

Transient osteoporosis of the hip: Presentation of (a)typical cases and a review of the literature

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ABSTRACT

Transient osteoporosis of the hip (TOH) is a rare disorder affecting primarily middle-aged men and women during the last trimester of pregnancy. The disease is characterized by pain in the involved joint with temporary osteopenia apparent on radiology without joint space narrowing or destruction, in the absence of other recognizable causes of synovitis or osteoporosis. Within a few months the pain as well as radiological abnormalities disappear spontaneously with complete resolution. In this paper the literature is reviewed, with particular focus on the topic of the role of magnetic resonance imaging (MRI) in the diagnostic procedure. Two patients with TOH, a father and daughter, are described. Such a familial appearance has not been reported before. Based on HLA-typing, the existence of an HLA-associated genetic predisposition nevertheless seems unlikely.

Introduction

Transient regional osteoporosis of the hip (TOH) is an uncommon clinical syndrome which is characterized by pain in the involved joint with a temporary osteopenia apparent on radiology without joint space narrowing or destruction, in the absence of other recognizable causes of synovitis or osteoporosis. The cause of TOH is unknown. Most patients are middle-aged men or women in their third

trimester of pregnancy. Thigh pain of gradual or rapid onset and limping are the most common symptoms (1-3). Within a few months the pain as well as the radiological abnormalities disappear spontaneously, with complete resolution of the condition (4-6). In this report we describe two TOH patients who were first degree relatives. The familial appearance of TOH has been reported only once before. The relevant literature is reviewed.

Case reports

Patient 1

In August 1996, during her last weeks of pregnancy, a 24-year-old white woman noticed pain in her right thigh and the upper part of her right leg. Till then she had been in good health, and these symptoms appeared spontaneously. After the delivery at the end of September, the pain worsened and was present also during the night. Weight-bearing was barely possible when she was seen for the first time in October 1996. She walked with crutches. On examination rotation of the right hip was limited. Furthermore, a significant atrophy of the quadriceps muscle was noticed. Plain roentgenograms showed demineralization of the femoral head. Magnetic resonance imaging of the right hip demonstrated diffusely decreased signal intensity in the femoral head on T1-weighted images (Fig. 1) and increased signal intensity of the same area on T2-weighted images.

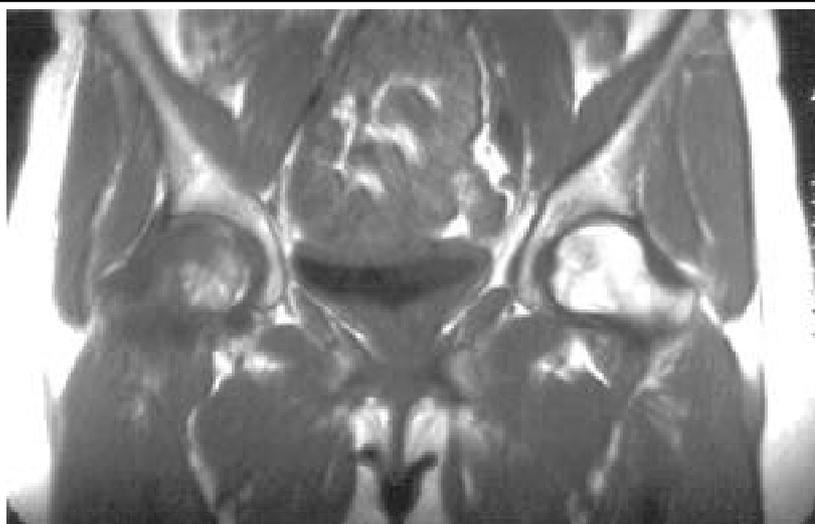


Fig. 1. Magnetic resonance imaging of the right hip in patient 1, demonstrating diffusely decreased signal intensity in the femoral head on T1-weighted images.

HLA typing showed A2, A9 (A24), B17(B57), B35, Bw4, Bw6, Cw4, DR6(DR13), DR7, DR52, DQ1(DQ6), DQ3(DQ9). Rest was advised and over the next two months the complaints gradually disappeared. Control roentgenograms in December 1996 showed that her condition had normalized. During follow up until February 1998 there were no signs of recurrence.

Patient 2

In December 1996, a 51-year-old white male, the father of patient 1 and a resident in the same village, noticed pain in his left thigh. The pain gradually worsened and was aggravated by walking. Except for the pain in his thigh, the patient denied complaints elsewhere. He had no fever or other signs of antecedent infection. A history of trauma was denied. His past history revealed only treatment for tuberculosis in 1949. On examination, rotation of the left hip was slightly restricted and painful. Laboratory investigations, including a complete blood count, erythrocyte sedimentation rate (ESR) and serum alkaline phosphatase were normal. HLA typing was performed and showed A2, B7, B17 (B57), Bw4, Bw6, Cw3, DR2(DR15), DR7, DR51, DQ1(DQ6), DQ3(DQ9). On roentgenograms, osteopenia of the left hip with poor delineation of the femoral head was seen. The joint space was normal. On bone scintigraphy a highly increased uptake in the left femoral head as well as in the acetabulum was seen. With a gradual increase of weight-bearing the symptoms disappeared completely within the next 6 months. Up till one year thereafter he has remained asymptomatic.

Discussion

Transient osteoporosis of the hip is a rare clinical syndrome. In 1959 the first patients were described. Curtiss and Kincaid reported 3 women in the last months of pregnancy who suffered from pain in the thigh, especially on weight-bearing. Roentgenograms showed osteopenia of the affected femoral head. No systemic metabolic disturbances could be found and after a few months both the symptoms and the radiological abnormalities disappeared spontaneously (7). This spe-

cific syndrome was named transient osteoporosis of the hip by Hunder and Kelly in 1967 (8). Since then, subsequent reports have referred to this clinical entity alternatively as regional osteoporosis, algodystrophy, transitory demineralization, idiopathic transient osteoporosis of the hip, migratory osteoporosis, migratory osteolysis, or reflex sympathetic dystrophy (RSD) of the hip (1, 2, 9-13). Because reflex sympathetic dystrophy can be distinguished from TOH on several grounds, it is debated whether TOH may perhaps be a variant of this disease (3, 11).

Clinical presentation and diagnosis

Two-thirds of patients are otherwise healthy, middle-aged men. The age at which the first symptoms present ranges from 24 to 75 years with most patients being between 40 and 60 years old (3). About one-third of the patients are female, the majority of whom are in the last trimester of pregnancy or in the early postpartum period (6). Children are rarely affected (14).

TOH is one among a group of entities referred to as transient regional osteoporosis (3). Although the hip is the most frequently affected joint (76%), others may be involved including the knee, foot, and ankle. In TOH, the presenting symptom is a dull and aching pain in the anterior thigh, buttock or groin region. The onset can be gradual or acute. Pain is absent or minimal at rest. On weight-bearing, however, it increases so that walking is hardly possible without stick or crutches. There are in general no precipitating factors. The left hip is slightly more affected than the right, especially in women (5, 9).

Physical examination is normal except for limited motion of the affected hip due to pain. Abduction and rotation are particularly impaired. Sometimes disuse atrophy of the quadriceps, buttock and calf is present (3, 6, 15).

Laboratory investigations, including the leucocyte count, serum phosphorus, serum calcium, serum alkaline phosphatase and parathyroid hormone levels are usually within normal limits (3, 6). Rheumatoid factors and tests for antinuclear antibodies are negative (3). In a minority of patients the ESR is elevated (3).

Urinary hydroxyproline excretion has been demonstrated to be elevated in one report (16), a finding which could not be confirmed by others (3, 17-19). Synovial fluid analysis does not yield additional information. In particular, no microorganisms have been found and leucocyte counts are low.

Roentgenograms are important for the diagnosis. The first roentgenological abnormalities are present 3 to 6 weeks after the onset of the symptoms. They consist of demineralization of the superoexternal, inferoexternal or whole femoral head without narrowing of the joint space. Sporadically the area involved includes the femoral neck and trochanters, and even extends to the acetabulum and iliac wing. Furthermore, bone hypertranslucency, accentuation of the force lines and poor delineation of the femoral head can be seen (6). Sometimes a mottled pattern is present (3). Computed tomography of the affected hip will confirm the osteopenia and preservation of a normal joint space.

Recent reports stress the importance of magnetic resonance imaging as part of the diagnostic investigations (20-28). MRI shows abnormal findings before conventional radiography, as early as 48 hours after the onset of TOH (29). Edema and fat necrosis in the femoral region result in a reduced T1 signal, whereas T2 signals are increased due to osteopenia. These alterations on MRI are suggestive for TOH, but not pathognomonic. Early stage osteonecrosis with bone marrow edema can mimic TOH features (28, 30). In the later stages, osteonecrosis may be distinguished from TOH since the classical abnormality in osteonecrosis develops in the anterosuperior segment of the femoral head surrounded by a double line on T2 weighted images (28). The extension of the signal intensity changes from the metaphysis to the epiphysis also favors TOH and differentiates the disease from neoplasm and osteomyelitis, both conditions which are usually located in the metaphysis (21). Radionuclide bone scans with ⁹⁹Tc-MDP are also helpful, especially early in the course of the disease. Within the first month, increased uptake in the femoral head can be seen. The uptake is homogeneous, with a typical maximum in the

center of the femoral head and a high femoral head/reference area uptake ratio, especially during the first 4 - 6 weeks (31). In this stage differentiation from osteonecrosis is possible because early cases of avascular bone necrosis usually yield a low femoral-head/reference area ratio due to the decreased uptake that characterizes necrotic bone (31, 32). Uptake in TOH may extend into the acetabulum, femoral neck and occasionally into the femoral shaft. Bone densitometry can be helpful for research purposes to quantitate the level of demineralization (33), but has no place in routine clinical practice.

Other diagnostic procedures are not contributory to the diagnosis. Synovial biopsies show non-inflammatory tissue. Only sporadic collections of leucocytes can be found (3). Bone biopsies reveal mild marrow fibrosis, fat necrosis, edema and osteoporosis with widely spaced, thin trabeculae (3, 23).

Differential diagnosis

The differential diagnosis of TOH includes inflammatory joint diseases, septic arthritis, osteonecrosis, stress fracture of the femoral neck, pigmented villonodular synovitis, synovial chondromatosis, carcinoma (either primary or metastatic), and multiple myeloma (6, 9, 19, 34). Laboratory investigations will discriminate between most of these conditions. The characteristic appearance of the roentgenograms and bone scans, together with the benign and self-limiting

course, will clarify the diagnosis.

Therapy and follow up

Therapy consists of prolonged rest, protected weight-bearing and the prescription of nonsteroidal anti-inflammatory drugs (NSAIDs). Sometimes physiotherapy is necessary to prevent contracture of the involved hip. These recommendations, however, do not seem to alter the natural course of the disease (5, 8, 14). Only calcitonin has been mentioned to reduce bone resorption and to accelerate recovery (18, 35), but this has been debated (3). Other drugs such as intravenous clodronate (15), prednisolone (11) and the bone-sparing steroid deflazacort (36) are used in the treatment of TOH, but as with calcitonin, the series reported thus far have been small and no controlled studies have been reported. Moreover, the time to complete recovery in the studies mentioned does not differ greatly from the natural course of the disease (Table I).

As stated, the disease is self-limited. After a period of rapid deterioration, which may last for approximately one month, the symptoms tend to stabilize. During the next 2 - 3 months pain and functional disability remain unchanged and roentgenographic osteopenia remains present. By 4 to 12 months, the symptoms as well as the osteopenia will gradually subside. Recovery will be complete. In 8 to 41% of patients more than one episode of TOH may occur, in which the same or the contralateral hip

may be involved (3, 15, 19). In addition, the recurrence of transient osteoporosis in joints other than the hip, such as the knee, ankle and foot, has been described (4, 8, 19, 36). This syndrome, called regional migratory osteoporosis (RMO), has clinical and radiological characteristics similar to those of TOH. In cases of multiparity, no reports are available regarding the recurrence of TOH in later pregnancies.

Pathophysiology

The cause of TOH is unknown. Several underlying abnormalities have been proposed as being important. Familial presentation has been described once before (37), where 3 brothers were presented with TOH, all with the same HLA grouping: A1-30 or 31, B8, B37, Bw4, Bw6, DR7-X, DR53. Combined with our patients the only HLA similarity is DR7. It is therefore not to be excluded that a particular HLA phenotype renders a person at risk to develop TOH but, as the incidence of TOH is very low, genetic predisposition as a major contributing factor seems to be unlikely.

Our patients, a father and daughter living in the same village, developed TOH a few months after one another, which could suggest an environmental cause. Careful evaluation, however, did not disclose any indicating clues.

Some authors mention the presence of type IV hyperlipidaemia in patients with TOH (38). Others have reported an association with cirrhosis (39), micro-

Table I. Literature overview of different therapeutical options in the treatment of transient osteoporosis of the hip.

Author	No.	Treatment	Dose	Duration	Outcome	Time
Lequesne (ref. 4)	6	Deltacortisone	30 mg (first 4 mos.)	Tapering in 3-6 weeks	Complete recovery, ineffective	2-6 mos.
Lakhanphal (ref. 3)	5	Prednisone	Up to 40 mg/day	?	Complete recovery, ineffective	?
Valenzuela (ref. 15)	2	Prednisone	20 mg/day	?	Complete recovery	2 1/2 mos.
Naides (ref. 19)	1	Prednisone	15 mg/day	4 weeks	Ineffective	
Carmona-Ortells (ref. 36)	2	Deflazacort	60 mg/day p.o.	1 wk., tapering over 1 mo.	Complete recovery, effective	2-4 wks.
Scheinberg (ref. 18)	1	Calcitonin	100 MRC every other day	6 weeks	Complete recovery, effective	2-4 mos.
Doury (ref. 35)	3	Calcitonin	160 MRC/day	20 days	Complete recovery, effective	3-12 days
Varena (ref. 33)	3	Clodronate	30 mg/day i.v.	10 days	Complete recovery	8-16 wks.

No. = number of patients treated; duration = number of days/weeks the treatment was given; outcome = final result reported (effective/ineffective denotes the opinion of the authors, if mentioned); time = number of weeks/months until the final result was reached.

trauma (5,7), acute muscle denervation (11) or vascular abnormalities (9). The association with the third trimester of pregnancy is intriguing. Several factors seem to predispose women to TOH during pregnancy, e.g. a negative calcium balance, increased activity of the adrenal cortex and an increased demand for protein and minerals (6). In addition, venous retention due to impaired venous return and leading to medullary hypertension, has been proposed as a contributing factor for the development of TOH in pregnancy (40). In conclusion, TOH is a rare disorder with a typical presentation and benign course. It is important to distinguish it from other diseases in order to prevent unnecessary diagnostic procedures and therapies. Diagnosis is possible based on the history and normal laboratory results, in combination with the typical aspect of plane roentgenograms and bone scintigraphy. Magnetic resonance imaging may also be helpful. Still, it has to be realized that no symptom or sign is pathognomonic for the presence of TOH. The pathogenesis is still unknown. A genetic predisposition linked to chromosome 6 cannot be excluded, but seems unlikely because of the merely discordant HLA pattern in the patients hitherto described.

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