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Clinical Case

Multiple Spontaneous Intracerebral Hematomas in a Child with Hemophilia and Sickle Cell Trait: A Case Report

Hématomes cérébraux spontanés multiples chez un enfant hémophile porteur du trait drépanocytaire : à propos d'un cas

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ABSTRACT

Intracranial hemorrhage (ICH) is a major life-threatening complication in hemophiliac patients but rather rarely encountered in sickle cell patients. It often occurs during childhood in response to a minimal head traumatism in hemophilia. Its diagnosis and therapeutic management can be difficult, especially in Africa where coagulation factor replacement is often lacking. We are reporting the case of an 8-year-old boy presenting with severe hemophilia A, sickle disease trait and Down's syndrome. Six days prior to his admission, the child reported severe headaches and visual disorders leading to a fall with loss of consciousness. Upon clinical examination, an intracranial hypertension syndrome was found. The Brain Computed Tomography revealed multiple intracranial hematomas associated with subarachnoid hemorrhage complicated by hydrocephalus. The patient benefited from a coagulation factor VIII substitution therapy and neurological monitoring. The outcome was favorable and the follow-up Brain CT scan showed a complete resorption of the hematomas. Spontaneous intracranial hematoma in sickle cell disease and hemophilia raises a diagnostic problem and its management remains difficult in Africa due to the unavailability of replacement therapy. Early diagnosis and appropriate management would reduce the morbidity and mortality associated with intracranial hypertension.

RÉSUMÉ

L'hémorragie intracérébrale est une complication redoutable de l'hémophilie, mais elle est rare chez l'enfant drépanocytaire. Elle survient généralement après un trauma minime chez l'hémophile. Le diagnostic et la prise en charge peuvent être difficiles en Afrique du fait du manque de composés sanguins appropriés. Nous reportons le cas d'un garçon de huit ans porteur d'une hémophilie A sévère, d'un trait drépanocytaire et d'un mongolisme. Six jours avant l'admission, l'enfant a signalé des céphalées sévères et des troubles visuels ayant conduit à une chute avec perte de conscience. L'examen clinique a montré un syndrome d'hypertension intracrânienne. Le scanner cérébral a mis en évidence de multiples hématomes intracrâniens et une hémorragie méningée compliquée dar une hydrocéphalie. Le traitement a associé un traitement à base de facteur de coagulation VIII et un monitoring neurologique. Le scanner de contrôle a montré une résolution complète des hémorragies. L'hémorragie cérébrale chez le sujet drépanocytaire hémophile pose des problèmes diagnostiques et son traitement reste délicat. Un diagnostic précoce et une prise en charge adaptée pourraient réduire sa morbidité et sa mortalité qui sont essentiellement liés au syndrome d'hypertension intracrânienne associé.

INTRODUCTION

Intracranial hemorrhage (ICH) is a major complication of hemophilia which often arises during childhood [1], and is rarely observed in patients with a sickle cell trait. In children with hemophilia, it usually occurs in the context of mild to moderate head trauma, whereas in patients with sickle cell disease the most frequent vascular complication is ischemia. ICH builds up a greatest challenge to the survival of severe hemophiliac patients, even in developed countries where these patients have the best quality of care [2]. The location of hemorrhage sunders approximately equally between subdural hematoma, intracerebral hemorrhage and subarachnoid hemorrhage (3). We are reporting the case of an 8-year-old boy who presented with multiple spontaneous ICHs with favorable outcome under medical treatment and neurological monitoring.

CASE PRESENTATION:

An 8-year-old boy not enrolled in school, and suffering from Down's syndrome and severe hemophilia A, carrying as well sickle cell trait (SCT) was admitted to our hospital emergency room. Since the age of 3.5, he started having frequent checks of his clinical status at the International Hemophilia Treatment Center (IHTC) and had ongoing prophylactic therapy. However, due to

family constraints, his treatment was discontinued three years later. He was admitted to the emergency ward 6 days after the onset of his symptoms. He reportedly had intense headaches, photophobia and recurrent consciousness disorders, which led to a fall with initial loss of consciousness along with 2 episodes of vomiting. The clinical examination on admission revealed pale mucous membranes, with a stable hemodynamic and ventilatory status. The neurological examination showed an impaired consciousness with a Glasgow Coma Scale assessed to 13, meningeal stiffness and a cerebellar syndrome. The craniofacial examination showed a right occipital subcutaneous hematoma. The emergency brain CT scan showed multiple hemorrhagic lesions: a bilateral cerebellar hematoma [Figure 1], a left temporal hematoma [Figure 2], and a meningeal hemorrhage complicated with early hydrocephalus [Figure 3]. The blood count revealed an anemia of 8.4 g/dl. Screening for inhibitors could not be performed.

The patient received coagulation factor replacement at a dose of 600 IU/kg as a loading dose, then 30 IU/kg/day for 7 days, associated with tranexamic acid. He also beneficiated from a transfusion of packed red blood cells, fresh frozen plasma for 3 days, analgesics and isotonic saline. A follow-up Brain CT scan performed after 2 weeks of treatment showed complete resorption of the hematomas. The child was transferred to hematology unit for further check-ups and screening of inhibitors factors.

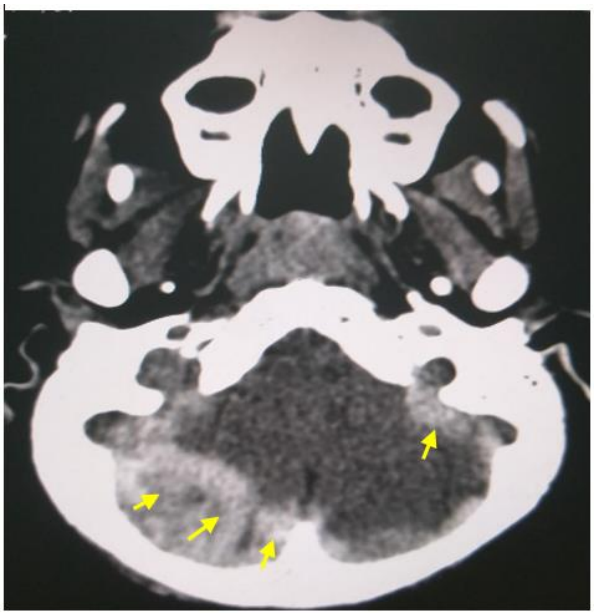

Figure 1: Brain CT axial section: Posterior fossa hematoma, more prominent on the right (yellow arrow)

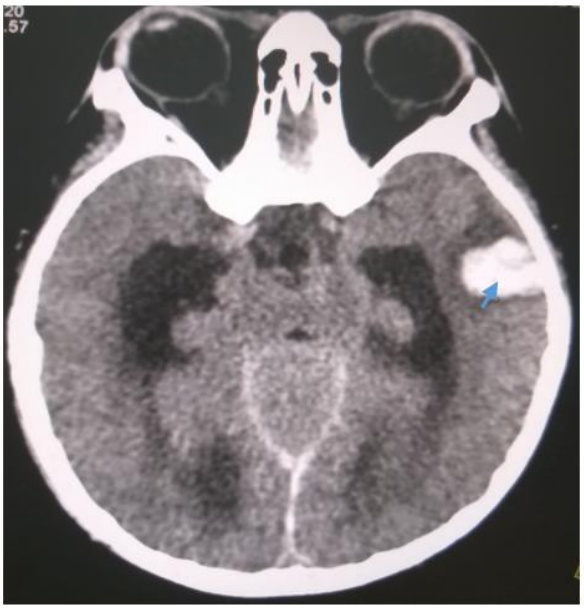

Figure 2: Brain CT axial section: left temporal hematoma (blue arrow)

DISCUSSION

Hemophilia is a genetical bleeding disorder whose gene is carried on the X chromosome, responsible for a deficiency of anti-hemophilic factor A (factor VIII) or anti-hemophilic factor B (factor IX). It is a ubiquitous disease with an incidence of 1 in 10,000 births worldwide. Hemophilia A is predominant (85%) while hemophilia B is only 15% [4]. ICH is among the leading causes of death in hemophiliac population and is responsible for 75% of neurological sequelae in survivors [5]. Cerebral complications such as ischemic stroke are the most widely described in children with sickle cell disease. In contrast, less than ten cases of spontaneous extradural [6] or subdural [7] hematoma in children with sickle cell disease have been described in the literature. In hemophiliac children, minor head traumatism is the main cause of ICH and is often overlooked. However, spontaneous ICH can occur in patients with severe hemophilia [8], which is thought to be attributable to coagulation factor deficiency. In sickle cell patients, ICH can occur in two ***major*** ways. On the one hand, a "vacuo" mechanism occurs on underlying ischemic cerebral atrophy leading to pericerebral effusion and tension of the bridging veins. On the other hand, a veno-occlusive mechanism is associated with a bone anomaly [9]. With regard to this case, since our patient's intellectual disability could cause falls during activities (games), we suggested the hypothesis of traumatism. Moreover, the consultation was delayed because of the enclosure of his village. The symptoms most frequently encountered in ICH are headaches (44.8%), vomiting (44.8%) and lethargy (41.3%). Other neurological manifestations can be observed such as convulsions (10.3%) and coma (10.3%) [10]. In patients with hemophilia, the diagnosis of ICH should not be ruled out on the basis of the absence of history of head injury or the absence of clinical signs [1]. For individuals with moderate or minor hemophilia, the risk of intracranial hemorrhage is two times lower than in patients with severe hemophilia [11]. ICH, which has an incidence of 3-12% [2], accounts for more than 30% of deaths in hemophiliacs [12] and 24-65% in sickle cell patients [13]. Mortality is more closely dependent on the location of the hemorrhage than to the severity of the hemopathy. Subdural hematoma

and subarachnoid hemorrhage are locations with a better prognosis [3].

Cranial CT or MRI is very useful. Its performance allows, in suspicious cases to diagnose and confirm ICH. This imaging allows visualization of the site, the amount of bleeding and predicts prognosis, but should not delay the administration of coagulation factors under any circumstances.

The coexistence of sickle cell trait and hemophilia is uncommon and rarely described in the literature, even in predominantly black populations, where the prevalence of both conditions is higher [14]. Few cases have been described in the literature: Glenn et al reported the simultaneous presence of hemophilia A and homozygous sickle cell disease in a 30-year-old black man [15], Kumar and Hareng reported an association of homozygous Sickle Cell Disease and hemophilia B, in a 15-year-old African-American man [16]. Many authors consider Sickle Cell Disease to be a hypercoagulable prothrombotic state and hypothesize that the association of sickle cell disease with hemophilia should alter the thrombo hemorrhagic balance and positively improve hemorrhagic hemophiliac phenotypes [17].

Bleeding disorders are contraindications to intracranial pressure monitoring (3). However, given the multitude of hemorrhagic lesions, the absence of a qualified anesthesiologist, the lack of an on-site hematologist, and the impossibility of emergency evacuation to the International Hematological Treatment Center, our patient was a candidate for neurologic monitoring. In addition, the availability of sufficient quantities of clotting factor concentrates must be ensured before major surgery is undertaken [18]. Some authors suggest that intracranial bleeding can be managed conservatively in most patients with hemophilia [2]. It is recommended in the literature to saturate at 100% at least during the first 5 days to ensure very rapid resorption of bleeding [4]. However, in our patient, we started clotting factor replacement with an initial dose of 60 IU/kg and then continued with a dose of 30 IU/kg because we did not have enough quantity in our hospital.

Our patient was used to be on prophylaxis therapy that was interrupted later on, due to family constraints (moving to live with his grandparents in a very remote village with no access to electricity). This case illustrates the difficulties of regular check-ups of that therapy in a rural environment, which lead to the discontinuation of treatment and the occurrence of intracranial hemorrhage. Nevertheless, this case shows the effectiveness of the management of a major hemorrhage, even at 450 km from the International Hematological Treatment Center (Dakar) with conservative treatment.

CONCLUSION

Intracranial hemorrhage is a serious complication of hemophilia with a high morbi-mortality but rather rare in sickle cell patients. Its management is multidisciplinary involving the hematologist and the neurosurgeons and represents a real challenge for a neurosurgery unit without an adequate technical platform.

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