

Musculoskeletal Infections In Patients Infected with Human Immunodeficiency Virus

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Abstract

Seventeen of 67 HIV-infected patients who had musculoskeletal symptoms were found to have musculoskeletal infections. Bacterial arthritis occurred in 10 patients in which *Salmonella enteritidis* was the most offending organisms followed by *Staphylococcus aureus*. Three patients had *Penicillium marneffii* septic arthritis and one had *P. marneffii* septic arthritis and osteomyelitis. One of these septic arthritis patients had double infection caused by *S. enteritidis* and *P. marneffii*. *Mycobacterium* spp. septic arthritis and osteomyelitis occurred in 2 patients. *Trichinella spiralis* myositis and *S. aureus* myositis each occurred in one patients. Eight patients died. Musculoskeletal infections in HIV-infected patients are not uncommon and have poor clinical outcome. (*J Infect Dis Antimicrob Agents* 1995;12:5-9)

Patients infected with human immunodeficiency virus (HIV) are usually associated with both local and systemic infections. However, musculoskeletal infections are considered rare (1-3). Most of the reported cases are caused by opportunistic pathogens or organisms that rarely cause infections in normal individuals. The organisms that have been reported to cause bone and joint infections in these patients are *Salmonella* spp., *Haemophilus influenzae*, *Streptococcus* spp., *Cryptococcus neoformans*, *Candida albicans*, *Sporothrix schenckii*, *Histoplasma capsulatum*, *Nocardia asteroides*, *Mycobacterium kansasii*, *M. avium intracellulare* complex (4-6). *Staphylococcus aureus* and *C. albicans* have been reported to be the most common offending organisms especially in HIV-infected intravenous drug users (IVDU) (7-9). Surprisingly, *Neisseria gonorrhoea* has rarely been reported as a cause of septic arthritis in HIV infected individuals (5).

Our experience has suggested that the incidence of musculoskeletal infections in HIV-infected individuals

might be higher than those reported in medical literature. This study was conducted to determine clinical features, responsible organisms and outcome of the musculoskeletal infections in patients infected with HIV

MATERIALS AND METHODS

From July 1990-March 1994, 67 HIV-infected patients of the Chiang Mai University Hospital who had musculoskeletal symptoms were consulted to the Division of Rheumatology, Department of Medicine, Faculty of Medicine, Chiang Mai University. Seventeen cases were found to have musculoskeletal infections. These patients were selected for this study.

The diagnosis of musculoskeletal infections was made by 1) the presence of organisms in the muscle, bone or joint tissues or fluids either by stained smears or cultures ; or 2) clinical suggestion of musculoskeletal infections and positive cultures from blood or other body tissue specimens and showed good response to appropriate antibiotics.

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A full history and physical examination with special attention to the musculoskeletal system were performed in all patients. Laboratory investigations including complete blood counts, urinalysis, synovial fluid (SF) analysis, bone and joint radiographs, liver and renal functions were determined as indicated clinically. All patients were found to be HIV seropositive by both indirect and competitive enzyme-link immunoabsorbent assays. Appropriate stained smears and cultures of blood, SF and tissue biopsy specimens were done by standard techniques with special attention to the possibility of opportunistic pathogens. The outcome of the treatment was classified as good, fair and poor if the clinical improvement was greater than 75%, between 25% and 75%, and less than 25% respectively.

RESULTS

Seventeen HIV-infected patients, 15 males and 2 females, were found to have musculoskeletal infections. Their average \pm SD of age was 27.1 ± 10.8 years. All male patients admitted having sex with prostitutes without using condom. Three male patients were also IVDU. One male patient was a splenectomized thalassemia, and was given

multiple blood transfusions. One female patient was a prostitute. All but 3 patients had fever at the time of presentation. The demographic data and the clinical features of the studied patients are shown in Table 1.

Ten patients had bacterial arthritis. The mean \pm SD of the duration of symptoms was 14.3 ± 8.9 days. The average number \pm SD of the involved joints was 2.3 ± 1.7 joints. The knee, elbow, hip, ankle, and shoulder were involved in 5, 3, 2, 2 and 2 cases respectively. The responsible microorganisms were *S. enteritidis* in 5, *S. aureus* in 3, *S. choleraesuis* in 1 and *Escherichia coli* in 1 case. One of the *S. enteritidis* septic arthritis also had *Penicillium marneffii* septic arthritis of the same joint (case 10). All of the *S. aureus* septic arthritis patients were IVDU. Periarticular soft tissue swelling and osteopenia with or without joint space narrowing were the most common findings on the radiographs of the affected joints. Blood cultures were positive in 9 of the 10 patients who had blood culture determination. SF analysis was performed in all patients. SF cell counts were available in 7 cases and had SF cell counts ranging between 3,900 to over 100,000 cells/mm³. SF of the other 3 patients were pus-like. Stained smears of the SF

Table 1. Musculoskeletal infections in 17 patients infected with HIV.

Case	Age/Sex	Risk group	Disease	Location	Organism			Outcome
					Stained smear (source)	Culture (SF)	Culture (blood)	
1	18 M	HT	septic arthritis	knee	negative (SF)	<i>E. coli</i>	<i>E. coli</i>	died
2	21 M	HT, IVDU	septic arthritis	shoulder, elbow, knee, ankle	gram-positive cocci (SF)	<i>S. aureus</i>	<i>S. aureus</i>	died
3	27 M	HT, IVDU	septic arthritis	knee	gram-positive cocci (SF)	<i>S. aureus</i>	<i>S. aureus</i>	died
4	25 M	HT, IVDU	septic arthritis	knee	gram-positive cocci (SF)	<i>S. aureus</i>	<i>S. aureus</i>	fair
5	16 M	HT	septic arthritis	sternoclavicular	gram-negative bacilli (SF)	<i>S. choleraesuis</i>	<i>S. choleraesuis</i>	good
6	17 F	HT*	septic arthritis	wrist, ankle	gram-negative bacilli (SF)	<i>S. enteritidis</i>	no growth	died
7	22 M	HT	septic arthritis	knee, hip	negative (SF)	<i>S. enteritidis</i>	<i>S. enteritidis</i>	poor
8	32 M	HT	septic arthritis	MCP, PIP	gram-negative bacilli (SF)	<i>S. enteritidis</i>	<i>S. enteritidis</i>	good
9	28 M	HT	septic arthritis	elbow	gram-negative bacilli (SF)	<i>S. enteritidis</i>	<i>S. enteritidis</i>	poor†
10	23 M	HT	septic arthritis	elbow	gram-negative bacilli (SF)	<i>S. enteritidis</i> + <i>P. marneffii</i>	<i>S. enteritidis</i>	poor†
11	33 F	HT	septic arthritis	knee	negative (SF)	<i>P. marneffii</i>	<i>P. marneffii</i>	good
12	21 M	HT	septic arthritis	elbow, wrist, MCP, PIP, knee, ankle, MTP	negative (SF)	<i>P. marneffii</i>	<i>P. marneffii</i> + <i>S. choleraesuis</i>	died
13	21 M	HT	septic arthritis and osteomyelitis	PIP of fingers and toes multiple osteolytic lesion	negative (SF)	<i>P. marneffii</i>	not done	good
14	21 M	HT	septic arthritis and osteomyelitis	wrist	acid fast bacilli (synovium)‡	-	-	fair
15	25 M	HT, Tx	septic arthritis	hip, sacroiliac	acid fast bacilli (sputum)§	-	-	good
16	34 M	HT	myositis	proximal & distal muscle group	<i>T. spiralis</i> (muscle)	-	-	good
17	27 M	HT	myositis	left thigh	negative (muscle)	<i>S. aureus</i> (muscle)¶	no growth	died

HT = heterosexual transmission, IVDU = intravenous drug users, Tx = blood transfusion, SF = synovial fluid, MCP = metacarpophalangeal, PIP = proximal interphalangeal, MTP = metatarsophalangeal, * = prostitute, † = returned home in terminal condition, ‡ = tissue cultures was missing, § = *M. tuberculosis* proven by culture, ¶ = cultures from muscle aspirate

were positive in 80% of cases but SF cultures were positive in all (100%).

Four patients died. The mean \pm SD of the duration of treatment was 5.5 ± 4.9 days. Septic shock, massive hemoptysis and progressive renal failure were the cause of death in 2, 1 and 1 case respectively. Two patients returned home in terminal condition. The outcome of the other 4 patients was good in 2, fair in 1 and poor in 1 case.

Four patients (including case 10) had fungal arthritis and osteomyelitis. All were caused by *P. marneffii*. The mean \pm SD of the duration of symptoms was 15.7 ± 9.0 days. The mean \pm SD of the involved joints was 2.2 ± 1.7 joints. The knee, elbow, ankle and wrist were involved in 2, 2, 1 and 1 case respectively. Involvement of the small joints of hands and feet was seen in 2 cases. One patient had osteomyelitis involving small bones of hands and feet. The osteomyelitis demonstrated multiple osteolytic lesions with minimal sclerotic border. No periosteal reactions were observed. One patient developed symmetrical polyarthritis probable related to HIV-associated arthropathy, but SF cultures from his knee and ankle grew *P. marneffii*. The other *P. marneffii* septic arthritis patient had SF cell counts only 200 cells/mm³. Blood cultures performed in 3 patients were positive in all. SF stained smears were not able to demonstrate the fungi but SF cultures were positive in all cases. All patients received itraconazole therapy. The outcome was good in 2 patients. One patient died after 9 days of treatment. *S. choleraesuis* bacteremia and septic shock could possibly be the cause of death in this case. The other patient (case 10) returned home in terminal condition after 2 weeks of therapy.

Mycobacterium spp. septic arthritis and osteomyelitis were seen in two patients. The first patient presented with chronic synovitis of the left wrist for 6 months. A radiograph of his wrist demonstrated narrow joint spaces with bony erosions. Acid fast bacilli were demonstrated in the granulomatous synovial tissue. Unfortunately, the synovial tissue for cultures was missing during laboratory handling. The second patient was a 25-year-old, splenectomized thalassemia, who presented with a 2-week history of fever and arthritis of the left sacroiliac and left hip joints. Bone scan showed increased activity at the painful areas. Sputum examination was positive for acid fast bacilli, proven to be *Mycobacterium tuberculosis* by cultures. He responded well to anti-tuberculous therapy.

Two patients had infectious myositis. One patient who presented with progressive symmetrical proximal weakness and mildly elevated serum muscle enzymes was found to have *Trichinella spiralis* myositis. A muscle biopsy from his left thigh showed multiple encysted larvae of *T. spiralis*. He responded well to high dose corticosteroid. The other patient developed *S. aureus* myositis of his left thigh. His illness was complicated by progressive renal failure and he died 4 days after hospitalization.

The mean \pm SD of hematocrit and of WBC counts of the studied patients were 25.7 ± 9.4 vol% and $8,900 \pm 6,900$ cells/mm³ respectively. Five patients were leukopenic (white blood cell counts $< 4,300$ cells/mm³), all had disseminated penicilliosis marneffeii. Mild to moderate degree of hepatitis was seen in 5 of 11 patients who had liver function determinations. Four patients had mild renal insufficiency. Oral candidiasis, oral hairy leukoplakia, lymphadenopathy, hepatomegaly and splenomegaly were seen in 13, 8, 5, 5 and 2 cases respectively.

DISCUSSION

We have described clinical features of musculoskeletal infections in patients with HIV infection. The prevalence of musculoskeletal infection in HIV-infected patients has been reported to be approximately 0.3% (5). The incidence of musculoskeletal infections has been reported to be 7.5-32% among HIV-infected individuals who had musculoskeletal symptoms (6,9). The higher incidence is seen in HIV-infected IVDU (9). Our series had an incidence of 25.37% despite majority of our patients acquire the HIV from heterosexual transmission. The difference in the incidence was not clear. The low incidence could possibly be because attention had not been focused to the musculoskeletal systems in the previous reported cases. The high prevalence of local and systemic infections seen in tropical countries could contribute to the high musculoskeletal infection rate in these immunocompromised patients.

S. aureus was the most common offending organisms among HIV-infected IVDU in our series, as expected. This result was similar to those that have been previously described in HIV-infected patients addicted to drugs (7,9). In non-IVDU HIV-infected patients, *S. enteritidis* was the most offending organisms. Salmonella septic arthritis and osteomyelitis are uncommon and usually associated with immunosuppressive state or underlying

diseases such as hemoglobinopathies, previous joint trauma, connective tissue diseases or lymphoma (10,11). Recently they have been reported to increase in patients with HIV infection (5,12-14). A mixed infection occurred in one patient. The clinical manifestations of bone and joint infections of our patients were similar to bacterial arthritis in non-HIV-infected individuals but tended to have more than one joint involvement. The organisms could be identified by blood or synovial fluid (SF) cultures in the majority of patients. The mortality rate of bacterial arthritis of our HIV-infected patients was high. These results differed from the previously reported cases with the low incidence of *S. enteritidis* septic arthritis in HIV-infected individuals and had good clinical outcome (3,7).

P. marneffii septic arthritis and osteomyelitis, to the best of our knowledge, has never been described in HIV-infected individuals. This fungus is endemic in Southeast Asia and the southern part of China (15). The incidence has been reported to increase among HIV-infected patients (16,17). All of our patients with *P. marneffii* bone and joint infections had evidence of systemic penicillosis including fever, lymphadenopathy, hepatosplenomegaly and skin lesions. Blood cultures were positive in the majority of cases. Hematogenous spreading could possibly be the cause of bone and joint infection of this fungus.

Three of the 4 patients with *P. marneffii* septic arthritis and osteomyelitis were of interest in that one had mixed infectious arthritis caused by *P. marneffii* and *S. enteritidis* in the same joint. The second patient developed septic arthritis in the presence of noninflammatory SF. Joint sepsis with acellular SF has been mentioned in HIV-infected patients (5). This finding suggests that early aggressive investigations for bone and joint infections are required. The third patient presented with polyarthritis which is unusual for fungal arthritis. However, SF analysis was performed only in 2 joints. *P. marneffii* septic arthritis superimposed on HIV-associated arthropathy could be possible in this case.

Infectious myositis is well recognized in patients with HIV infection (5,18,19). Most of the reported cases are caused by *S. aureus*. A case of *Microsporidia* spp. myositis has been described (20). We have recently described a case of *T. spiralis* myositis presenting as polymyositis in an HIV-infected patient (21).

In conclusion, musculoskeletal infections in patients with HIV infection are not uncommon, especially in

developing countries. The responsible pathogens differ from those reported from the western countries. The mortality rate of musculoskeletal infections in HIV-infected patients is high and signifies the poor prognosis.

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