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CASE REPORT

Iliopsoas Hematoma as Unusually Early Onset of Hemophilia A in a Young Infant

Coppo D[1], Rossi L[2], Raffaldi I[3], Aguzzi S[3], Castagno E[3], Ricca I[4] and Bondone C[3]*

[1]*Università degli Studi di Torino, Turin, Italy*

[2]*Department of Pediatrics and Neonatology, Ospedale Civile Ciriè, Turin, Italy*

[3]*Department of Pediatric Emergency, Regina Margherita Children's Hospital, A.O.U. Città della Salute e della Scienza di Torino, Turin, Italy*

[4]*Transfusion Medicine, Department of Diagnostic, Regina Margherita Children's Hospital of Turin, Italy*

***Corresponding author:** *Irene Raffaldi, MD, Department of Pediatric Emergency, Regina Margherita Children's Hospital, A.O.U. Città della Salute e della Scienza di Torino, Turin, Italy, Tel: +39011-313-5205, Fax: +39011-313-5060*

Abstract

A 2-month-old infant was admitted for irritability and hypomobility of the left lower limb. Ultrasound revealed a deep hematoma of the iliopsoas muscle and coagulation tests showed increased activated partial thromboplastin time (aPTT). The finding of marked reduction of blood coagulation factor VIII (FVIII) led to the diagnosis of severe Hemophilia A. The infants were promptly put on i.v. factor VIII concentrates, resulting in rapid clinical improvement. As far as known, this is the first documented case of iliopsoas hematoma in such a young infant as early onset of Hemophilia A. Timely diagnosis of hemophilia is crucial to start prompt appropriate treatment, in order to avoid severe bleeding and long-term complications.

Keywords

Hemophilia A, Iliopsoas hematoma, Infant, Inherited bleeding disorders

Introduction

Hemophilia A can is an X-linked inherited bleeding disorder caused by the deficiency of coagulation factor VIII (FVIII). Hemorrhagic episodes mainly affect joints and muscles and can be either spontaneous or derived from trauma [1]. Iliopsoas hematoma stands among possible, though rare, onsets of Hemophilia A in children, representing a diagnostic challenge for pediatricians, on the grounds that clinical features are usually slight and not specific, especially when affecting young infants [2]. Clinical onset in the first months of life, before infants start to crawl, is very rare. We report the case of a young infant with hemophilia A diagnosed at the Emergency Department after spontaneous iliopsoas hematoma.

Case Description

A 2-month-old male infant is admitted to the pediatric emergency department showing irritability and prolonged crying in apyrexia. The anamnesis revealed that the child was born at term by spontaneous delivery, that maternal vaginal culture was positive for Streptococcus agalactiae, and that intrapartum antibiotic prophylaxis was incomplete; whereas no personal problems were referred.

According to family history, the mother has been affected by metrorrhagia and postpartum hemorrhage even though the finding of the screening performed during postpartum stage was normal coagulation test; the other son, the patient's 4-year-old brother, is in good health.

Upon arrival, the patient is in good general health, apyretic, with normal cardiopulmonary examination, meteoric and painful abdomen and spontaneous fluid motility. In the suspicion of abdominal colic, a rectal enema is performed with benefit and the patient is discharged from the hospital.

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After two days, the patient is taken back to the emergency department for the appearance of hypomobility of the lower left limb, associated with the reappearance of inconsolable crying, especially at the diaper change. No trauma is reported. At physical examination, the lower left limb is semi-flexed, apparently in analgesic posture; no other clinical anomalies are identified. The negativity of the inflammatory markers and radiological investigations (abdomen and hip ultrasound) enables to exclude in the first instance the presence of hip infectious processes and space-occupying lesions. On the other hand, coagulation tests show an unexpected increase in the activated partial thromboplastin time (aPTT) amounting to 126.9 seconds (normal values 25-38 seconds), with an aPTT ratio of 4.09. In the clinical suspicion of hemorrhagic coagulopathy, coagulation factors VIII, IX, XI, XII and von Willebrand are dosed and an ultrasound is repeated to check the iliopsoas muscle. Blood tests show a marked deficit of FVIII of 0.2 percent (%) (normal values: 50-200%) and the ultrasound reveals a hematoma affecting the iliopsoas muscle. The clinical and laboratory picture is compatible with severe Hemophilia A.

The infusion of recombinant FVIII is promptly started and carried out for 9 days with a progressive improvement of the clinical condition and an increase in FVIII blood levels. The patient starts a follow-up at the Hemophilia Center of Regina Margherita Hospital and is submitted to anti-hemorrhagic prophylaxis with periodic infusions of recombinant FVIII.

Genetic analysis identifies the intron 22 inversion mutation in the FVIII gene in the infant and in his mother.

After 4 months from the beginning of the prophylaxis, the infant develops FVIII inhibiting antibodies and a considerable difficulty to have a stable venous access emerges. Therefore, the prophylaxis is replaced with the weekly subcutaneous administration of Emicizumab, a bispecific antibody which mimics the co-factor function of FVIII. The patient is currently well and has not showed any further bleeding.

Hemophilia A can be defined as an X-linked hemorrhagic disease caused by a mutation in the FVIII gene, resulting into the deficiency or dysfunction of clotting FVIII. The disease at issue can be considered rare as it occurs in live male births with a frequency approximately ranging from 1 in 4000 to 1 in 5000. The gene mutation is usually inherited, yet sporadic disease, presumed due to a new mutation, is common in 30-55% of cases [1]. Depending on the percentage plasma level of FVIII, Hemophilia is classified as mild, moderate or severe (FVIII levels respectively 6-40%, 1-5%, < 1% of normal). Severe Hemophilia A affects almost exclusively males, although milder clinical pictures are described also in female carriers [2].

The main clinical presentation is characterized by acute hemorrhagic disorders and the most frequently affected sites are the joints, in particular the knees, ankles and elbows. The recurrence of joint bleeding, if not properly treated with the infusion of the deficient factor, can lead over time to the progressive damage of the joint cavity with the development of hemophilic arthropathy [3]. Moreover, hemorrhages under the form of deep hematomas can affect the muscular system, above all the quadriceps and iliopsoas muscles, like in the case at issue. Further areas possibly involved by the bleeding are the nasal, oral and gastrointestinal mucosa. Urogenital involvement can lead to hematuria and renal colic caused by clots. Intracranial bleeding is rare, but it constitutes the main cause of mortality in these patients [3]. As mentioned above, the bleeding can be spontaneous, as happens in the most severe forms, or it can be caused by trauma, even if of a minor entity, in the mild and moderate forms. Severe forms of Hemophilia A generally emerge within the first 12-36 months of life, with a wide age range for the appearance of the first bleeding. Newborns rarely show bleedings at the time of delivery and the most frequently affected areas are the central nervous system, cephalohematomas and venipuncture sites. In most cases the onset occurs following even minor injuries in conjunction with crawling or the start of walking with bruising or joint and musculoskeletal bleeding in 10-25% [4,5].

The clinical case at issue concerns a serious A Hemophilia in a 2-month-old child bearing the following features: Early onset of the disease; unusual clinical picture characterized by the presence of a deep hematoma in the iliopsoas muscle (likely to be caused by reiterated micro-traumas related to diaper changing). The peculiar nature of the mentioned clinical condition can be reasonably inferred from the scarcity of scholarly studies devoted to pediatric patients with a hematoma affecting the muscle at issue [2,6,7]. As far as known, no case of iliopsoas muscle hematoma has been reported before the one at issue in patients affected by hemophilia younger than 6 years of age. The clinical manifestation of iliopsoas hematoma in infants can be slight and unspecific, which entails a real diagnostic challenge for pediatricians: The mentioned features are likely to delay the identification of the disease and to induce an underestimation of its real incidence. The main clinical symptoms that have been recorded for school-age children are the following: pain in the lower abdominal quadrants, in the groin and lumbar area; paresthesia on the medial side of the thigh, or a palpable mass or rope in the inguinal region. As potentially life-threatening complications one could mention anemia and hypovolemia [8]. In younger children, the symptoms of psoas hematoma can be limited to inconsolable crying crisis and irritability; only in the most advanced stages, the patients can show reduced mobility of the lower limb [2,7].

In order to exclude other pathological conditions that may share a similar clinical presentation (such

as hip arthritis and abdominal compressive masses) pediatricians are required to perform blood chemistries tests and radiological examination (abdominal and hip ultrasonography) [9]. Besides, to identify a possible unknown coagulopathy a coagulation test is recommended. Moreover, in the clinical and hematological suspicion of a hemorrhagic disorder, a muscle ultrasound scan of the iliopsoas muscle is indicated to identify a possible deep hematoma and proceed to the correct diagnosis [10].

Hemophilia should be considered in all male children with bleeding and suggestive family history. Nevertheless, it should be borne in mind that around a third of affected patients have a negative family history, which is explained by a *de novo* mutation in the mother or child [3]. In the case here illustrated, the patient's mother reported a history of metrorrhagia and postpartum hemorrhage with normal coagulation tests. One possible reason for the erroneous normality resulting from the hemorrhagic coagulopathy test undertaken in the post-partum stage lies in the stressful context related to pregnancy and delivery, which may reasonably lead to the overcoming of the normal FVIII levels [11].

When the presence of a prolonged aPTT in a child raises the suspicion of a hemorrhagic coagulopathy, the undertaking of a mixture test is recommended: In the event of a non-correction of the aPPT, pediatricians must consider the possibility of a circulating anticoagulant, whereas, in the opposite event, they are required to perform the dosage of those coagulation factors absent which the length of aPTT may increase, i.e. FVIII, von Willebrand, factor IX, factor XI, factor XII [12].

In case of FVIII deficiency, Hemophilia A can be diagnosed and a genetic analysis shall be performed to identify the presence of a specific mutation [1]. Hemophilia A therapy is based on factor VIII replacement with plasma derivatives or recombinant protein. The mentioned treatment can be undertaken following the demand to treat active bleedings, or as a prophylaxis aimed at preventing hemorrhages [5]. In the suspicion of iliopsoas hematoma associated with Hemophilia A, FVIII infusion therapy should be promptly administered at the dose of 40-50 IU/kg of factor, such as in case of hematomas or hemarthrosis [13].

A consensus emerges from medical literature on the efficiency of a long-term prophylaxis with factor VIII to prevent dangerous hemorrhages such as intracranial and the development of hemophilic arthropathy. Such prophylaxis is generally started after the first year of life, that normally matches with the period of time in which the child takes his/her first steps, and must be carried out throughout his/her life. In the case here-illustrated, the patient has started the prophylaxis earlier, due to the premature onset of Hemophilia [5].

About 25% of patients with severe Haemophilia A develop FVIII inhibiting antibodies that hinder the effectiveness of the mentioned therapeutic program [14]. Emicizumab is a recombinant humanized monoclonal antibody capable of building a bridge between the activated factor IX and the coagulation factor X, in order to restore the function of the missing activated FVIII. It is approved for prophylaxis in individuals affected by hemophilia A, with or without inhibitors, and it is administrated by subcutaneous way [15]. The choice of the adequate therapies should be case-by-case and tailor-made, i.e. designed on individual safety, risk of inhibitor development, pharmacokinetics and wealth. Gene therapy is currently under development [5].

Conclusion

In light of the above-undertaken analysis of the mentioned clinical case, time is ripe to draw the following conclusions: hemophilia A is a rare genetic hemorrhagic disorder caused by deficiency of FVIII; it causes exaggerated bleeding especially involving muscles and joints; hematoma of the iliopsoas constitutes one of the possible manifestations and must always be considered by pediatricians in an infant showing evident signs of irritability; early diagnosis and prophylaxis or treatment are essential to avoid serious bleeding and the development of long-term complications. To that purpose, coagulation tests and ultrasound reveal to be helpful tools. In young children affected by difficult venous access, with or without inhibitors, Emicizumab may constitute a valid subcutaneous alternative to prophylaxis.

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