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The management of musculoskeletal infection in HIV carriers

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Over a three-year period, the authors prospectively implemented a protocol for management of musculoskeletal sepsis (MSS) in HIV carriers in Yaounde, Cameroon. The diagnosis of MSS was based on conventional criteria. HIV carriage was screened by an ELISA test and confirmed with the Western Blot technique. The immune status was based on CD4 lymphocyte count by flow cytometry ; patients were classified as non-immunodepressed (NID), mildly immunodepressed (MID), or severely immunodepressed (SID) based on their CD4 lymphocyte count, as the latter was respectively over 500, between 200 and 500 or less than 200 per ml. Infection was treated by surgical debridement followed by a long-course targeted antibiotic therapy. All SID patients and some MID patients with AIDS-related symptoms also had standard antiretroviral (ARV) therapy. Thirty-one of 294 patients seen with musculoskeletal sepsis during the study period and tested for HIV were found to be HIV carriers. Their mean age was 33 years ; the male/female ratio was 1.58. The following clinical pictures were observed : chronic osteomyelitis (COM) in 32.3% of the cases, septic arthritis (SA) in 38.7%, soft tissue infection (STI) in 25.8% ; the last case was a severe leg complication of Buruli Ulcer (BU). Among these 31 patients, 38.7% were classified as SID (5 COM, 4 SA, 2 STI and the BU patient), 25.8% as MID (2 COM, 4 SA, 2 STI) and 35.5% as NID (3 COM, 6 SA, 2 STI). The organisms involved were not specific. Fifteen patients were managed conventionally, while the other 16 had the usual treatment associated with ARV therapy. The immediate outcome of MSS was good in 29 patients, after a mean hospital stay of five weeks; in two cases of septic arthritis of the knee, a second debridement was needed, due to persistent drainage, and the sinuses all closed. Three months after discharge, one patient with COM of the humerus developed a low-flow fistula which was closed after a revision sequestrectomy. After one year, none of the patients complained of any symptom suggesting reactivation of their MSS.

There is no evidence that HIV carriage is in itself a high risk factor for musculoskeletal sepsis ; the incidence of HIV carriage was indeed virtually similar in the 294 patients with MSS and in the general population, i.e. around 10%. However, in order to improve the outcome following musculoskeletal infections in patients with HIV, their management should take into account their immune status, based on a CD4 lymphocyte count. NID patients should be treated as any other patients with MSS, while SID should

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have additional standard ARV treatment. For those who are MID, the indication for antiretroviral therapy should depend on the presence of one or more AIDS-related signs.

INTRODUCTION

The issue of musculoskeletal sepsis (MSS) in HIV seropositive patients has been the source of some controversies during the past decade. Some authors have reported that HIV infection makes patients more susceptible to musculoskeletal infections, especially myositis, arthritis and osteomyelitis *(6,7,9)* ; on the contrary, others have stated that HIV seropositivity does not *per se* expose patients to bone and joint infections, compared to seronegative individuals *(10,11)*. In all these series, the musculoskeletal infection was managed by conventional debridement and targeted antibiotherapy with a good outcome in up to 90% of cases *(2)* ; how far these patients were immunocompromised is however not clear. There is therefore a lack of reported evidence on the treatment and outcome of MSS in cases where it is combined with severe immunodeficiency. Our opinion is that such reports are needed and should be encouraged.

The purpose of this paper was to report our method of management of MSS in HIV carriers, and its mid-term outcome, as it was prospectively applied, especially in severely immunocompromised patients.

METHODS

Over a period of three years, from March 2000 to March 2003, we prospectively implemented a protocol of management of musculoskeletal infections diagnosed in HIV carriers in the Central Hospital and General Hospital of Yaounde. All patients observed with MSS were screened for HIV infection whenever they presented an evident risk factor, on their own demand or upon advice from the staff. The diagnosis of MSS was based on classical clinical signs in combination with roentgenographic examination of the limbs, puncture of joints or soft tissues, complete blood count and erythrocyte sedimentation rate (ESR). The HIV screening test used was the ELISA test ; whenever it appeared positive, a Western blot test was carried out for confirmation. In case of confirmation, the patient was elected for the protocol and was registered on a special form with demographic, clinical, biological, treatment and outcome data. Any one refusing the screening was normally treated, but excluded from the study as well as any ones who were lost from the process before the confirmation test. After registration, the next step was a CD4 lymphocytes count by the flux cytometry technique and routine hepatitis B serology. Based on the CD4 count and the age (5), patients were classified as non immunodepressed (NID), mildly immunodepressed (MID), or severely immunodepressed (SID) according to whether they had respectively more than 500, 500 to 200 or less than 200 lymphocytes per ml of blood.

All patients underwent surgical débridement, and a specimen of pus or necrotic tissue was taken for bacteriological analysis. A prolonged and targeted antibiotic therapy was carried out postoperatively on the basis of the isolated germ and its sensitivity ; it lasted until normalisation of the ESR. When a patient was classified as NID or as MID without any AIDS-related symptom, no further treatment was prescribed, but a counselling on specific way of life and regular check up was undertaken by the HIV/AIDS team. All those classified as SID and some MID with AIDS-related diseases benefited from anti- retroviral therapy (ARV) prescribed by the HIV/AIDS team. The patients were advised never to stop the ARV drugs when started. Upon discharge, they were instructed to attend the check up at 8 weeks, at which time the antibiotic therapy was stopped based on the normalisation of the infection markers. They were further seen at 6 and 12 months for clinical and radiological control of the affected limb. The follow-up of the HIV infection was continued by the specialised consultant.

The special forms were finally collected and entered into a computer data base. Frequency calculations were made, and the results were expressed with a confidence interval (CI) of 95 %. When necessary, a comparison of two frequencies was done using the X^2-test ; differences were considered non significant if $p < 1.96$.

RESULTS

Demography

During the three year - period of the study in both hospitals, 303 patients were diagnosed with musculoskeletal infection. Two hundred and ninety four of them underwent HIV screening for different

reasons. Thirty three were screened positive, i.e. 11.22% (CI = 11.33 to 11.11) ; one of them, a 4-year-old child, died suddenly of cerebral malaria before the confirmation test and another one, an adult, was lost to follow-up very early. Our final study group therefore included 31 patients, 19 males and 12 females, with a sex ratio of 1.6. The youngest patient was 18 years old and the oldest 52 years ; the mean age was 33.5 years. There was no history of IV drug use or homosexuality. Twenty patients presented HIV-related factors: recent herpes zoster infection in six cases, recent death of the partner from unknown cause in three cases, recent major weight loss in five cases, recurrent soft tissue infection in three cases, and long-lasting scratching dermatitis in three cases. Three patients were already known to be seropositive, and nine were screened on their own request or upon demand from the staff.

Clinical presentation

Ten (32.25%) of the 31 MSS cases were classified as chronic osteomyelitis (COM), twelve (38.70%) as septic arthritis (SA), and eight (25.80%) as soft tissue infections (STI) ; the thirty-first case was a severe leg complication of Buruli Ulcer (BU). In the patients with chronic osteomyelitis, the presenting complaints were pain, functional impairment and sinus formation; the infection sites were the femur in seven cases, the tibial shaft, the humeral shaft and the fibula in one case each. Patients with septic arthritis all presented with fever, pain and swelling of the joint, which was the knee in six cases, the ankle in three, the shoulder in two, and a metatarsophalangeal joint in a single case. The soft tissue infections were abscesses in six patients, and cellulitis and erysipelas in one patient each. As independent co-morbidities, we found one known diabetes and one sickle cell anaemia.

Paraclinical features

The radiological changes were not specific, the virus was HIV 1 in all cases, and the hepatitis serology was negative in all cases. The CD4 counts ranged from 162 to 988 cells/ml, with 12 patients (38.7%) being classified as SID (5 COM, 4 SA, 2 STI and the BU patient), 8 (25.8%) as MID (2 COM, 4 SA, & 2 STI) and 11 (35.5%) as NID (3 COM, 6 SA, & 2 STI) (table I).

Table I. — Relative rates of the three categories of immune status in the 31 patients, based on their CD4 count

	NID	**MID**	**SID**	**TOTAL**
COM	3	2	5	10
SA	6	4	4	14
STI	2	2	2	6
BU	0	0	1	1
Total	11 **(35.5)**	8 **(25.8)**	12 **(38.7)**	31 **(100.0%)**

The mean value of the ESR was 63.4 mm after the first hour. The organisms involved were *Staphylococcus aureus* in 17 cases (54.8%), *Proteus mirabilis* in 6 (19.3%), *Pseudomonas* alone in four (12%), and *Pseudomonas* associated with *E. Coli* in one case, *E. Coli*, *Streptococcus agalactiae* and S*almonella* subgroup in a single patient each.

Management

As far as the MSS was concerned, the two patients with erysipelas and cellulitis were treated with intravenous penicillin and bed rest, while all the others underwent surgery followed by targeted antibiotherapy. The surgery consisted of conventional debridement through a direct approach for abscesses or by conventional arthrotomy for septic arthritis. The seven patients with femoral COM and the one with humeral COM had two-stage surgery consisting of debridement, followed by skin grafting after a few weeks of daily dressing, while the one with tibial infection underwent a three-stage programme of surgical debridement, autologous bone grafting and finally, soft tissue reconstruction by a musculo cutaneous flap from the medial part of the gastrocnemius. Whenever present, internal fixation devices were removed. The patient with fibular COM, which was related to BU, underwent a two-stage procedure consisting of subtotal fibulectomy and débridement of all necrotic muscles, followed by skin grafting after one month of

daily dressing. The antibiotic treatment was cefuroxine in 13 cases, rifampicine + ciprofloxacine in 9 cases, amoxicilline +clavulanic acid in 7 cases and finally, cloxacilline or rifampicine alone in one case each.

Regarding the immune status, antiretroviral therapy was prescribed to the 12 SID patients and to the five who were MID, but with AIDS-related symptoms (recurrent herpes zoster infection in two, unexplained recent loss of more than 5% of weight in two and chronic scratching dermatitis in one), but two of them refused it. There was also one NID patient with a COM who presented with a three-year history of ARV therapy ; he was encouraged to continue, which makes a total of 16 HIV carriers with MSS under ARV therapy in this series. The ARV therapy was a triple association of Effavirenz + Zidovudine + Lamivudine in four cases, Indinavir + Lamivudine + Zidovudine in eigth patients, Niverapine + Lamivudine + Stavudine in three and Seocnin + Lamivir in the last one (table II).

Outcome

The immediate outcome of the MSS was good in 29 patients, after a mean hospital stay of five weeks. Subjectively, they had significant decrease or complete resolution of pain. Objectively, all the wounds dried and closed ; the ESR returned to normal after an average of 5 weeks. However, in two cases of SA of the knee, a second débridement was needed owing to persistent discharge, but all sinuses finally closed.

Three months after discharge, all patients were seen for check up. Thirty of them appeared clinically, radiologically and biologically normalised. At this date, and under these conditions, the MSS was declared “under control” and antibiotic treatment was stopped. The thirty-first patient was not cured at this stage. He presented a low flow fistula that closed later on, after a revision sequestrectomy, performed on an ambulatory basis.

After one year, none of the patients complained of any sign or symptom related to reactivation of their MSS ; their general status was also good except in two cases who later consulted for an anal fistula and a facial palsy respectively.

DISCUSSION

This prospective study describes the management of MSS in a consecutive series of 31 HIV carriers, among whom 16, who were either SID, or MID but with AIDS-related symptoms underwent surgery and antiretroviral therapy while the other group of 15, who were either NID or MID with no AIDS-related disease only had surgical treatment. The MSS was soon under control in 28 patients (90.3%). The other three patients (9.7%) needed a revision procedure, but one year later no patient presented any symptom related to his previous sepsis. There are scarce data in the literature on the treatment or outcome of musculoskeletal sepsis in AIDS patients. Our opinion is that clinical trials should be encouraged, in order to improve our knowledge on this challenging issue. We did not randomise the trial because it would not have been ethically acceptable.

Regarding the prevalence of 11.2% HIV carriers in our sample of 294 patients with MSS, it did not differ significantly from that in the general population, which is 11% *(8)*. It may therefore be possible that HIV infection is not *per se* a risk factor for MSS and we believe with Casado *et al* *(3)* and Vasilopoulos *et al* *(10)* that, whenever observed, this association should be considered fortuitous. The other epidemiological data in the study are similar to those in existing literature, except for the absence of intravenous drug abuse and homosexuality as risk factors ; this may be explained by the cultural and economic differences between the local and western communities. The clinical, biological and radiological features did not present any specificity compared to the usual findings in HIV-negative patients ; Espinosa *et al* *(4)* and Belzunegui *et al* *(2)* also found such a similarity. Regarding treatment, osteomyelitis was managed as stated in our protocol *(1)* based on the status of the soft tissue coverage, while septic arthritis and soft tissue infection were conventionally treated. Antiretroviral therapy was prescribed only to immunodepressed patients, with a good immediate and mid-term outcome ; all infections were controlled regardless of the association or not of ARV therapy. This was also true in two MID patients

Table II. — Data of the 16 patients with MSS who received an ARV therapy

Patient	Age / sex	Indication for screening	Past surgical history	Location & type of MSS	CD4 count	Immune status	Organism involved	Surgery	Antibiotic therapy	Anti-retroviral therapy	Hospital stay	Immediate local result (3 months)
N° 1	49 M	Already known	Internal fixation	COM Femur	586	NID	Pseudo-monas + E.coli	2-stage surgery with plate and screws removal	Rifampicine Cipro-floxacine	Effavirenz Zidovudine Lamivudine	38 days	Good
N° 2	38 F	Recent death of the partner	Open fracture externally fixed	COM Femur	181	SID	E. coli	2-stage surgery	Amoxicilline clavulanic acid	Indinavir Lamivudine Zidovudine	36 days	Good
N° 3	26 M	facial zoster infection	Osteomye-litis in childhood	COM Humerus	182	SID	Staph aureus	2-stage surgery	Cloxacilline	Niverapine, Stavudine Lamivudine	36 days	revision sequestrec-tomy 3 months later
N° 4	31 F	Recent weight loss	none	COM Femur	172	SID	Staph Aureus	2-stage surgery	Cefuroxime	Indinavir Lamivudine Zidovudine	42 days	Good
N° 5	32 F	Recent weight loss	None	COM Femur	203	MID	Proteus mirabilis	2-stage surgery	Cefuroxime	Indinavir Lamivudine Zidovudine	45days	Good
N° 6	19 F	Long lasting scratching dermatitis	None	COM Femur	212	MID	Staph aureus	2-stage surgery	Rifampicine Cipro-floxacine	Niverapine, Stavudine, Lamivudine	36 days	Good
N° 7	30 M	Routine screening	osteomye-litis in childhood	COM Tibia	172	SID	Staph aureus	2-stage surgery	Cefuroxime	Effavirenz Zidovudine Lamivudine	36 days	Good
N° 8	42 F	Severe weight loss	none	COM Fibula	162	SID	Staph aureus	2-stage surgery	Rifampicine	Seocnin + Lamivir	90 days	Good
N° 9	25 F	Weight loss	Recurrent joint punctures	SA Knee	192	SID	Proteus mirabilis	debridement	Amoxicilline clavulanic acid	Indinavir lamivudine Zidovudine	28 days	Good
N° 10	32 M	Routine screening	Joint infiltration	SA Knee	180	SID	Staph aureus	debridement	Cefuroxime	Effavirenz Zidovudine Lamivudine	45 days	Revision débridement after 14 days
N° 11	22 F	Fatigue	Joints scarifica-tions	SA Knee	190	SID	Pseudo-monas	debridement	Rifampicine Cipro-floxacine	Indinavir lamivudine Zidovudine	45 days	Revision débridement after 18 days
N° 12	42 M	Spontan-eous request	Shoulder arthro-graphy	SA Shoulder	192	SID	Staph aureus	débridement	Cefuroxime	Indinavir lamivudine Zidovudine	14 days	Good
N° 13	27M	Staff councel-ling	Recent soft tissue abscess	Abscess of psoas muscle	185	SID	Strepto agalactiae & E. Coli.	débridement	Rifampicine Cipro-floxacine	Effavirenz Zidovudine Lamivudine	10 days	Good
N° 14	18 M	Recurrent herpes zoster	None	Abscess of quadriceps	208	MID	Staph aureus	débridement	Cefuroxime	Indinavir Lamivudine Zidovudine	10 days	Good
N° 15	22M	Sponta-neous request	none	SA Ankle	194	SID	Staph aureus	débridement	Rifampicine Cipro-floxacine	Indinavir Lamivudine Zidovudine	18 days	Good
N° 16	18 M	Chest zoster infection	none	SA Ankle	188	SID	Proteus mirabilis	débridement	Amoxicilline clavulanic acid	Niverapine, Stavudine, Lamivudine	27 days	Good
Mean value	29.5	——	——	——	212.43		——-	——	——	—-	34.76	——

with AIDS-related symptoms, whose infection was controlled without any associated treatment against their viral infection. One of these two patients later developed an anal fistula while the other developed facial palsy ; these complications might not have occurred if they had been under ARV therapy. It may therefore be possible that, when musculoskeletal infections are properly treated by conventional surgical débridement and targeted antibiotic therapy, HIV carriage does not worsen their course, provided the patient is not immunodeficient. For those patients who are severely immunodeficient and those who are moderately immunodeficient but with AIDS-related symptoms, associated antiretroviral therapy may contribute to improve the overall outcome.

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