Goldbloom's Syndrome – a case report

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ABSTRACT

The Goldbloom's syndrome (GS) is a rare clinical condition of unknown aetiology, occurring exclusively in the pediatric population. It consists in an idiopathic periosteal hyperostosis with dysproteinemia, whose symptoms can mimic a neoplastic disease. We present a case report illustrating the diagnostic challenge of this condition. The exclusion of the common causes of bone pain, associated with generalized periostitis and increased gammaglobulins suggested the diagnosis of GS. The self-limited symptoms, the resolution of radiological findings in four months and the normalization of laboratory abnormalities within ten months, allowed to establish definitely the diagnosis of GS. GS must be considered when diffuse bone pain, prolonged fever and weight loss are present after exclusion of malignant disease with bone involvement.

Keywords: Goldbloom's Syndrome; Difuse Periostitis; Bone Pain; Dysproteinemia; Child.

INTRODUCTION

The Goldbloom's syndrome (GS) is an idiopathic periosteal hyperostosis associated with dysproteinemia[1-5].This is a rare clinical condition affecting only the pediatric population, without gender preference, with limited number of cases reported in the literature[1-5]. The clinical, laboratorial and radiological recovery is complete with only supportive care but may last months to years[1-5].

We describe the case of a two-year-old girl with fever, bone pain and weight loss, whose investigation and follow-up led to the diagnosis of GS. This is the only case of GS described in the Portuguese literature. Taken this into consideration, the authors present a brief description of some cases of GS published.

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CASE REPORT

A two and a half year old girl was first admitted to a local community hospital with one month history of pain localized to the limbs' diaphysis, refusal to walk, intermittent fever and weight loss (two kilograms). The pain was described as occurring all day long and over night, reaching the upper and lower limbs, making it impossible for her to go up and down stairs and even to hold a spoon. The progressive clinical deterioration led to the inability to walk. Additionally, she had a daily peak of fever (maximum 38 °C), anorexia, fatigue, cutaneous pallor, night sweats, as well as occasional headache, with photo and phonophobia. There were no respiratory, cardiac, gastrointestinal or urinary symptoms.

The past medical history was unremarkable and the stature-weight growth was in the fifth percentile. About a month before the beginning of the symptoms, she had a febrile suppurative otitis, treated with amoxicillin with clavulanic acid. The family history was irrelevant. Complementary investigation showed: normochromic normocytic anaemia (haemoglobin 10,3 g/dl), normal peripheral blood smear, thrombocytosis (798,000/ /mcL); erythrocyte sedimentation rate (ESR) of 102 mm/1st hour and C-reactive protein (CRP) of 9,4 mg/dl. The values of lactate dehydrogenase, alkaline phosphatase, uric acid and serum ferritin were within normal limits. Blood cultures and Mantoux test (two UI) were negative and serological tests for cytomegalovirus and toxoplasmosis did not show acute infection. The anti-nuclear antibodies, ENA screen and anti-DNA antibodies and fractions of the C3 and C4 complement were also negative.

On the third day of hospitalization (D3), temperature reached values of 39°C associated with periods of either irritability or prostration. An abdominal ultrasound, a chest X-ray and a dorsal-lumbar magnetic resonance (MRI) were performed and were considered normal. At D9, she was transferred to the Central Hospital. The physical examination revealed a "sick look", cutaneous pallor and intense pain on palpation of the limbs' diaphysis. The echocardiogram was normal. Ho-

TABLE I. CASES DESCRIBED IN THE INTERNATIONAL LITERATURE, TO WHICH WE ADD OUR CASE

	Gender	Age	Prior intercurrent	Clinical manifestations	Analytical changes	Radiological changes	Evolution
Goldbloom et al[1]	♂	14 years	Scarlet fever	- Bone pain SL, IL, jaw - Fever - Weight loss	- Anemia NN - Increased ESR - Increaded dysproteinemia: hypoalbuminemia, α and γ globulins	Periosteal reaction, ulna, shinbone, femur, mandible, humerus, fibula, metatarsus and metacarpus	Laboratorial and radiological normalization 5.5 years later
	♀	10 years	Tonsillitis	- Bone pain IL - Fever	- Anemia - Increased dysproteinemia: hypoalbuminemia, α2 and γ globulins	Periosteal reaction ulna, femur, fibula and shinbone	Clinical resolution in two weeks
Cameron et al[2]	♂	12 years	Pharyngitis	- Anorexia - Fever - Weight loss - Bone pain hand, wrist, ankle and jaw	- Anemia NN - Normal ESR - Increased CRP - Increased hypoalbuminemia, α1,α2 and γ globulins	Periosteal reaction mandible, radium, ulna, shinbone and fibula and phalanx	Clinical and radiological improvement; but after two years kept the dysproteinemia
Rodríguez et al[3]	♀	13 years	Upper Respiratory Infection	- Extremities pain - Weight loss	- Anemia NN - Increased ESR - Increased hypoalbuminemia, γ globulin	Periosteal reaction ulnas, radium, tibia, metatarsus and metacarpus	Complete resolution eleven months later
Gerscovich et al[4]	♂	3 years	Upper Respiratory Infection	- Forearm pain - Fever	- Anemia - Increased ESR - Increased hypoalbuminemia, α1, α2 and γ globulins	Periosteal reaction of the ulna, radium and femur	Complete resolution one year later
Kuwashima et al[5]	♀	4 months	NS	- Fever - Pain and swelling knee, elbow, wrist and fingers (migratory pain)	- Increased ESR and CRP - Increased hypoalbuminemia, γ globulin	Periosteal reaction humerus, ulna, radium and phalanx	NS
Santos S et al	♀	2.5 years	Febrile Suppurative Otitis	- Fever - Bone pains SL and IL - Weight loss - Anorexia	- Anemia NN - Increased ESR and - Increased α1, α2 and γ globulins	Periosteal reaction radium, ulna, tibia, and fibula	- Clinical and radiological resolution in four months - Analytical resolution in ten months

Legend: NS - Not stated, SL – Superior Limbs, IL – Inferior Limbs, ESR – Erythrocyte Sedimentation Rate, CRP - C-reactive protein; NN - normochromic normocytic

wever, X-rays of the long bones (Figures 1a and 2a) and bone scintigraphy (Figure 3) revealed signs of diffuse periostitis. Further laboratorial investigation an high total proteins value of 89.3 g/L [Reference value (RV) 54-75 g/L] and protein electrophoresis revealed a reduction in the percentage of albumin 37.1% (N 60-70%) and increased alpha fraction 1 [4.3% (RV 1.4-2.9%)], alpha 2 [17.2% (RV 7-11%)], beta [14.5% (RV 8-13%)] and gammaglobulin [26.9% (RV 9-16%)] by polyclonal hypergammaglobulinemia. The serological screening for syphilis was negative and the bone marrow examination was normal.

The diagnosis of GS was made, she was treated with ibuprofen (10 mg/kg/dose 3 id), being discharged from the hospital four days later. Four months later on follow-up she showed complete clinical and radiological remission, but laboratory abnormalities only normalized after ten months of disease duration.

She maintained rheumatological follow-up until she was four years of age with clinical, laboratorial and radiological resolution (Figures 1b and 2b) and with a good/regular growth.

DISCUSSION

In 1966, Goldbloom *et al.* reported two cases of fever and bone pain in a ten and a fourteen year old child, with periostitis and dysproteinemia in both, which designated as idiopathic periosteal hyperostosis associated with dysproteinemia[1]. Later this entity was recognized in other pediatric patients as Goldbloom's Syndrome[2-5]. In Table I are described schematically the cases published since 1966, to which we add our case. More than 40 years after the description of the first two cases of GS[1], its aetiology remains undetermined[2,5]. The virusal aetiology is the most probable, although there are cases reported with evidence of previous streptococcal infection (see Table I). In our patient, an infectious cause was considered since the symptoms were preceded by a suppurative otitis.

The bone pain often disproportionate to clinical findings is the most obvious sign[1-5]. Fever[1,2,4,5] and weight loss[1-3] are common features in GS, and were also present in our patient.

Radiologically, the signs of periostitis are typical, affecting preferencially long bones, in decreasing order of involvement: radio, femur, humerus, ulna and tibia[5]. This was demonstrated in our case report (Figure 1a and 2a). The involvement of short tubular bones[2,3,5] or the mandible[1,2] is rare. Radiological changes are confined to the periosteum, although plasma cell infiltration can occur at bone marrow level[2].

The differential diagnosis of GS, due to the presence of fever, bone pain and radiological findings of periostitis must be done with lymphoproliferative disease[6-11], malignant bone disease[6,8] and osteomyelitis[4-6] with one or more focus. Therefore a thorough investigation should be performed and should reveal a normal white blood cell count, peripheral blood smear

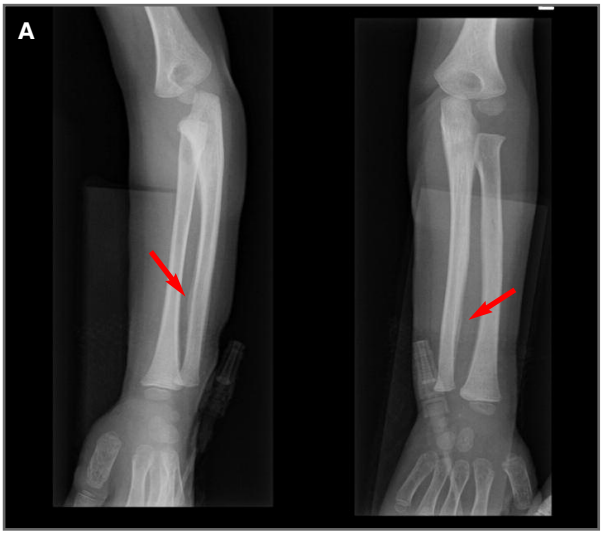

FIGURE 1a. Signs of periostitis of the upper limb (marked with arrow) in November 2007

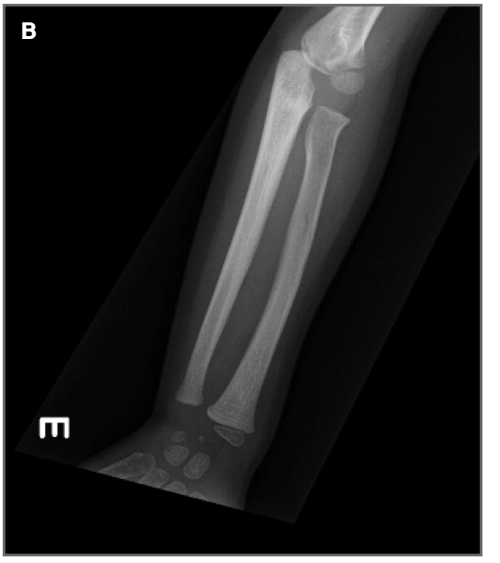

FIGURE 1b. Radiological resolution in March 2008

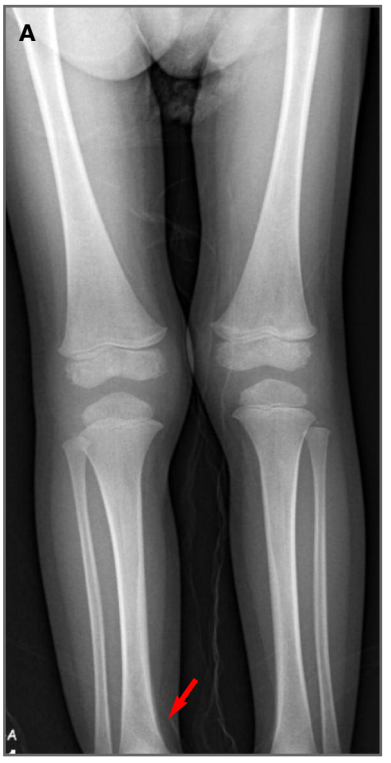

FIGURE 2a. Signs of periostitis of the lower limb (marked with arrow) in November 2007

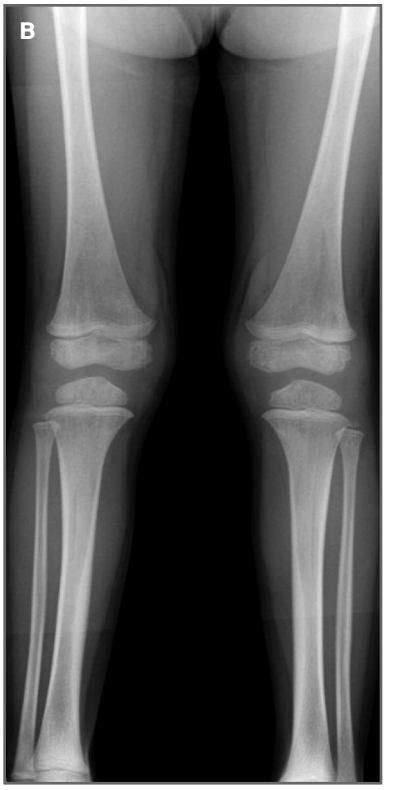

FIGURE 2b. Radiological resolution in March 2008

and bone marrow examination and a negative blood culture. Periostitis is a radiologic manifestation present in about 1.9% to 35% of acute lymphoblastic leukemia (ALL)[11]. Thus, the association of periostitis, bone pain and fever requires malignancy to be excluded, especially ALL[7-11].

No specific laboratory test exists for GS but universal findings include: increased acute phase reactants (ESR and CRP)[1-5], anaemia[1-4] (mainly normocytic normochromic), dysproteinemia with hypoalbuminemia, increased gamaglobulins and variable values of alpha 1, alpha 2 and beta globulins[1-5]. Such laboratorial abnormalities were found in our patient. These findings, together with the radiological abnormalities and after exclusion of other clinical entities, allowed to evoke the diagnosis of GS.

Other differential diagnoses to consider are: Caffey disease[12] (child cortical hyperostosis), occurring in infants with preferential involvement of the mandible but without dysproteinemia[4] and chronic intoxication by vitamin A, which may present with bone pain and radiological abnormalities but without fever[13]. These entities were immediately excluded, due to the child's age and absence of relevant personal history or vitamin A chronic ingestion. The pachydermoperiostosis (or Touraine-Solente-Golé Syndrome) is an autosomal dominant disease characterized by periostitis in addition

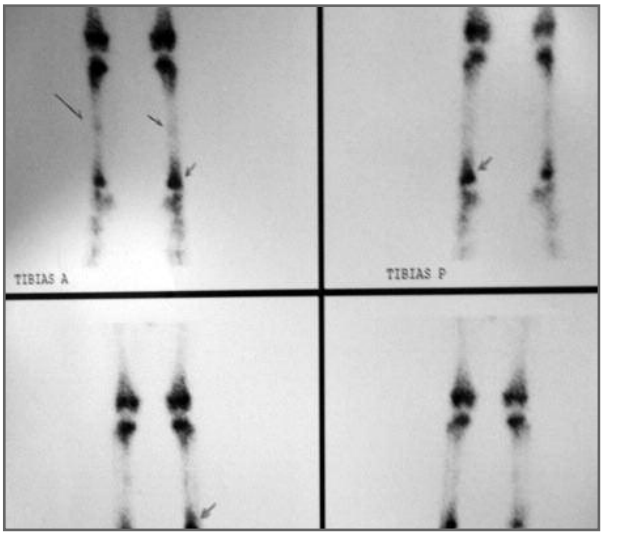

FIGURE 3. Areas of hyperfixation on bone scintigraphy

to digital clubbing and coarse facial features[4,6], that didn't exist in this case. Secondary hypertrophic osteoarthropathy was also excluded since there weren't signs of cardiac, respiratory or digestive involvement which could suggest a chronic disease[14].

The treatment of the GS is symptomatic and the prognosis is good, with clinical improvement in weeks to several months, although complete laboratorial and radiological normalization may take years[1,2,4,14]. Our patient, after four months on follow-up showed both clinical and radiological recovery. However laboratory abnormalities have normalized only after ten months.

The GS is a rare clinical entity and may be underdiagnosed. Therefore it is important to consider GS as a possible diagnosis when symptoms of diffuse bone pain, prolonged fever and weight loss are present, and malignancy with bone involvement or infectious diseases, such as osteomyelitis, are ruled out.

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