Netherlands
The Journal of Medicine

PHOTO QUIZ

Shoulder pain in two HIV-seropositive patients

A. Verbon[1]*, J.M. Prins[2]

[1]Department of Internal Medicine, Erasmus MC, Rotterdam, the Netherlands, [2]Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Center, Amsterdam, the Netherlands, *corresponding author: e-mail: a.verbon@erasmusmc.nl

CASE 1

Patient K, born in 1967, started complaining about progressive pain in his left paretic shoulder in the summer of 2008. Both passive and active movements were painful. The X-ray is shown in *figure 1A*. The patient's medical history was remarkable for the diagnosis of *Pneumocystis jiroveci* pneumonia (PJP) in 2002, with a CD4 count of 1 x 10^6/l and a plasma HIV-RNA of 140,000 copies/ml. After treatment of the PJP, antiretroviral therapy consisting of stavudine, lamivudine and lopinavir/ritonavir was started; after one year lopinavir/ritonavir was substituted by nevirapine because of a cholesterol of 5.9 mmol/l. His HIV-RNA became undetectable (<40 copies/ml) and his CD4 count increased steadily to 520 x 10^6/l. In 2003 he suffered from a cerebrovascular accident. An MRI showed infarction in the area of the left medial cerebral artery, and multiple T2 hyperintense lesions of gray and white matter in the basal ganglia and peripheral parts of the brain. With the presumed diagnosis of vasculitis, prednisone was started and patient received a cumulative dose of 10.5 gram between 2003 and 2004. In this period alendronine acid was started.

CASE 2

Patient L, born in 1963, was diagnosed with HIV infection in 1999. At that time the CD4 count was 40 x 10^6/l, and toxoplasmosis cerebri was diagnosed. After treatment, antiretroviral therapy was started with stavudine, lamivudine and indinavir/ritonavir. Within a few months the plasma HIV-RNA declined below the detection level, and within one year the CD4 count increased to 500 x 10^6/l. In June 2005, she had reactivation of the toxoplasmosis, i.e. on a CT scan oedema surrounding the calcified old toxoplasmosis lesion. She was successfully treated with sulfadiazine/pyrimethamine and dexamethasone. Steroids were gradually tapered and stopped in the summer of 2006. In the summer of 2008 she developed pain in the upper left arm. The X-ray is shown in *figure 1B*.

Figure 1A. *X-ray of left humerus of patient K showing sclerotic changes centrally*

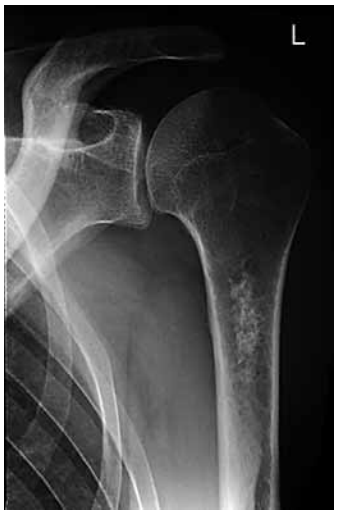
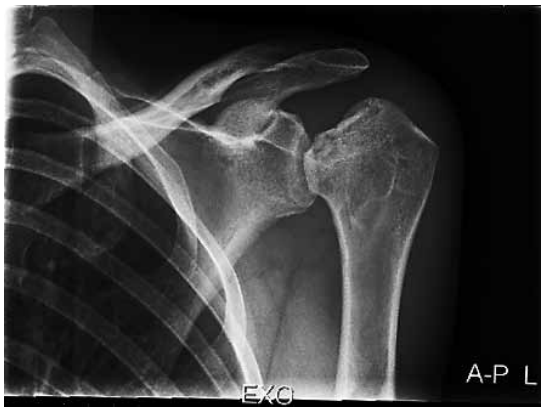


Figure 1B. *X-ray of left humerus of patient L showing subchondral collapse*



WHAT IS YOUR DIAGNOSIS?

See page 325 for the answer to this photo quiz.

DIAGNOSIS

In case 1, the X-ray of the shoulder showed sclerotic changes central in the left humerus without cortical changes or osteolysis and was compatible with avascular necrosis. In case 2, the X-ray showed avascular necrosis of the left upper humerus, with subchondral collapse. Avascular necrosis (AVN) of the bone has been described in HIV-infected patients since 1990 and the incidence seems to be increasing.[1] An annual incidence as high as 1.19 per 1000 patients has been reported, which is 29-fold higher than the population-based incidence.[1] In HIV-negative patients, the majority of AVN is of the femoral head, but it has also been described in humerus, knee, ankle and smaller joints.[2] The explanation for the high percentage of AVN occurring in the femoral head is multifactorial, but mechanical stress probably plays an important role.[2] This was shown in rats that were forced to stand on their hind legs while being fed; 33% developed AVN.[2] AVN has been associated with more than ten different disease entities, trauma being the most frequently occurring aetiology.[2] Of non-traumatic causes, use of corticosteroids is most commonly reported, but also the consumption of alcohol, infections (among which HIV infection), hyperbaric events, storage disorders, marrow infiltrating diseases, coagulation defects and some autoimmune diseases have been described.[2] The final common pathway for the development of AVN is a compromise in the blood flow to the bone. In non-traumatic AVN, epidemiology suggests that pathogenesis is often multifactorial. The concept of cumulative cell stress stems from data that show a higher rate of steroid-induced AVN in systematically ill patients. Both patients described here fit this theory, since they had used high cumulative doses of steroids, were infected with HIV for a long period, and had hypercholesterolaemia (patient K). Whether there is a causal association with HIV infection or antiretroviral treatment has not been completely elucidated. Prior corticosteroid use has been reported to be a significant risk factor, although traditional risk factors such as alcoholism, radiation therapy, hypercholesterolaemia, and hypertriglyceridaemia were also described.[2] In a case-control study from France[3] describing 12 HIV-seropositive patients with AVN, in the multivariate analysis only prior steroid use and alcohol abuse were associated with AVN. CD4 count nadir, the use of highly active antiretroviral therapy (HAART), use of protease inhibitors, duration of antiretroviral therapy, or HIV load over 500 copies/ml were not statistically significantly associated with AVN, and neither were HAART-induced metabolic disorders such as fat wasting, fat accumulation, high cholesterol or hypertriglyceridaemia or diabetes mellitus.[3] In another case-control study of 26 patients with HIV and AVN, a lower CD4 count nadir and previous opportunistic infections were associated with AVN, whereas duration of therapy was not.[4]

To our knowledge, our patients are the first reported HIV-infected patients with AVN of the upper humerus. Early imaging of painful bones and joints in HIV patients with concurrent or prior steroid or alcohol use seems warranted.

REFERENCES

1. Gutiérrez F, Padilla S, Ortega E, García JA, Flores J, Galera C, et al. Avascular necrosis of the bone in HIV-infected patients: incidence and associated factors. AIDS. 2002;6:481-3.
2. Assouline-Dayan Y, Chang C, Greenspan A, Shoenfeld Y, Gershwin ME. Pathogenesis and natural history of osteonecrosis. Semin Arthr Rheum. 2002;32:94-124.
3. Lawson-Ayayi S, Bonnet F, Bernardin E, Ragnaud JM, Lacoste D, Malvy D, et al. for Groupe d'Epidémiologie Clinique du SIDA en Aquitaine. Avascular necrosis in HIV infected patients: a case-control study from the Aquitaine Cohort, 1997-2002, France. Clin Infect Dis. 2005;40:1188-93.
4. Hasse B, Ledergerber B, Egger M, Flepp M, Bachmann S, Bernasconi E, et al. Swiss HIV Cohort Study. Antiretroviral treatment and osteonecrosis in patients of the Swiss HIV Cohort Study: a nested case-control study. AIDS Res Hum Retrovir. 2004;20:909-15.