Intracranial Hemorrhage (ICH) in a 5-years-old Child with Severe Hemophilia B and Inhibitors with Anaphylaxis: Treatment Issues

SÃO JOÃO

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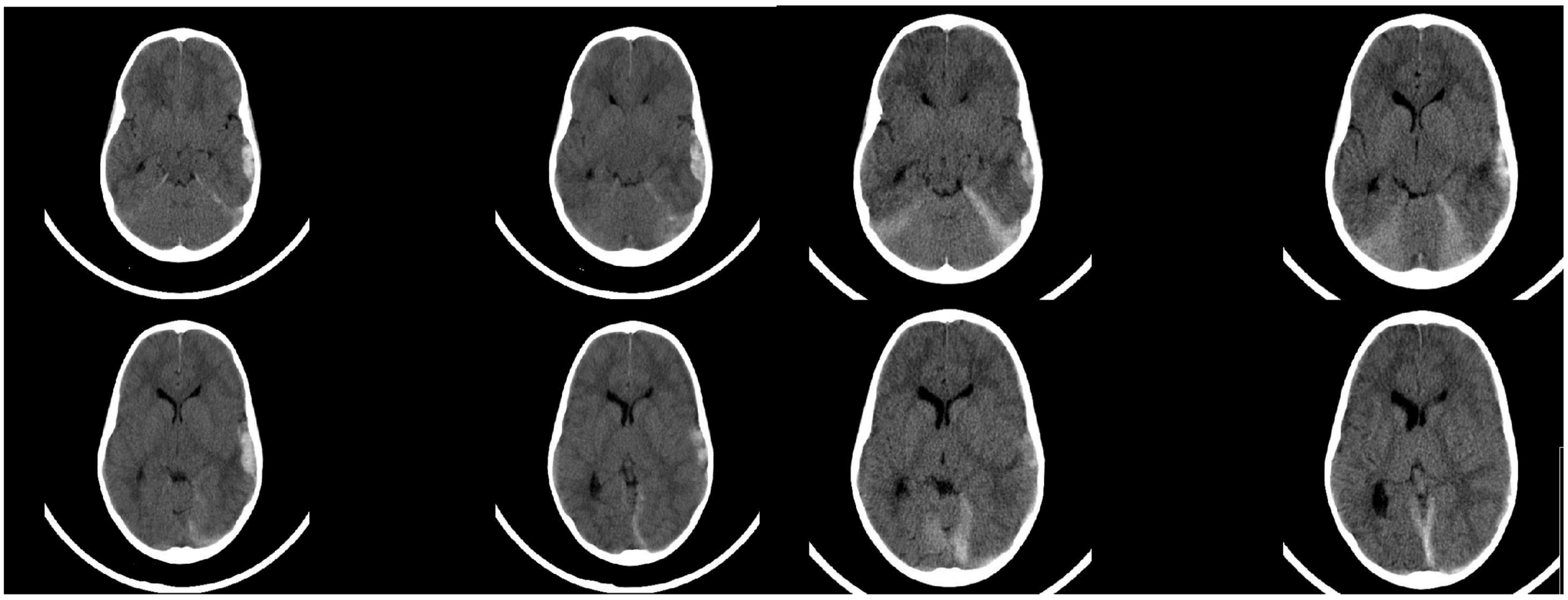
Background:

Intracranial haemorrhage (ICH) is a potential life-threatening complication in patients with severe haemophilia and inhibitors which develops spontaneously in most situations. Treatment to achieve haemostasis includes bypassing agents, such as FEIBA® or recombinant activated factor VII (rFVIIa) and should be urgently instituted.

Case Report:

A 5-year-old male, with no previous family history, was diagnosed with severe hemophilia B at the age of 4 months, due to unusual ecchymoses and a prolonged aPTT. He had been followed at our centre and replacement therapy was only needed 14 months after diagnosis. A plasma-derived FIX concentrate (OctanineF)® was instituted on bleeding episodes and after 4 exposure days (ED), he developed inhibitors with anaphylaxis. Since then, he has been treated with rFVIIa (NovoSeven)® and due to frequent bleeding situations, he began prophylaxis with 160 µg/kg 3 times/week.

On October 2011, he was admitted to the pediatric urgency with intense headache persisting after acetaminophen, photophobia and drowsiness. The computed tomography (CT) scan showed a frontal contusion and a left fronto-temporo-parietal acute subdural hematoma. Mannitol 20% and intravenous morphine was started and a megadose bolus of 270 µg/kg rFVIIa was given. He was maintained on clinical surveillance and it was scheduled bolus of 90 µg/kg q2h for 48h, on day 3 q3h, with the dosing interval increasing thereafter. No change observed in the CT scans 24h and 48h after admission. On day 10, after an effort to defecate due to morphine constipation, patient was more prostrated, with intense headache and a CT scan was performed. A new intracranial subarachnoid hemorrhage was observed as an expansion of the the previous hematoma. As the scheduled interval between doses on that particular day was 8 hours, a megadose bolus of 240 µg/kg rFVIIa was given and the interval between doses again shortened and maintained 110 µg/kg q2h for 5 days (until consistent clinical improvement). The interval between doses was subsequently extended. CT scans performed on day 18 and 24 showed marked reduction of hematoma and subarachnoid hemorrhage. The patient was discharged on day 25, without neurological sequelae and full recover. The total dose of rFVIIa spent was 17 mg/kg on 152 infusions.



Day 1 Day 10

Comments and Issues:

No thrombotic complications appeared, despite intensive treatment with rFVIIa. Although schedule replacement therapy after intracranial hemorrhage in hemophilic patients with inhibitors, is still a matter of discussion our patient remains on prophylaxis with rFVIIa 90 µg/kg daily, for at least 6 months and then every other day. Pharmacoeconomic impact in this scenario is a challenge, as cost for treating this patient until discharge was 265.000 € and daily prophylaxis for 6 months, 252.000 €.

Despite low rate successful achievement of immune tolerance in hemophilia B patients, a more recent approach in the management of patients with inhibitors includes the use of anti-CD20 monoclonal antibody, rituximab. We are now proposing for this patient immune tolerance induction including a desensitization programme with increasing doses of FIX and rituximab.

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