Multiple Distal Pseudotumours in a Patient with Severe Hemophilia A and High Titer Inhibitors

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Introduction

Hemophilic pseudotumours (PTs), first described by Fernandez de Valderrama and Matthews [7], are rare complications of bleedings: 1-2% of patients in a large study over 25 years [1]; 1.89% in a study on 212 patients from Romania, aged between 0-25 years, followed for 11 years [15]. PTs develop after repeated, unresolved muscular hematomas, or subperiosteal hemorrhages [5, 16, 17]. The distinct clinical features of PTs are progressive enlargement, with destruction of the adjacent structures (bones, vessels, nerves) compressed by, or included within the PT. Pathologically, the PTs are blood collection in different states of organization, with a liquid or solid content, having one or more cavities; PTs are surrounded by a fibrous capsule with very rich blood supply, usually originating from more than one artery; calcifications, and ossification of the capsule, inflammatory cells, many histiocytes containing copious amounts of siderin may be seen [2, 4, 16].

Objectives, Patients

The study aims to analyze the characteristics (favoring factors, locations, imagistic aspects, evolution) and to evaluate the results of the medical and surgical approaches in a rare case of multiple consecutive distal PTs appeared in a single patient. The patient (G.E.) with severe familial hemophilia A (factor VIII:C <0.2%) was diagnosed at 9 months of age (1990), and treated in the IIIrd Pediatric Clinic, and respectively, in the Pediatric Surgical and Orthopedic Clinic Timișoara. Very high titre inhibitors were first diagnosed in 1998, and persisted at high levels (>10 BU). No treatment for immune tolerance induction (ITI) was applied. The molecular defect is not known. Inhibitors were absent in a patient’s affected cousin, with only a few exposures to FVIII.

The patient developed five consecutive distal PTs with different locations, between his ages of 8-13 years. The conservative measures were inefficient (progressive bone destruction, infection, hemorrhage), and radical surgical interventions were necessary in order to save the patient’s life. Replacement therapy with rFVIIa, and aPCC was used. An antiangiogenic treatment with Interferon alpha (IFNα) was applied for eight months, apparently with good results.
Results and Discussions

There are two types of PTs described by Gilbert [6]. **Proximal PTs** occur more frequently in adults, are localized in the proximal axial skeleton, especially around the femur and pelvis, probably start in the soft tissue and than secondarily erode the bones, and have a slow evolution, presenting as painless, firm, expanding mass. **Distal PTs** affect usually young, skeletally immature patients (children, adolescents), being located especially in the small cancellous bones (calcaneus, talus and metatarsals of the feet, seldom the carpus or other locations). Distal PTs are generally the result of direct trauma, are most probably secondary to unresolved intraosseous hemorrhages, and are characterized by rapid and painful evolution [6].

The extension, dimensions, content, and the number of cavities may be evaluated by x-ray, ultrasounds, CT, and MRI investigations; the epiphyseal, or the epiphysio-metaphysary distal PTs usually have multiple cavities, while the diaphyseal, or diaphyso-methaphysary PTs have a single cavity [2, 16, 17].

Multiple PTs were extremely rare described [8]. The presented patient is the single one in our experience with this type of complication. The PTs appeared consecutively, between the patients’ age of 8-13 years, being located at the both foots, the left knee, and the right shank.

The patient G.E. was diagnosed at the age of 9 months (1990) presenting a muscular hematoma after intramuscularly injection, and severe anemia. It’s important to underline that the familial care was inadequate (low socio-economic level, alcoholic father with advanced tuberculosis, unemployed, two brothers at school ages, mother working all days long), the patient being admitted many times with multiple muscular hematomas, advanced hemarthroses of the knees, opened wounds, gingival, lingual, and pharyngeal hemorrhages, epistaxis, epicranial hematomas, frequently with severe anemia or hemorrhagic shock. Chronic arthropathy of the knees and ankles developed in time. The replacement treatment with plasma, cryoprecipitate, and erythrocyte concentrate in his first two years of life was complicated with HCV infection (donors screening for HCV was introduced in our transfusions center in 1992), but he remained HIV negative (donors screening for HIV was introduced in our transfusions center in 1990); between 1992-1997 he was treated only with factor VIII concentrates, with good clinical response, although one surgical intervention for an infected hematoma, performed in 1995 under FVIII concentrate coverage, was complicated by severe hemorrhage. The psychological disturbances, repeated urinary tract infections with *E.coli*, and *Proteus spp.*, pulmonary tuberculosis (contact with father), and multiple dental problems complicated the patient’s state.

In July 1998, the patient (8 years old) was admitted presenting a tumoral mass of the left heel, intense pain, with obvious signs of infection, and the imminence of spontaneous rupture. The problem has been neglected, the patient being previously taken care in a related family (Moldavia) for two months. The x-ray showed destruction of the calcaneus (Fig. 1-A), and the presence of a distal PT was not recognized, the case being initially interpreted as osteomyelitis. The surgical intervention (evacuation) under FVIII concentrate coverage and antibiotics was complicated by severe hemorrhage; repeated evacuations, application of local hemostatics and anti-