LETTER TO THE EDITOR

To The Editor

"The Other Side of the Coin": Hemorrhagic Stroke in Congenital Hypofibrinogenemia

Keywords: Anti-coagulation, Bleeding disorder, Coagulopathy, Congenital, Hypofibrinogenemia, Intracranial hemorrhage, Stroke

We read with great interest the article published by Nathoo et al.[1] Congenital fibrinogen disorders can present with both thrombotic and bleeding events. As pointed out by the authors, ischemic stroke is a major cause of morbidity. However, hemorrhagic stroke is also a catastrophic event that has been rarely reported in this patient population. We would like to enrich the discussion of neurological manifestations in rare bleeding disorders by presenting the other side of the spectrum in the case of a young woman who developed acute intracranial hemorrhage (ICH) secondary to congenital hypofibrinogenemia.

An 18-year-old woman was admitted to our hospital due to acute left hemiplegia and somnolence, which had appeared a day before. She experienced thunderclap headache just before the symptoms begun. On examination, her vital signs were normal, but she had left facial paralysis and hemiplegia with an ipsilateral Babinski sign. There were no other significant clinical findings.

She had a history of congenital hypofibrinogenemia that was diagnosed during the neonatal period due to umbilical and gingival bleeding unresponsive to vitamin K, prolonged coagulation time (with normal levels of coagulation factors and platelets), and low fibrinogen levels (0.005 g/L, normal 1.9–4.1 g/L). She had a history of easy bruising and multiple admissions for epistaxis, gingival bleeding, and hypermenorrhea requiring blood transfusions at a local pediatric hospital. No other family members were apparently affected.

Urgent non-contrast CT revealed right frontoparietal intraparenchymal hemorrhage with fluid levels (Figure 1) and bilateral subarachnoid hemorrhage toward the convexity with subfalcine herniation and slight midline shift (Figure 2). Additional imaging studies (including angiography) showed no aneurysms, tumor, or arteriovenous malformation. Further laboratory studies were relevant for normal platelet levels, prolonged coagulation times, and low fibrinogen levels at 0.3 g/L (Normal 1.9–4.1 g/L). Urgent treatment with cryoprecipitate and fibrinogen was implemented, reaching therapeutic fibrinogen levels within the first week.

Her hospital course was further complicated by pneumonia and urinary tract infection. She was discharged home a month later on palliative care (with the use of a gastrostomy tube) with a modified Rankin scale (mRs) of 5 points (Severe disability; bedridden and requiring constant nursing care and attention).

Congenital fibrinogen deficiencies are a heterogenous group of disorders that include afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia. Afibrinogenemia has a prevalence of one in a million, with undetectable fibrinogen levels, bleeding events, and rarely thrombosis.[2] Hypofibrinogenemia is more frequent, but its prevalence is difficult to establish due to large number of asymptomatic cases with low levels of fibrinogen.[3] Dysfibrinogenemia has normal or slightly diminished levels of malfunctional fibrinogen.[3]

Patients with hypofibrinogenemia are usually asymptomatic, but this depends on fibrinogen levels. The bleeding profile in severe hypofibrinogenemic patients can be similar to afibrinogenemia. Spontaneous bleeding can be observed among patients with fibrinogen levels lower than <0.5 g/L.[3] Episodes of epistaxis, menorrhagia, hemarthrosis, as well as umbilical, skin, and muscular bleedings are common, while intracranial hemorrhage is rare[4] but it is considered the most common cause of death.[5] ICH has been reported in 5% of the patients with afibrinogenemia but it can be also observed in patients with hypofibrinogenemia. Over 90% of these cases exhibit intraparenchymal hemorrhage.[5] Fluid–blood levels in acute intracerebral hemorrhage on CT scan are highly specific for coagulopathy-related disorders and should prompt an urgent cause.[6]

Current guidelines recommend management of cerebral bleeding with fibrinogen, with a minimal target peak fibrinogen level of 1.5 g/L.[7] Most experts agree that secondary prevention should be started after a first life-threatening hemorrhage with a suggested fibrinogen level goal of ≥0.5 g/L.[7]

Congenital fibrinogen deficiency disorders have a wide clinical spectrum. Thrombosis is hypothesized to occur as a consequence of low fibrinogen levels that favor an increase in thrombin and a prothrombotic state.[1] On the other side, fibrin is primarily involved in clot formation and its absolute deficiency may be involved in spontaneous bleeding, as presented in our case.

In conclusion, most cases of hypofibrinogenemia are asymptomatic; however, some patients exhibit catastrophic bleeding such as intracranial hemorrhage, while others may present as thrombotic occlusion of cerebral vessels.[3] As practicing clinicians, we should be aware of the highly varied clinical spectrum in these rare bleeding disorders since treatment strategies differ depending on the affected side of the coagulation cascade.

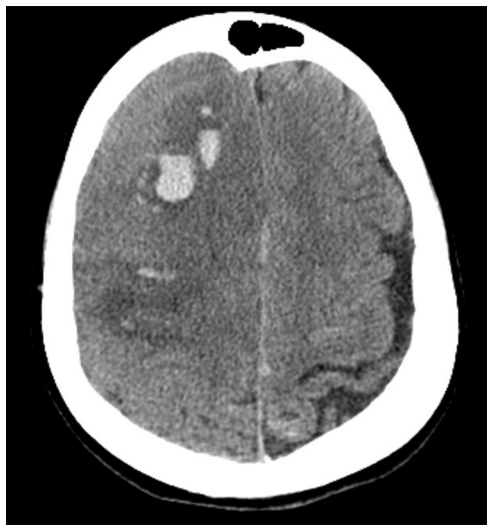

Figure 1: *CT scan. Right frontoparietal fluid levels and subarachnoid hemorrhage.*

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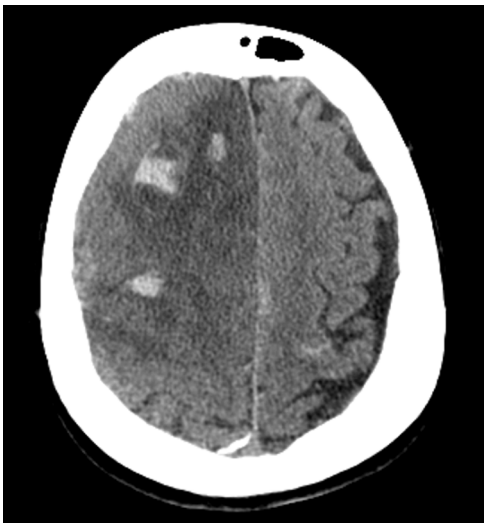

Figure 2: *CT scan. Right frontoparietal hemorrhage with marked perilesional edema and fluid levels. Left subarachnoid hemorrhage.*

Disclosures

The authors do not have anything to disclose.

Statement of authorship

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