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ORIGINAL STUDY

Evaluation of results of conservative therapy in patients with transient osteoporosis of hip

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The present study aimed to review the general characteristics of 18 cases diagnosed with transient osteoporosis of the hip (TOH) in our hospital within a 3-year period and to present their follow-up results after conservative treatment. A retrospective evaluation was made of the treatment and results of follow-up of TOH cases using physical examination and laboratory findings, hip radiographs and magnetic resonance imaging (MRI) and Harris Hip Scores (HHS). The mean duration of complaints of 6 females (mean age, 34.3 ± 4.3 years) and 12 males (mean age, 40.7 ± 10.5 years) was 6.1 ± 2.7 weeks before the treatment. Three female patients had a history of giving birth by cesarean delivery. None of the patients had any history of trauma. MRI revealed increased intensity in T2 sequences and decreased intensity in T1 sequences in the proximal aspect of the femur. None of the patients had subchondral collapse or intra-articular effusion. For 3 female patients who were breastfeeding, no medical therapy was given, but only hyperbaric oxygen (HBO) therapy and forearm crutches. As standard management, the other patients were prevented from weight-bearing with the use of forearm crutches and medical therapy of diclofenac sodium, acetylsalicylic acid, and risedronate sodium was administered and additional HBO therapy. Clinical and radiological improvements were observed in all patients. None of the patients had avascular necrosis (AVN) of the femoral head. There was no record of therapy-related complications. While HHS was 55.6 ± 7.8 before the treatment, it increased to 88.8 ± 5.8 in the 3rd month and to 96.0 ± 1.8 in the 6th month after the treatment. This change in score over time was found to be significant.

Keywords : transient osteoporosis ; bisphosphonate ; risedronate ; hyperbaric oxygen.

INTRODUCTION

Transient osteoporosis of the hip (TOH) is a self-limiting condition with good prognosis in general and with poorly enlightened etiology and pathophysiology (*24*). More than 200 cases have been reported in literature since 1959 when it was first defined by Curtiss and Kincaid (*3*) in pregnant

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women (*24*). The etiology and pathophysiology of transient osteoporosis of hip remains unclear. Although pregnancy has been reported as the unique risk factor associated with TOH, the disease has also been reported in non-pregnant women and in middle-aged males (*24*). The main clinical symptom is unexplained joint pain. Magnetic resonance imaging (MRI) is the most beneficial method in diagnosis. Osteonecrosis or avascular necrosis (AVN) has been reported as the most important diseases in the differential diagnosis of TOH and some researchers have propounded that TOH might be an early reversible phase of AVN (*14,15*). Since prognosis and treatment vary, the differentiation of AVN from TOH is important. Surgical interventions have a substantial place in the treatment of AVN (*26*). However, TOH is a condition that does not require surgical intervention and is treated by supportive and conservative therapies including analgesics, non-steroid anti-inflammatory drugs (NSAIDs), benzodiazepines, rest, graduated physiotherapy to prevent contractures of the involved hip, and protected weight bearing (possibly with crutches) (*24*).

The aim of the present study was to review the general characteristics of 18 TOH cases and to present their follow-up results after conservative treatment.

MATERIAL AND METHODS

The study comprised 18 patients who were admitted to the orthopedics polyclinic with thigh and inguinal pain and were diagnosed with TOH. The hospital records of the patients between January 2010 and December 2012 were retrospectively evaluated. Approval for the study was granted by the Local Ethics Committee.

A record was made of the physical examination and laboratory results of the patients, hip radiographs and MRI results, HHSs, and results of treatment and follow-up. Clinical improvement of the patients was assessed according to the classical information (*2*). The disappearance of the initial presenting complaints and the range of motion of the hip joint becoming normal when compared to the contralateral hip were considered clinical improvement. Radiological improvement was considered to be the disappearance of the initial findings on the control MRI scans.

The Harris Hip Score was calculated by scoring pain, function (type of walking, usage of support, range of walk, sitting, ability to get on a public transport vehicle, ability to wear shoes and socks, ability to climb stairs), and deformity and range of movement (flexion, extension, abduction, adduction, rotation) (*7*). The Harris Hip Score is graded as follows : < 70 : poor, 70-79 : fair, 80-89 : good, and 90-100 : excellent (*12*).

Only hyperbaric oxygen (HBO) therapy and forearm crutches, but no medical therapy, were recommended for 3 females who were breastfeeding. As standard management, the other patients avoided weight-bearing with the use of forearm crutches and received diclofenac sodium (100 mg/day) as an anti-inflammatory agent until the alleviation of pain and risedronate sodium (150 mg/month) for 6 months. In addition, HBO therapy was applied at a dose of 2.5 ATA at 2 hours per day for 30 days (30 session/60 hours) and acetylsalicylic acid was given at a dose of 100 mg/day for 3 months.

The patients were assessed at 4-week intervals in the first 6 months and at 3-month intervals in the second 6 months and thereafter at one-year intervals. The patients underwent hip radiographs + MRI at 3-month intervals in the first 6 months and MRI of the hip at 3-month intervals in the second 6 months. The Harris Hip Score was assessed before the treatment, in the 3rd month after the treatment, in the month when complaints disappeared, and in the 6th month after the treatment. Dual-energy X-ray absorptiometry was not performed.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc. Chicago, IL, USA) version 15.0 for Windows. Descriptive statistics were expressed as frequency tables and cross tables for categorical variables and as mean ± standard deviation for numerical variables. Paired group comparison of independent numerical variables was performed using the Mann-Whitney U test where distribution was not normal. Multiple repeated measurement analyses of dependent variables were performed using the Friedman test when distribution was not normal. The repeated measures test was used to analyze the changes over time between the groups. Subgroup analyses were performed using the Wilcoxon test with Bonferroni correction. The level of statistical significance was set at $p < 0.05$.

RESULTS

Of the total 18 patients, 6 were female (mean age, 34.3 ± 4.3 years) and 12 were male (mean age, 40.7 ± 10.5 years). The mean duration of complaints

of the patients before the treatment was 6.1 ± 2.7 weeks. None of the patients had any history of trauma. Three females had a history of giving birth by cesarean delivery without trauma associated with delivery. On physical examination, movements of the hip joint of the patients were observed to be painful and restricted. All patients had osteopenia or demineralization on hip radigraphs and normal joint space. MRI revealed increased intensity in T2 sequences and low signal intensity in T1 sequences in the proximal aspect of the femur. Subchondral collapse or intra-articular effusion was not present in any of the patients. Complete blood count, C-reactive protein, brucella immunoglobulin G, and purified protein derivative tests, which were performed to exclude septic arthritis, inflammatory arthritis, and malignancy in the differential diagnosis of patients, revealed no pathological findings. Technetium 99 whole body bone scintigraphy demonstrated increased diffuse homogeneous intensity.

Clinical and radiological improvements were observed in all patients (Fig. 1, 2). None of the patients had AVN of the femoral head. There was no record of therapy-related complications. The demographic and disease characteristics of the patients are summarized in Table I.

No statistically significant difference was determined between gender groups in terms of the mean age, duration of clinical improvement, duration of radiological improvement, and duration of follow-up (Table II).

While HHS was 55.6 ± 7.8 before the treatment, it increased to 88.8 ± 5.8 in the 3rd month and to 96.0 ± 1.8 in the 6th month after the treatment. The change in HHS over time was statistically significant (Table III). No statistically significant difference was determined between genders in terms of change in HHS over time (Table IV).

DISCUSSION

Transient osteoporosis of hip is a clinical entity that is not uncommon but is thought to be underdiagnosed. In literature, it is usually presented in the form of case reports and it has been reported to be more frequent in middle-aged healthy males and that the male : female ratio is 3:1 (*11,19,21*). Of the

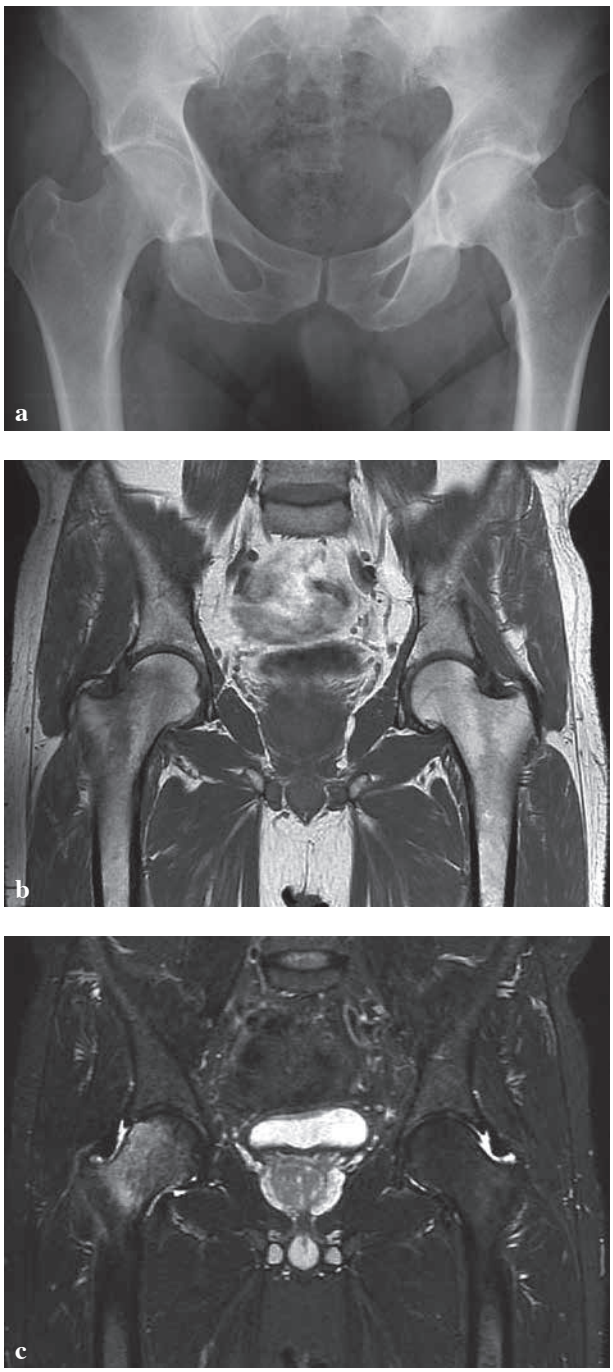

Fig. 1. — (a) Osteopenia in the right femoral head and neck on hip X-Ray examination. The left hip is normal. (b) The coronal T1-weighted image of the hip joint shows a low signal intensity lesion in the right femoral head (arrow). (c) high signal intensity lesion on fat suppressed coronal T2 weighted image (arrow).

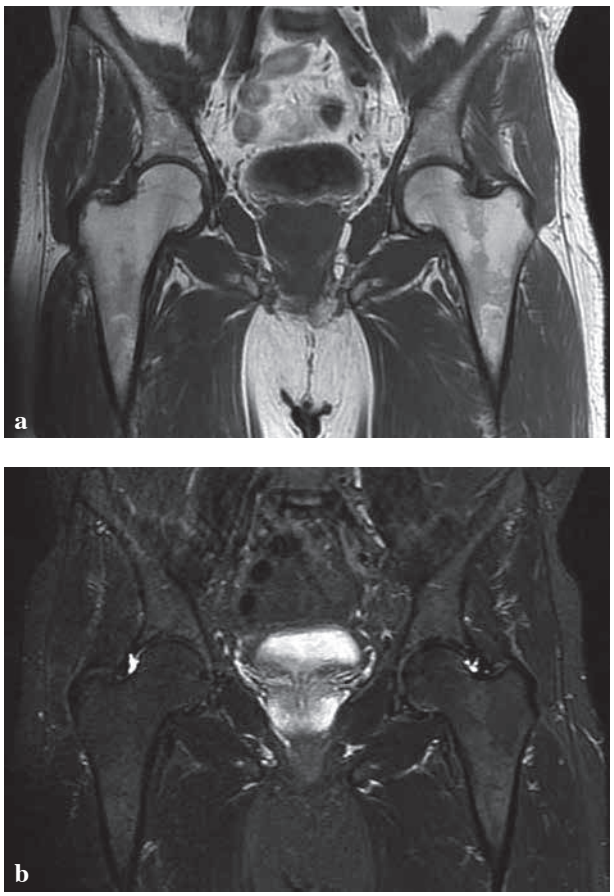

Fig. 2. — (a-b). Follow-up hip MRI showing no abnormal lesion in both femoral heads.

present 18 patients, 66.7% were male and 3 of 6 females had a history of caesarean delivery and presented during the postpartum period. Although it is known that TOH can develop in late pregnancy or in the postpartum period in females, it has also been reported in non-pregnant women without any preceding infection or trauma (*8,11*).

Table I. — Characteristics of patients with transient osteoporosis of hip

Gender	
Female	6 (33.3)
Male	12 (66.7)
Age, year	38.6 ± 9.3
Involved hip	
Left	10 (55.6)
Right	8 (44.4)
Pretreatment duration of complaints, week	6.1 ± 2.7
Duration of follow-up, month	17.8 ± 5.3
Duration of clinical improvement, month	3.9 ± 0.9
Duration of radiological improvement, month	8.3 ± 2.2

The etiology and pathophysiology of TOH has not been clearly defined. Etiological factors implicated in TOH include a genetic predisposition, mechanical compression of obturator nerve, reflex sympathetic dystrophy, bone medullary hypertension and small vessel ischaemia, fatty marrow conversion of the proximal femoral metaphysis, and chemical or hormonal factors related to pregnancy. Angiographical and scintigraphical studies show that nutrient arteries of the femoral head are dilated and that perfusion is higher than in the unaffected contralateral side. These findings suggest that TOH may be the result of a vasomotor response to an undisclosed etiological factor, though ischaemia is most likely. Further risk factors include cigarette smoking, steroid intake, alcoholism, obesity, hemoglobinopathies, and pregnancy. Hypothyroidism may be implicated in the etiology of TOH as well as iatrogenic hyperthyroxinemia. Minor trauma preceding hip pain which may have caused a period of transient ischemia could precipitate to TOH (*8,11, 13,34*).

Table II. — Characteristics of the patients according to genders

	Female (n = 6) (Mean ± SD)	Male (n = 12) (Mean ± SD)	p
Age (year)	34.3 ± 4.3	40.7 ± 10.5	0.159
Duration of clinical improvement (month)	4.2 ± 1	3.8 ± 0.8	0.455
Duration of radiological improvement (month)	8.0 ± 2.4	8.5 ± 2.2	0.612
Duration of follow-up (month)	19.7 ± 6	16.9 ± 4.9	0.470

Table III. — Harris hip scores before and after the treatment

	Mean ± SD	p
Before the treatment	55.6 ± 7.8	< 0.001
Month 3 after the treatment	88.8 ± 5.8	
Month 6 after the treatment	96.0 ± 1.8	

Although TOH is usually unilateral, occasional cases of bilateral involvement have also been reported. Xyda *et al* (*34*) reported postpartum bilateral TOH in 3 cases. In the present study, all the patients had unilateral involvement, with 55.6% left hip and 44.4% right hip.

In clinical practice, there are difficulties in differentiating TOH from AVN (*1,13*). While TOH improves spontaneously or with symptomatic treatment, AVN may display a progressive course and may require early surgical intervention (23, 31). MRI is the preferred method for differential diagnosis of painful conditions of the hip (*22*). MRI characteristics in TOH cases include low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (*32*). In the present study, the MRIs of all patients consistently revealed high signal intensity in T2 sequences and low signal intensity in T1 sequences in the proximal aspect of the femur. Subchondral collapse or intra-articular effusion was not present in any of the patients. The mean duration of clinical improvement was 3.9 ± 0.9 months and the mean duration of radiological improvement was 8.3 ± 2.2 months. There was no difference in these durations between the genders. Balakrishnan *et al* (*1*) evaluated 10 TOH cases, all of which were male, and reported the mean duration of radiological improvement as 7.5 months (range, 4-11 months). The mean duration of spontaneous improvement of symptoms was reported to be 5.8 months (range, 2-10 months). No focal or subchondral changes were detected on the MRIs of 10 patients.

It has been reported that some TOH cases have been treated by the restriction of weight-bearing only (*21*). However, there are also reports on the benefits of various additional medical therapies. Fabbriciani *et al* (*9*) reported improvement of symptoms and MRI findings with teriparatide therapy in a 62-year old male case. Seok *et al* (*27*) reported a TOH case improved with a single dose bisphosphonate (zoledronate 5 mg) therapy. La Montagna *et al* (*17*) found neridronate, a third-generation amiobisphosphonate, therapy to be successful in a case with bilateral TOH. Schapira *et al* (*25*) reported successful treatment of a TOH case with intravenous bisphosphonate. Kibbi *et al* (*16*) reported 3 patients diagnosed with transient osteoporosis (hip in 2 patients and knee in 1 patient), for whom oral weekly alendronate was effective in shortening the disease duration. Emad *et al* (*6*) reported radiological improvement demonstrated by MRI in 8 TOH cases treated with alendronate. Varenna *et al* (*33*) reported that effective and rapid results were obtained with pamidronate therapy in 16 TOH cases. In the present study, acetylsalicylic acid and diclofenac sodium was used for the analgesic and anti-inflammatory effect and risedronate, which is a bisphosphonate, was also used. Bisphosphonates modulate bone turnover and reduce remodeling in cases of excessive resorption. The bisphosphonate group of drugs have increasingly been used in many bone conditions, such as Paget's disease, osteoporosis, and metastatic cancer (*10*). Risedronate is an oral bisphosphonate, which became available after alendronate, and is approved by the United States Food

Table IV. — Harris hip scores according to the genders before and after the treatment

	Female (n = 6) (Mean ± SD)	Male (n = 12) (Mean ± SD)	p
Before the treatment	53.6 ± 3.9	56.6 ± 9.2	0.511
Month 3 after the treatment	88.4 ± 6.6	88.9 ± 5.7	0.888
Month 6 after the treatment	96.5 ± 2.1	95.7 ± 1.7	0.372
p	0.675		

and Drug Administration (FDA) for the treatment of Paget's disease of the bones and the prevention and treatment of postmenopausal osteoporosis and glucocorticoid-induced osteoporosis. Risedronate shows its clinical effects by binding to hydroxyapatite in bone tissue and inhibiting osteoclast activity (*30*).

In the present study, HBO was performed in addition to standard therapy. HBO therapy has been reported to reverse cellular ischemia by enhancing the oxygen concentration of the extracellular fluid and to reduce edema by inducing vasoconstriction (*23*). There have been reported cases of TOH where benefit has been gained from HBO therapy. Accelerated recovery was observed in the patients with TOH treated with HBO. HBO would be effective for accelerated recovery time in patients with transient osteoporosis of the hip by suppression of oedema, lowering the intraosseous pressure, restoring venous drainage, and rapidly improving the microcirculation (*5,20*).

Although TOH, which is a self-limiting condition with good prognosis, can be completely improved with conservative therapy, complications may be encountered occasionally. Lamarca *et al* (*18*) reported a displaced subcapital fracture, which was treated by total hip arthroplasty, as a rare complication of TOH. This complication due to weakness of the bone in TOH also might suggests that a period of nonweightbearing or protected weightbearing may be a reasonable component of routine conservative management.

In the present study, no complications were observed in any of the patients. According to the HHS, the hip status of the patients was poor before the treatment (mean score, 55.6 ± 7.8 and excellent (mean score, 96.0 ± 1.8) at the 6^{th} month after the treatment. The improvement in HHS over time showed no difference between the genders.

Suresh *et al* (*28*) reported a patient who was successfully treated for TOH but then developed TOH in the opposite hip 14 months after the initial admission and it was emphasized that TOH cases needed long-term follow-up. Diwanji *et al* (*4*) reported no osteonecrosis over the course of a 2-year follow-up period in 2 middle-aged female cases with TOH, who were diagnosed on the basis of MRI findings and were treated conservatively. Uematsu *et al* (*29*) reported 4 TOH cases, who developed TOH during pregnancy and showed clinical and radiological improvements without recurrence over the course of a mean 70.8 month follow-up period. In the present study, all patients also improved without recurrence over the course of a mean 17.8 ± 5.3-month follow-up period.

In conclusion, it is important to make an early and accurate diagnosis by MRI in TOH cases, which are likely to completely recover with conservative therapies without surgical intervention. Early differentiation of TOH from AVN will avoid unnecessary surgical intervention and ensure appropriate treatment. In the present retrospective study in which 18 patients were evaluated, it was determined that the patients were conservatively treated and followed-up for approximately 2 years. All the patients were observed to have improved without any complications with no significant difference between the genders.

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