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Case report

Hemarthrosis subtalar, a rare diagnosis☆

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ABSTRACT

Type B hemophilia usually affects patients with a family history of this disease and has a typical clinical picture. However, in the present case it appeared in a patient outside the typical age with no family history of hematologic malignancies and with an unusual clinical picture.

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Hemartrose subtalar, um diagnóstico raro

Palavras-chave:
Hemofilia B
Hemartrose
Articulação do tornozelo

RESUMO

A hemofilia do tipo B afeta normalmente pacientes com história familiar positiva para a doença e se apresenta com quadro clínico típico. No presente caso, no entanto, o diagnóstico se deu em um paciente fora da idade típica, sem histórico familiar de doenças hematológicas e quadro clínico diferente do habitual.

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Introduction

Hemophilias are hematologic diseases that results in changes in the coagulation process, due to deficiency of a clotting factor. The disease has a genetic cause and the most common hemophilias are type A (factor VIII deficiency) and type B (factor IX deficiency).

Type B (or Christmas disease) accounts for 14% of cases, equivalent to one case per 30,000 births of male children.[1,2] The disease is highly associated with males due to the fact

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that the altered gene is located in the long arm of the X chromosome. The most common signs are bleeding, often in the mucous membranes, joints, and subcutaneous tissue. Symptoms include hemarthrosis, bruisings, hematuria, and gastrointestinal bleeding.[3] The diagnosis is made by tests that assess the coagulation cascade: prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT). If the intrinsic pathway of coagulation is affected, the PT will be normal, but the aPTT will be higher. To confirm factor IXdeficiency, the factor itself should be measured.[3,4]

Hemarthrosis is a bleeding in the joints and can be of traumatic, hematological or neurological origin, among others.[5] The most common cause is trauma to articular regions. In cases where it courses with neurological problems, they are usually associated with the Charcot joint, an alteration in which there is no articular proprioceptive (neurological) perception. The hematological etiology may be induced by drugs or acquired hematological diseases (myeloproliferative diseases and thrombocytopenia, among others), or be hereditary (hemophilia). The most common bleeding sites are the knee, elbow, and tibio-talar joints.[6,7] The initial symptoms are redness and swelling, sometimes associated with paresthesia, and the process may progress to severe pain.[8] If the hemarthrosis is not treated, the inflammatory process will become chronic and may lead to functional impairment. The diagnosis can be made using imaging tests such as ultrasonography, CT scan, or magnetic resonance imaging (MRI); however, the gold standard is the aspiration of the joint fluid.[7,9,10]

Hemarthroses in patients with hemophilia B are usually indicators of moderate or severe factor IX deficiency. When the ankles are affected, it is difficult to exclusively use the symptoms to distinguish which specific joint was affected. According to Rodriguez-Merchan[11] and Lofqvist et al.,[12] the subtalar joint may be associated in approximately 50% of the cases. However, it is rarely involved and reported in isolation. The clinical picture in these patients may be unclear, since many do not experience severe pain or significant functional gait limitation.

This study aimed to describe the difficulty in the diagnosis of hemophilia B in an extremely rare event of isolated hemarthrosis of the subtalar joint.

Case report

Male patient, aged 1 year and 8 months, born and raised in São Paulo, Brazil, white, and of no declared religion. His mother reported he had been having difficulty to walk for eight days, due to problems in weight bearing and dorsiflexion of the left foot. The mother also reported an abrupt and progressive swelling in the lateral and posterior region of his ankle. He remained afebrile at all times and was prescribed Predsim® (sodium prednisolone phosphate) and Hixizine® (hydroxyzine hydrochloride) for suspected insect bite (Fig. 1).

The mother denied changes in other systems, routine use of medications, and history of chronic diseases in the family. The vaccine immunizations pertinent to his age range were up-to-date. The child had a history of bronchiolitis at 5 months; coxsackievirus infection at 8 months, and an episode of transient hip synovitis at age 1 year and 2 months, which resolved itself in a short period of time.

At the general physical examination, there were no cardiovascular, pulmonary, abdominal, or neurological changes.

The orthopedic physical examination showed increased volume throughout the ankle, but without local temperature increase or redness. The gait was altered, with left side limping and impaired weight bearing.

The results of the initial tests were as follows: C-reactive protein (CRP), 8.22 mg/L; capillary glucose, 87 mg/L; and erythrocyte sedimentation rate (ESR), 15 mm. The complete blood

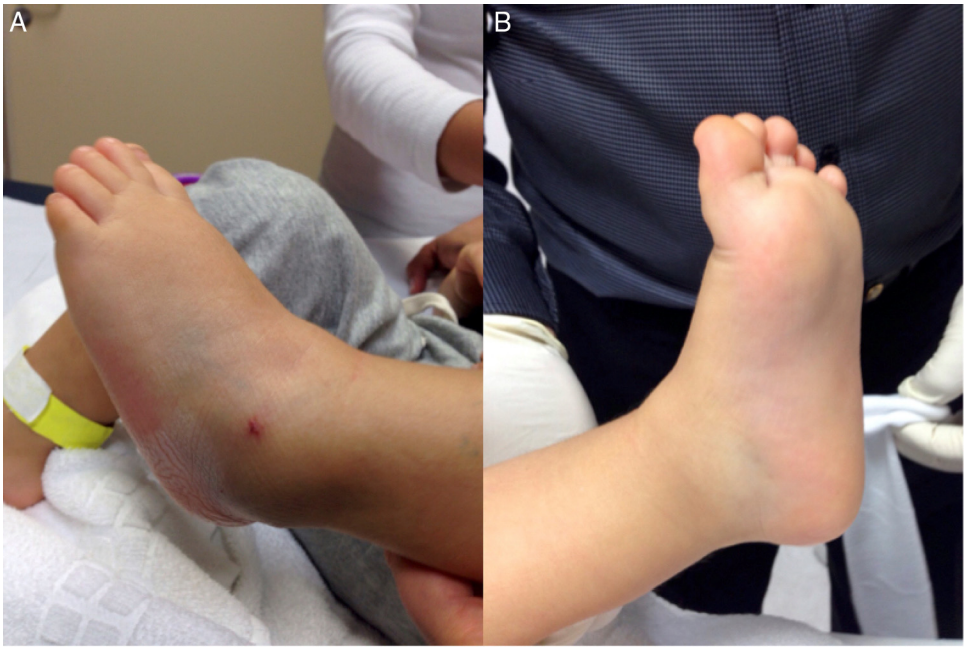

Fig. 1 – (A) Lateral view of the patient's foot at admission; (B) medial view of the foot at admission.

count results were as follows: hemoglobin (Hb), 11.9 g/dL; hematocrit (Ht), 34.9%; mean corpuscular volume (MCV), 70.6 fl; mean corpuscular hemoglobin (MCH), 24.1 pg; mean corpuscular hemoglobin concentration (MCHC) 34.1 g/dL; red cell distribution width (RDW), 15.2; leukocytes, 15.98×10^3 uL, showing a predominance of lymphocytes with 7447 uL; neutrophils, 7015 uL; and monocytes, 1135 uL. In addition, the platelets count was 460×10^3 uL.

Comparative radiographs of the ankles were performed, which did not demonstrate bone lesion; however, it was possible to visualize the increase in soft tissue densification in the lower portion of Kager's fat pat and of the entire lateral periarticular region of the hindfoot.

Ultrasound examination of the left foot and ankle evidenced the thickening of the long fibular tendon, which was hypoechoic and heterogenic (tendinopathy), but without ruptures. There was also mild skin and subcutaneous edema in the peri- and infra-malleolar lateral region and absence of joint effusion.

As these data were of low relevance for the diagnosis, an MRI was requested, and the initial report in the emergency department showed a joint effusion in the posterior subtalar joint with signs of synovitis in the tibial talar joint, associated with adjacent soft tissue edema that extended to the sinus tarsi and to Kager's fat pad. Another noteworthy finding was a nodulariform image of likely synovial proliferation adjacent to the lateral contour of the tarsal sinus, which measured approximately 1.5 cm in the longest axis.

The alterations were observed mainly in the retromalleolar topography, in the fibular region.

Diagnostic hypotheses of allergy to insect or spider bite due to localized hyperemia (Fig. 1), to villonodular synovitis, or to the inflammatory/infectious process were raised.

Punctures were then made on the ankle in the operation room, guided by fluoroscopy. The first puncture was made in the lateral region, anterior to the malleolus, along the sinus tarsi; another puncture was made posteriorly (between the fibular tendons and the malleolus), and the third laterally in the infra-malleolar region.

At the first puncture the aspect was of synovial fluid, less thick and more fluid, with transudate characteristics. In turn, in the second puncture, constant blood dripping of venous aspect and continuous flow was observed. The last puncture, made for triangulation and an attempt to lavage the space, resulted negative, without flow or backflow. All collected fluid was sent for anatomopathological and laboratory analysis.

The cytological analysis of the transudate collected in the first puncture indicated 42% neutrophils, 34% lymphocytes, and 20% monocytes. In the second puncture, lymphocytes predominated (51%), followed by neutrophils (38%) and monocytes (7%). In both culture, the results were negative for aerobic, anaerobic, and acid-alcohol resistant bacilli (no growth).

During the surgical procedure, new laboratory exams were requested (two days after the first exams), including coagulation; however, there was not enough blood for this exam, due to the difficulty in collecting and to the rupture of punctured vessels. The other exams indicated higher inflammatory markers: CRP, 11 mg/L, and ESR, 18 mm. Furthermore, uric acid, creatine phosphokinase (CPK), aldolase, and creatinine were also outside the normal range: 2.8 mg/dL, 52 U/L, 7.9 U/L, and 0.27 mg/dL, respectively. Urea, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) had normal values at 228 mg/dL, 33 U/L, and 21 U/L, respectively. Finally, the complete blood count showed no alterations: Hb, 11.5 g/dL; Ht, 33.3%; MCV, 70.3 fl; MCH, 24.3 pg; MCHC, 34.5 g/dL; RDW, 15.3%; leukocytes, 13.6×10^3 uL, with a predominance of neutrophils (46%) and lymphocytes (42.6%); and platelets, 406×10^3 uL. In addition to these tests, the serologies for hepatitis A (IgM), hepatitis B (HBS antigen, HBE antigen, anti-HBS, anti-HBE, anti-HBC), hepatitis C (anti-HCV), Epstein Barr, cytomegalovirus, toxoplasmosis, erythrovirus, and HIV were all non-reactive.

Prophylactic antibiotic therapy with cefuroxime was performed after the surgical procedure.

In the 24 h following the procedure, the highvolume outflow of the bloody fluid persisted, staining the plaster in the first dressing change.

After the procedure, the ankle had its volume stabilized, mobility improved and pain decreased, but extensive ecchymosis appeared, including on the posterior region of the knee due to "cast friction" (Fig. 2), as well as in other regions.

Due to the presence of these symptoms, which are indicative of bleeding, and the fact that the examination was not performed due to the low volume of blood collected in the surgical center, a new coagulogram was requested, which showed a decreased PT of 11.9 s, as well as a reduced INR of 0.86. The aTTP was higher, at 85.5 s, with an increased patient/normal laboratory ratio of 2.52 and a standard platelet count of 433,000/mm^3. When assessed, the coagulation factors indicated that factor VIII was slightly increased at 201% (200% is the reference value), Von Willebrand factor was within the normal range (87%), and that the patient had a significant factor IX deficiency, with less than 1% activity (the minimum reference value is 60%).

Discussion

The incidence of type B hemophilia in the population is 1 in 20,000–30,000 live births and its prevalence of 5.3 per 1,000,000 men.[1] This hematologic disease accounts for 15% of cases of hemophilia, representing the second most common type. No predominance has been evidenced in any ethnic group.[6] Hemarthrosis corresponds to 85% of bleeding in these patients, often occurring in the second decade of life. The ankle is affected in 45% of the cases; of these, the subtalar joint is affected in 55%, but rarely in isolation.[6,12,13] The most common symptoms are pain, loss of mobility and joint function, axis deviation, and finally, ankylosis.[14]

The diagnosis is confirmed exclusively by laboratory alterations in the coagulogram, but some imaging tests help to establish the clinical picture. Radiography is an examination of low sensitivity and specificity for diagnosis. The effectiveness of the ultrasound examination is questioned in the literature; the authors who defend its use argue that it is a low-cost, non-invasive exam that can detect the presence of intra-articular fluid with ease.[7] MRI is considered the most sensitive test for detecting early changes; it can also highlight the difference in fluid effusions and synovial hypertrophy.[15] In the present

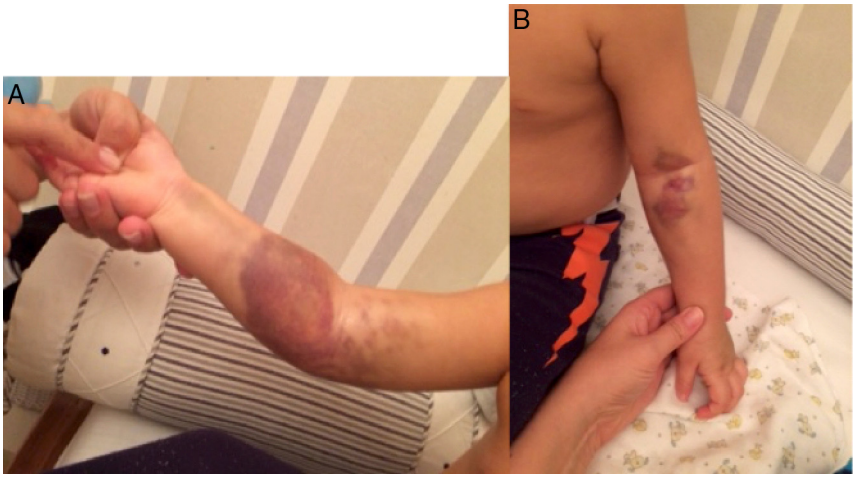

Fig. 2 – Ecchymosis after retention. (A) right arm; (B) left arm.

case, as the patient was a young child requiring anesthesia for the performance of the exam, an ultrasound was requested.

The image aspect indicates the possibility of alteration of the inflammatory nature, reinforcing the need to consider infectious etiologies in the differential diagnosis. These alterations were observed in all planes of the T1- and T2-weighted images. Reassessing the case, the authors highlighted the fact that, in addition to the synovial inflammation, the signal of the synovial fluid was heterogeneous, especially in T2-weighted images, which could correspond to intra-articular clots, thus raising the possibility of a coagulopathy (Fig. 3).

Type B hemophiliacs have normal PT with increased aTTP and factor IXdeficiency.[16] This was marginally different from that observed in the present patient, who had slightly decreased PT.

Differential diagnoses for cases of hemarthrosis are subdivided into traumatic and non-traumatic. Traumatic situations are easier to diagnose, due to the history of recent trauma in the region. Non-traumatic diseases include infectious diseases, as well as neurological, vascular, and hematological neoplasias. In order to establish a diagnosis, other signs and symptoms should be investigated, as well as possible laboratory changes. Among the hematological alterations, the origin of the deficiency must also be determined, in order to establish the most adequate treatment.

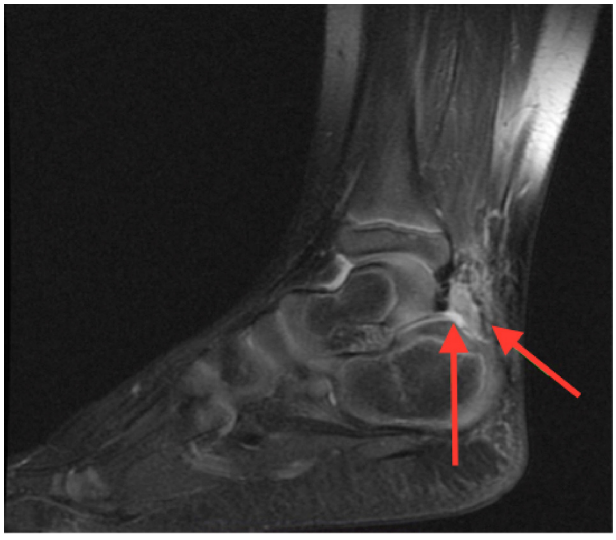

Fig. 3 – Sagittal MRI T2-weighted image. The tip of the arrow indicates nodulariform formation and clot.

Based on the increased aTTP, together with a close-to-normal PT and a very significant factor IX deficiency, the diagnosis of type B hemophilia was made and the specific treatment was initiated.

The importance of this report is to describe the possibility of the association of hemophilia with isolated hemarthrosis of the subtalar joint. No other cases with this specific combination were retrieved in the literature, which explains the initial difficulty to achieve the diagnosis. Epidemiology proves this rarity, as this was a patient in the first decade of life (under 2 years), in whom only the subtalar joint was affected, with a non-characteristic clinical picture and a patient who was not collaborative for the exam; moreover, there was no family history of the disease.

The authors conclude that that it is not uncommon to have patients in the pediatric age group with ankle volume increase and difficulty to walk. Therefore, the knowledge of similar cases and treatment strategies is relevant for the differential diagnosis.

Conflicts of interest

The authors declare no conflicts of interest.

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