sided hemiparesis. Blood pressure was 160/100 mmHg, with evidence for hypertension-related end-organ damage (microalbuminuria, mild ventricular hypertrophy). Laboratory analysis demonstrated a marked and persistent prolongation of activated partial thromboplastin time (aPTT, between 100 and 140 s; n.r. 20–37 s) with a normal prothrombin time (PT) (104%, n.r. 70–140%). Since coagulation tests showed complete aPTT correction with heterologous normal plasma, specific clotting factor assays were performed. Factor VIII and factor IX were normal, while factor XI (FXI) level was 5 U/dl (i.e. 5%, n.r. 70–140). The diagnosis of severe FXI deficiency was made and the patient was repeatedly infused with fresh frozen plasma (FFP), until aPTT normalization. Moreover, anti-hypertensive treatment was potentiated (ACE-inhibitor dosage increase, addition of calcium-channel and beta-blocker drugs), until reaching values stably below 125/80 mmHg. On the contrary, no stenting of the basilary artery stenosis was performed in consideration of the risks associated with the procedure, including the requirement of a long-term intensive antiplatelet therapy.

Patient’s clinical condition progressively improved. After the infusion of FFP was ceased, aPTT reverted to over 100 s, but no rebleeding or new bleeding was observed. At discharge, we recommended the prophylactic or therapeutic FXI replacement with FFP or FXI concentrates, in the case of surgery, trauma or major bleedings.

The deficiency of FXI is a rare autosomal recessive disorder representing less than 10% of all
hereditary coagulation factor deficiencies.\textsuperscript{1} Spontaneous bleeding, except for menorrhagia, is a very uncommon event also in patients with severe FIX deficiency.

This is the second description of a spontaneous cerebellar haemorrhage, and one of the few reports of FXI deficiency-associated non-traumatic intracranial bleeding.\textsuperscript{1–5} Interestingly, in our case the occurrence of the haemorrhagic event and its localization may be the result of the unpredictable concomitance of three synergistic factors, i.e. chronic hypertension, FXI deficiency and dysplastic basilar artery stenosis, each one per se probably not sufficient to provoke a major spontaneous bleeding in the brain. A hypothetic pathogenic cascade is the following: by increasing the upstream pressure regimen, the basilar artery stenosis, as situated immediately after the origin of the artery site of bleeding (right anterior–inferior cerebellar artery), could have amplified locally the mechanical impact on vascular wall of poorly controlled systemic hypertension, thus putatively contributing to haemorrhage development and localization. Notably, in patients with fibromuscular dysplasia of cerebral arteries, the prevalence of intracranial aneurysms and the risk of subarachnoid or intracerebral haemorrhage is higher than in the general population.\textsuperscript{6} In this context, a small fissuring lesion in the right anterior–inferior cerebellar artery may be occurred, but its consequences in terms of bleeding extension might have been critically amplified by the concomitant coagulation disorder.

In conclusion: (i) subjects with FXI deficiency have a low, although actual risk of spontaneous

\textbf{Figure 1.} (A) Computed tomographic images on admission demonstrated right paramedian cerebellar haemorrhage. (B, C) Cerebral angiography showed a focal stenosis of basilar artery, immediately after the origin of anterior inferior cerebellar arteries (white arrows); no evidence of aneurism or arteriovenous malformations.
Brain haemorrhage; (ii) such a risk may be significantly enhanced in the presence of one or more concomitant synergistic factors, particularly hypertension and vascular abnormalities, which therefore should be carefully searched and, if present, intensively treated; (iii) silent FXI deficiency should be considered in young patients even in the case of a typical hypertensive haemorrhage when aPTT is abnormally prolonged.

Conflict of interest: None declared.

References


