Clinical Article

Hip arthroplasty in HIV-infected patients

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Summary

We conducted a prospective study evaluating the clinical outcome of the arthroplasty in HIV-infected patients. Between July 2000 to August 2001, 14 patients (mean age 42 years) underwent uncemented total hip replacement for osteonecrosis (10 patients) and neglected neck of femur fractures (four patients). Patients were classified according to the WHO and CDC classification and were operated by a single surgeon using the Hardinge approach. At a mean follow-up of 72 months, all patients were fully ambulant. The mean total lymphocyte count (TLC) was 2.24 cells/mm^3, CD4-425 cells/mm^3, CD8-873 cells/mm^3 and CD4 /CD8-0.52. In three patients the CD4 counts declined to <200 and they are presently receiving antiretroviral therapy. There was no loosening, infection or dislocation. One patient sustained a periprosthetic fracture which was treated successfully non-operatively.

We conclude that total hip replacement in HIV-infected patients who have not progressed to WHO stage IV can be rewarding and the procedure does not carry an increased risk of postoperative infection.

Introduction

The increased prevalence of HIV has increased awareness and concern for the diagnosis and treatment of patients requiring total joint arthroplasty. Collective experience with HIV and arthroplasty at any institution is small and limited. HIV-positive patients suffer progressive deterioration in immunity as indicated by a fall in the CD4 count.

Joint replacement in HIV-positive patients with haemophilia carries a higher risk of infection.[1] Despite reports of increased frequency of infection in haemophilic patients who are HIV-positive, little is known about the relationship between HIV and arthroplasty in non-haemophilic patients.[2,3]

Studies report that in such patients the risk of immune status deteriorates.[4,5] The literature on surgical complications in HIV-infected patients is retrospective and inconsistent, with reports documenting both favourable and unfavourable outcomes.[6] The earlier studies of Hoekman *et al* and Jellis suggested that symptomatic HIV-positive patients developed a high incidence of wound infection (24% and 40% respectively) after implant surgery following trauma.[7]

Materials and methods

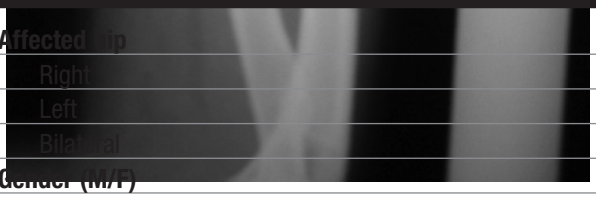
Between July 2000 and August 2001, we performed 15 uncemented total hip replacement in 14 patients (four female) and the mean age was 42 years (range 29-45).

Details regarding patients' gender, age, bodyweight, WHO classification, CDC and follow-up are listed in *Table I.*

Informed consent was obtained before HIV testing, and counselling was provided for all patients. The pre-operative haemoglobin was 10.5 gm/dl (range 9.7-12.5 gm/dl)and serum albumin was 32 gm/dl (range 29-35 gm/dl). Pre-operative nutritional support was provided for all patients requiring a high protein diet in consultation with a dietician who was actively involved in the treatment and management of these patients. Uncemented total hip replacement was preferred because they were younger patients with good bone stock and was performed by a single surgeon (SB) using the Hardinge approach.

Duraloc acetabular components and coral femoral stems were used.

Table I: Clinical data



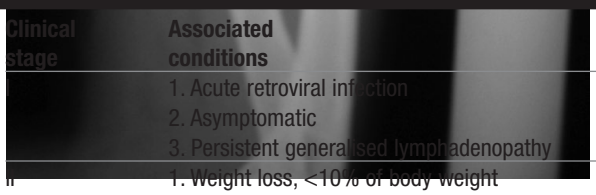
Affected hip	
Right	9
Left	5
Bilateral	1
Gender (M/F)	10/4
Age (years)	42 (range 29-45)
Osteonecrosis	10
Neglected neck of femur fracture	4
Body weight (kg)	61 kg (range 52-102)
WHO staging *(Table II)*	I – 11
	II – 1
	III – 2
CDC staging *(Table III)*	A1 – 7
	A2 – 4
	A3 – 3
Follow-up (years)	6 years (range 5 – 7years)

Peri-operative parenteral cefril was administered in all patients (three doses). In addition patients were routinely given rifampicin for 9 months as prophylaxis against tuberculosis and to prevent bacterial adherence to implants. This was suggested and prescribed by our local infectious disease expert while knowing full well that this is unscientific with no articles to support the use in these patients.

Clexane was given routinely, until patient was mobilised (average five days).

Collective experience with HIV and arthroplasty at any institution is small and limited

Table II: World Health Organisation staging system for HIV infection and disease



Clinical stage	Associated conditions	Performance scale
I	1. Acute retroviral infection 2. Asymptomatic 3. Persistent generalised lymphadenopathy	Scale 1 Asymptomatic Normal activity
II	1. Weight loss, <10% of body weight 2. Minor mucocutaneous manifestations 3. Herpes zoster within last 5 years 4. Recurrent upper respiratory tract infections	And/or scale 2 Symptomatic Normal activity
III	1. Weight loss > 10% of body weight 2. Unexplained chronic diarrhoea > 1 month 3. Unexplained prolonged fever (intermittent or constant) > 1 month 4. Oral candidiasis 5. Vulvo-vaginal candidiasis, chronic (> 1 month) or poorly responsive to therapy 6. Oral hairy leukoplakia 7. Pulmonary tuberculosis, within the past year 8. Severe bacterial infection (e.g. pneumonia)	And/or scale 4: Bedridden: >50% of the day during the last month
IV (AIDS-defining conditions)	1. HIV wasting syndrome 2. *Pneumocystis carinii* pneumonia 3. Toxoplasmosis of the brain > 1 month 4. Cryptosporidiosis with diarrhoea 5. Cryptosporidiosis, extrapulmonary 6. Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes) 7. Herpes simplex infection, mucocutaneous > 1 month, or visceral any duration 8. Progressive multifocal leuco-encephalopathy 9. Any disseminated endemic mycosis, e.g. histoplasmosis 10. Candidiasis of the oesophagus, trachea, bronchi or lungs 11. Atypical mycobacteriosis, disseminated 12. Non-typhoidal salmonella septicaemia 13. Extrapulmonary tuberculosis 14. Lymphoma, Kaposi's sarcoma 15. HIV encephalopathy	And/or scale 4 : Bedridden: 50% of day during the last month

Table III: AIDS surveillance case definition for adolescents and adults (Centres for Disease Control and Prevention, 1993 revision)

	Clinical categories		
$CD4^+$ Cell count categories	**A** Documented asymptomatic HIV infection, including peripheral generalised lymphadenopathy or acute retroviral syndrome	**B** Symptomatic HIV infection, including conditions not listed in clinical Category C but which are either: attributed to HIV infection; indicative of a defect in cell-mediated immunity, or considered to have a clinical course or management that is complicated by HIV infection	**C** Symptomatic HIV infection with an AIDS indicator condition. Once a Category C condition has occurred the individual remains in Category
$CD4^+$ count of > 500 cells/mm^3 or $CD4^+$ cell percentage of > 2	A1	B1	C1
$CD4^+$ count of 200-499 cells/mm^3 or $CD4^+$ cell percentage of 14-28%	A2	B2	C2
$CD4^+$ count of <200 cells/mm^3 or $CD4^+$ cell percentage of < 14%	A3	B3	C3

Patients were mobilised after surgery but remained partial weight-bearing with an ambulatory aid for a period of 3 months.

Follow-up was done at six weeks, three months and biannually thereafter. Clinically hip ratings were evaluated according to Merle d' Aubigne and Postel for pain, walking ability and range of motion (ROM) with a maximal score of 18 points (6 points for each item).[8]

Radiographic evaluation was done by examining the antero-posterior and lateral radiographs taken pre-operatively, immediately postoperative and at each follow-up. The acetabular component was considered to be unstable if there was definite migration or a change in position. The stability of the femoral component was evaluated as described by Eng.[9] The distribution of osteolysis on the femoral side was recorded according to the zonal system described by Delee and Charley[10] and on the femoral sides by Gruen.[11]

Results and outcome

The results are summarised in *Table IV*. In fourteen patients the mean follow-up was 72 months (range 60-76 months). The estimated blood loss averaged 350 ml (range 250 ml-675 ml) and there did not appear to be any predisposing conditions that resulted in excessive intra-operative blood loss. Five patients required blood transfusion. The average hospital stay was nine (6-14) days.

The mean pre-lymphocyte subject analysis was TLC 2.24 mm^3, CD4 -425 mm^3; CD8 873 mm^3; CD4/CD8 -0.52 and the mean post-lymphocyte analysis at six years was TLC 1.98, CD4-350 mm^3, and CD8-724 mm^3.

In three patients the CD4 counts declined to below 200 (average 113.6) and are presenting receiving highly active antiretroviral therapy (HAART) consisting of zidovudine, didanosine and lopinavir which was commenced in 2005. Five patients have gone back to their employment while the others are on a disability grant.

Clinical

There were no revisions, the mean Merle d' Aubigne and Postel hip score was 17 points at the final evaluation (pain 6, walking 5, range of movement 6).The incidence of the thigh pain was very low (three patients).

Radiological

There was no migration or circumferential radiolucent zone greater than 2 mm in the uncemented cups. Femoral osteolysis was seen in two patients, Gruen zones 1 and 7. Examples of a few of our patients are included *(Figures 1a-c, Figures 2a-b).*

Complications

One patient who sustained a periprosthetic fracture following a high energy traffic accident was treated successfully non-operatively for two months on traction.

Table IV: Summary of results at six years

Haematological		
Mean lymphocyte subset analysis	**Pre-op**	**Post-op**
TLC	2.24 mm³	1.98 mm³
CD4	425 mm³	323 mm³
CD8	873 mm³	724 mm³
CD4:CD8 ratio	0.52	0.48
Clinical		
Number of revisions or loosening	none	
Hip score	17	
Pain	6	
Walking	5	
Range of movement	6	
Radiological		
Stability		
Bone in growth	Cup	15 (100%)
	Stem	15 (100%)
Osteolysis	Pelvis	0
	Femur	2

There was no late infection, nerve palsy or deep vein thrombosis.

Discussion

There are very few reports of total hip arthroplasty in HIV-infected patients. Most reports are confined to joint replacement in HIV-positive patients with haemophilia carrying a considerable risk of infection and implant wound healing.[1,2,11,12] In a multicentre retrospective study by Kesley *et al*,[13] three of 27 patients developed deep infections; all three were HIV-positive at the time of infection. Lehman *et al* evaluated deep periprosthetic infection after total joint replacement in patients with HIV and intravenous drug users (IVDU). Of 28 HIV positive patients undergoing joint replacement four developed infections, seven patients with IVDU developed an infection, 11% of patients with both IVDU and HIV developed a deep infection.[14]

Ragni *et al* reported rate of infection of 26.1% in a group of HIV-positive patients in whom CD4 count was below 200 cells/ml³ in patients requiring arthroplasty.[15] Our study has demonstrated a zero infection rate at six years particularly in three of our patients with their CD4 count declined below 200 cells/mm³ (average 113.6 cells/mm³). Our situation is different from Lehman's study in that the IVDU are exposed to multiple episodes of bacteraemia associated with percutaneous injections and from Ragni's report in haemophilic patients who are prone to recurrent bleeds and frequent factor transfusions.

Although HIV infection typically takes approximately 10 to 12 years from initial infection to death, this period varies considerable between individuals.

In a small proportion (5% to 10%) of HIV-infected individuals ("rapid progressors"), progression to AIDS is much more rapid, perhaps taking as little as 2 years in some individuals.[16] In about 5% of cases ("long-term non-progressors"), progression to AIDS is much slower and may be postponed indefinitely.[16] Rapid progressors appear to experience severe symptomatic primary infection rather than mild or asymptomatic primary infection.[16]

Long-term survival is a reality for patients requiring total joint arthroplasty and we do not suggest that an absolute value for the CD4 count should be used to decide whether or not to offer surgery

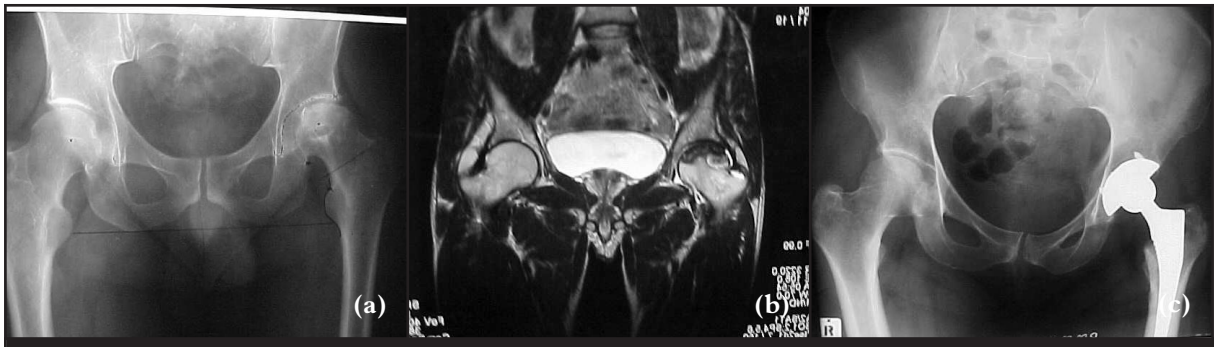


Figure 1:
(a) Antero-posterior radiograph - osteonecrosis of the hip
(b) MRI
(c) Follow-up at six years after THR hip score of 17

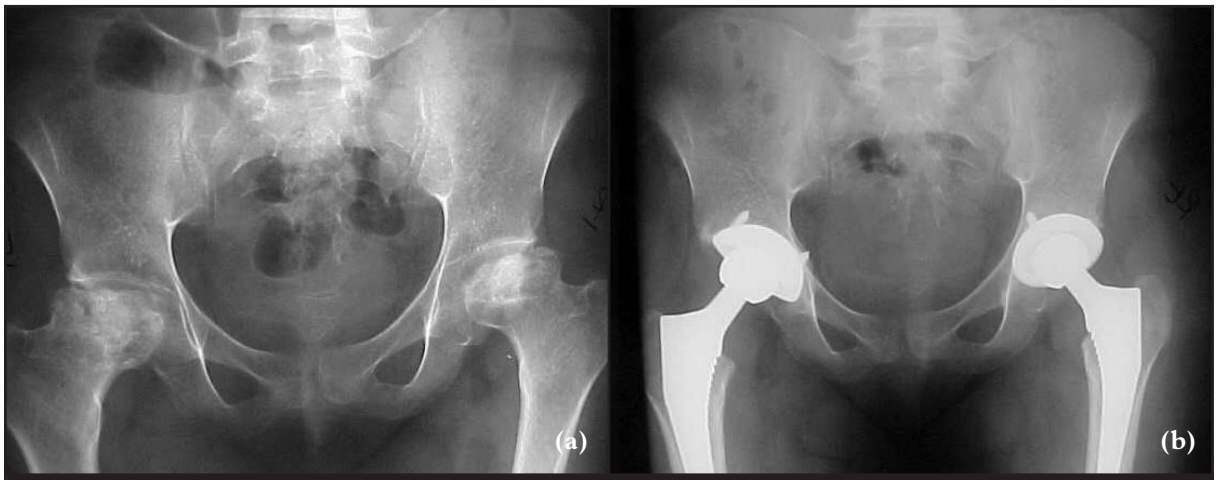


Figure 2(a): Antero-postero radiograph of osteonecrosis of bilateral hips
Figure 2(b): Follow-up at six years after THR hip score of 17

Rapid progressors show a decline in CD4 cell counts and non-cytolytic CD8 suppressor activity over two to three years whereas long-term non-progressors show no declines. However at present the relative contribution of immunological, genetic and virological factors in determining which individuals become long-term non-progressors is controversial. Three patients in this series were rapid progressors. The only consistent physical examination in these patients is a persistent inguinal lymphadenopathy, dermatological abnormalities, hyperpigmentation and minor constitutional symptoms like fatigue and myalgia. Hence, the decision to perform a total joint replacement does not depend on the CD4 count, rather on whether the individual is a rapid progressor or a long-term non-progressor and the stage of the disease. It is also advisable to maintain careful vigilance for early signs of infection and to institute early, systemic antibiotics and to commence anti-retroviral therapy which is effective at improving the immune status. It is now clear that long-term survival is a reality for patients requiring total joint arthroplasty and we do not suggest that an absolute value for the CD4 count should be used to decide whether or not to offer surgery. The outcome of total joint arthroplasty will depend on the nutritional status, stage of the disease and co-morbidity. Increasing emphasis is being put on providing infected individuals with nutritional advice, evaluation and support as early as possible after diagnosis.

Osteonecrosis of the femoral head associated with HIV was first reported in 1990 (Goorney *et al*),[17] and has been shown to occur with increased incidence in patients infected with HIV. Recent studies on symptomatic osteonecrosis in HIV-positive individuals by Kerruly *et al* have reported an annual incidence of about 1%.[18] Several mechanisms have been proposed as causes of avascular necrosis (AVN) in HIV-infected patients. HIV is associated with elevated levels of anticardiolipin antibodies, particularly the IgG type.[19] These antibodies are often elevated in patients with arterial and venous thrombosis, and in thrombocytopaenia. In the HIV-positive population with elevated ACAI, one study in which 73 homosexual men were enrolled demonstrated no venous thrombosis[19] and a second study revealed only one episode of deep venous thrombosis.[20] Solomon *et al*[21] reported five HIV-positive patients with AVN and elevated ACA, and stated that elevated ACA should be interpreted with caution, as they are elevated in 80-90% of patients with AIDS. There are patients with HIV infection who develop AVN with no other known risk factors for AVN.[22,23] Antiviral therapy (protease inhibitors) is thought to be responsible for the development of AVN in HIV patients since antiviral drugs may cause hyperlipidaemia and osteoporosis.[24]

On the other hand, in some of these patients AVN may develop before antiviral therapy. It has been suggested that the HIV itself or some other factors may increase the risk of development of AVN in those patients, although antiphospholipid antibodies (APLA) are often detected in HIV-positive patients; the clinical importance of this condition is not clear.[25]

In this cohort of patients with osteonecrosis, it was difficult to define reasons for AVN in individual patients, because most of the patients had multiple risk factors. Known risk factors in our patients were corticosteroid use (eczema in one patient), alcohol abuse (six patients), smoking (ten patients), hypercholesterolaemia (two patients) and antiviral therapy (three).

The neck of femur fractures in this young cohort of patients were due to motor vehicle accidents and the fractures were stabilised with an onlay device (pin and plate). The above patients presented to me with failed implants and neglected non-unions. At the initial surgery neck osteotomy or bone grafting were not performed. In these patients an uncemented total hip replacement were performed as a single stage surgery.

Conclusion

Cementless total hip replacement in HIV-infected patients who have not progressed to clinical stage IV (WHO) can be rewarding and does not carry an increased risk of post-operative infection.

Despite the decline in the CD4, we feel that joint replacement can be of considerable value in improving the quality of life in HIV-infected patients, particularly when surgery is performed in specialist centres in close consultation with physicians involved in the treatment of infectious diseases. The decision to perform a total joint replacement must always be analysed on the basis of the risk-benefit ratio for the patient and on informed decision by the patients and physician. The outcome in this patient population reveals that total hip arthroplasty can be safely performed with minimum complications in compliant patients who have not progressed to an AIDS-defining disease (stage IV).

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Bibliography

Bueher *et al.* Wound infection rates after invasive procedure in HIV-1 seropositive versus HIV-1 seronegative haemophilias. *Ann Surg* April 1990;492-98.

Centres for disease control and prevention. 1994 revised classification system for human immunodeficiency virus infection among adolescents and adults. *Morbidity & Mortality weekly reports* 1992;**41**(RR-17;1-5.

Mahoney Cr, Glesby MJ, Di Carlo EF, Peterson MGE & Bostnam MP. Total hip arthroplasty in patients with human immunodeficiency virus infection-pathologic findings and surgical outcomes. *Acta Orthop* 2005;**76**(2):198-203.

Masur H, Miller K, Jores E *et al.* High prevalence of avascular necrosis (AVN) of the hip in HIV Infection: Magnetic resonance imaging of 339 asymptomatic patients. Abstracts of 38th Annual Meeting of the infection disease society of America. September 7-10;2000;New Orleans: Abstract 15.

WHO global programme o AIDS. Proposed World Health Organisation staging system for HIV infection and disease. *Aids* 1993;**7**:868-9.

References

1. Hick JL, Ribbans WJ, Buzzard B, Kelly SS, Toft L, Torri Cr, Wiedel JD, York J. Infected joint replacements in HIV-positive patients with haemophilia. *J Bone Joint Surg (BR)* 2001;**83**:1050.
2. Luck JV, Logan LR, Benson DR, Glasser DB. Human immunodeficiency Virus infection: complications and outcome of orthopaedic surgery. *JM Acad Ortho Surg* 1996;**4**;297-304.
3. Harrison WJ. HIV/AIDS in trauma and orthopaedic surgery. (Br) 2005;87B:1178-81.
4. Savioz D, Chilcot M, Sudvig C *et al.* Preoperative counts of CD4 T-lymphocytes and early postoperative infective complications in HIV positive patients. *Aus J Surg* 1998;**164**;483-7.
5. Tran HS, Moncure M, Tarnott M *et al.* Predictors of operative outcome in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. *Am J Surg* 2000;**180**;228-33.
6. Green WB, De Gnor LT, White GC. Orthopaedic procedure and progress in haemophilia patients who are seropositive for human immunodeficiency virus. *Am J of Bone & Joint Surg* 1990;**724**:2-11.
7. Hoekman P, Van Der Perre P, Nelissen J. Increased frequency of infection after open reduction of fractures in patients who are seropositive for human immunodeficiency virus. *Am J of Bone & Joint Surg* 1991;**73A**:675-9.
8. Merle A, d'Aubigne R, Postel M. Functional results of hip arthroplasty with acrytic prosthesis. *J Bone Joint Surg* 1954;**36-A**:451-75.
9. Eng CA, MAssin P, Suthers KE. Roentgenographic assessment of the biologic fixation of porous-surfaced femoral components. *Chin Orthop 1990;***257**:107-28.
10. Delee JG, Charley J. Radiological demarcation of cemented sockets in total hip replacement. *Chin Orthop* 1976;**121**:20-32.
11. Gruen TA, McNeice GM, Amstutz HC. Modes of failure of cemented stem type of loosening components: a radiographic analysis of loosening. *Chin Orthop* 1979;**141**:17-27.
12. Luck JV, Karpe EK. Surgical management of advanced haemophilic Arthropathy: an overview of 20 years experience. *Chin Orthop* 1989;**242**:60-82.
13. Kesley SK, Jachiewicz PF, Gilbert MS, *et al.* Hip arthroplasty in haemophilic arthroplasty. *Chin Orthop* 1992;**276**:210.
14. Lehman CR, Ries MD, Pairment GD, Davidson AB. Infection after total joint arthroplasty in patients with human immunodeficiency virus or intravenous drug use. *J Arthroplasty* 2001;**16**:330-5.
15. Ragni MV, Crossett LS, Herndon JH. Postoperative infection following orthopaedic surgery in human immunodeficiency virus-infected haemophiliacs with CD4 count $\leq$ 200/mm^3. *J Arthroplasty* 1995;**10**.716-21.
16. Haynes BF. Immune responses to human immunodeficiency virus infection. In AIDS: Etiology, Diagnosis, Treatment and Prevention, 1997; pp89-99 edited by VT De Vita Jr, S Hellman & S Rosenberg. Philadelphia: Lippincott – Raven.
17. Goorney BP, Lacey H, Thuairajasingam S, Brown JDK. Avascular necrosis of the hip with HIV infection. *Genitourim Med* 1990;**66**:451-2.
18. Kerruly JC, Chaisson RE, Moore RD. Increasing incidence of avascular necrosis of the hip in HIV infected patients. *J Acquir Immune Def Syndr* 2001;**28**:101-2.
19. Bloom EJ, Abrams DI, Rodgers G. Lupus anticoagulant in the acquired immunodeficiency syndrome. *JAMA* 1986;**265**:491-93.
20. Canoso RT, Zonli, Goofan JE. Anticardiolipin antibodies associated with HTLV-III infection. *Bar's. Haematol* 1987;**65**:495-98.
21. Solomon G; Brancatol, Winchester R. An approach to human immunodeficiency virus positive patients with spondyloarthritic disease. *Rheum Chin North Am* 1991;**17**:43-58.
22. Belmonte MA, Garcia-Partales R, Domenech I *et al.* Avascular necrosis of bone in human immunodeficiency virus infection and antiphospholipid antibodies. *J Rheumatol* 1993;**20**:1425-8.
23. Rademaker J, Debro JS, Solomon G. Osteonecrosis and human immunodeficiency virus infection. *J Rheumatol* 197;**24**:601-4.
24. Brown P, Crare L. Avascular necrosis of bone in patients with human immunodeficiency virus and osteonecrosis of the femoral head. *J Arthroplasty* 2002;**17**:135-9.
25. Atahan A, Gatay A, Reyhan *et al.* Human immunodeficiency virus and avascular necrosis of femoral head; a case report. *Chinese Med J* 2004;**117**(9):1437-40.