Characteristics of septic arthritis in human immunodeficiency virus-infected haemophiliacs versus other risk groups

A. Barzilai, D. Varon, U. Martinowitz, M. Heim and S. Schulman

The National Hemophilia Centre, Chaim Sheba Medical Center, Tel Hashomer, Israel

Abstract

The cases are presented of four haemophiliacs infected with human immunodeficiency virus (HIV) and with septic arthritis among the 340 patients followed at our centre. The data of these cases and 39 additional HIV-infected haemophiliacs with septic arthritis, identified in a literature search, are reviewed. The spectrum of bacterial pathogens is limited and somewhat different from that in other risk groups. The localization is exclusively to joints affected by haemophilic arthropathy. The laboratory picture is characterized by the absence of peripheral leucocytosis, varying CD4-helper cell counts, a high erythrocyte sedimentation rate and fever. The clinical picture mimics that of haemarthrosis, often causing a delay in diagnosis. Treatment with systemic antibiotics is often sufficient, obviating the need for arthrotomy and open drainage. Prognosis related to the joint function is relatively good, but poor when related to the medium- to long-term survival of the patient.

Key words: Septic arthritis, Haemophilia, HIV, Diagnosis, Aetiology.

Septic arthritis is an unusual manifestation in patients infected with human immunodeficiency virus (HIV) or with fully developed AIDS. It was previously rarely observed in haemophiliacs, but during the past decade the complication has become more frequent, probably as a consequence of the HIV epidemic in this group. It is plausible that at least some of the 10 haemophiliacs with septic arthritis reported during the years 1981–1987 [1] were also infected with HIV, but this was never verified. During the past 10 yr, several case reports have focused our attention on how septic arthritis was unexpectedly demonstrated in haemophiliacs suspected to have a typical haemarthrosis, but without the usual response to replacement therapy with factor concentrates. The majority of these patients were also infected with HIV. With the increasing incidence, septic arthritis must be a first-line differential diagnosis in the HIV-infected haemophiliac with a swollen and warm joint, typical of haemarthrosis.

In addition to the presentation of four cases from our clinic with haemophilia, HIV infection and septic arthritis, we wanted to identify some typical features of this combination in comparison with other risk groups.

Case reports

At the National Hemophilia Centre in Israel, all 340 haemophiliacs in the country are followed. Eighty-six were infected with HIV ~ 15 yr ago. Over the past 5 yr, four cases of single-joint septic arthritis were diagnosed, exclusively in HIV-infected haemophiliacs. The clinical, microbiological and immunological characteristics of these patients are summarized in Table 1. All these patients were also infected by hepatitis B and C; none of them were carriers of hepatitis B virus, but all of them had chronic hepatitis. The delay until the correct diagnosis was reached varied from a few days to several weeks. In the most remarkable case, the 37-yr-old patient, there was no fever or leucocytosis. There were only moderate local symptoms, mainly pain. The patient was examined by the orthopaedic surgeon, who considered the diagnosis of an extra-articular, localized inflammation and injected lidocaine at the insertion site of the collateral ligament. Owing to increasing pain and complete inability to use the knee, the patient was taken to the operating theatre 2 weeks later. Only upon accessing the joint space, when pus emerged, was it realized that the diagnosis was septic arthritis.

Methods

Through a literature search via Medline and from the abstracts of the congresses of the World Federation of Hemophilia since 1985, an additional 39 reported cases of HIV-infected haemophiliacs with septic arthritis were identified [1–10]. The data on the cases presented in abstract form were limited, as well as on some of the patients reported in the articles.
Table 1. Characteristics of our own haemophiliacs with HIV and septic arthritis. Cell counts are $\times 10^6/l$

<table>
<thead>
<tr>
<th>Haemophilia</th>
<th>Age (yr)</th>
<th>Anti-HIV treatment</th>
<th>CD4 count</th>
<th>CD4/CD8</th>
<th>WBC$^a$</th>
<th>Affected joint</th>
<th>Agent</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>A severe</td>
<td>30</td>
<td>Zidovudine</td>
<td>406</td>
<td>0.38</td>
<td>4500</td>
<td>Ankle + elbow</td>
<td>Salmonella</td>
<td>Blood culture</td>
<td>Ampicillin</td>
<td>3 yr</td>
</tr>
<tr>
<td>A severe</td>
<td>30</td>
<td>Non-compliant</td>
<td>22</td>
<td>0.03</td>
<td>14000</td>
<td>Elbow</td>
<td>Salmonella group D</td>
<td>Blood culture</td>
<td>Ampicillin and ofloxacin</td>
<td>1 yr</td>
</tr>
<tr>
<td>A severe</td>
<td>51</td>
<td>Zidovudine</td>
<td>0</td>
<td>0.00</td>
<td>3100</td>
<td>Elbow</td>
<td>Campylobacter</td>
<td>Joint aspirate</td>
<td>Erythromycin</td>
<td>2 yr</td>
</tr>
<tr>
<td>A severe</td>
<td>37</td>
<td>Zidovudine and didanosine</td>
<td>12</td>
<td>0.38</td>
<td>3500</td>
<td>Knee</td>
<td>Staphylococcus aureus</td>
<td>At surgery</td>
<td>Oxacillin</td>
<td>Alive</td>
</tr>
</tbody>
</table>

$^a$White blood cell count.

$^b$Gallium scan also showed increased uptake over the distal femur and mastoid process.

Table 2. Characteristics of the 43 haemophiliacs with HIV infection and septic arthritis reviewed, including 39 cases in the literature [1–10] and our own four. Cell counts are $\times 10^6/l$

<table>
<thead>
<tr>
<th>Haemophilia</th>
<th>Age (yr)$^a$</th>
<th>Aetiology of septic arthritis</th>
<th>Affected joints</th>
<th>CD4 count$^a$</th>
<th>WBC$^a$</th>
<th>ESR (mm/h)$^a$</th>
<th>Fever (°C)$^a$</th>
<th>Survival$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases with data available</td>
<td>25 for severity</td>
<td>25</td>
<td>43</td>
<td>43$^b$</td>
<td>36</td>
<td>20</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>Severe: 22</td>
<td>26</td>
<td>Streptococcus pneumoniae: 8, Klebsiella: 2</td>
<td>Ankles: 6, Shoulders 3</td>
<td>210</td>
<td>113</td>
<td>39.2</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Moderate: 3</td>
<td>1</td>
<td>Streptococcus group A, group C, S. viridans, Campylobacter 1 each</td>
<td>Wrist: 1, Hip: 1</td>
<td>4600</td>
<td>4600</td>
<td>4600</td>
<td>4600</td>
<td>4600</td>
</tr>
</tbody>
</table>

$^a$Range and median.

$^b$Adds up to 55 joints due to oligoarthritis in 5 cases.
Results

The data from the 39 cases, together with those of our four cases, are presented in Table 2. The most common pathogenic agent in the material reviewed was Staphylococcus aureus in 53% (23/43), followed by streptococci in 26% (11/43), of which five were Streptococcus pneumoniae, salmonellae in 19% (8/43) and one case of Campylobacter.

Septic arthritis occurred in 24 of the 55 sites in the knees (44%), in 20 elbows (36%), six ankles (11%), three shoulders (5%), and once each in the hip and wrist joint. These are the joints typically affected by haemophilic arthropathy. Oligoarticular involvement occurred in five of the 43 HIV-infected haemophiliacs [3, 7, 8] (Table 1).

Severe immunosuppression, as assessed by the CD4-cell count, did not play a major role as a risk factor for the development of septic arthritis. This information was available in 36 of the 43 cases and the count was >400 x 10^9/l in five and >200 in another 15 cases, whereas it was below 100 in 14 cases. Other clinical features were the absence of leucocytosis in peripheral blood, an elevated erythrocyte sedimentation rate (ESR) and a symptomatology similar to haemarthrosis. The white blood cell count in the 20 HIV-infected patients, where this was reported, ranged from 1.8 to 14.3 x 10^9/l (median 4.6). The ESR was only reported in six cases, but with the exception of one who had only 28 mm/h, there was a significant elevation above 60 mm/h. This was not necessarily caused by the septic arthritis since HIV-infected patients often have an elevated ESR due to opportunistic or other infections.

Arthroscopy and open drainage have often been recommended for the treatment of septic arthritis [3], but were only performed in seven of the cases. In 12 of 14 cases with follow-up, the patient had died within 40 months from the septic arthritis.

Discussion

HIV can cause a wide variety of rheumatic manifestations [11–18], oligoarthritis of the lower limbs being the most common significant reported problem and bone infection being one of the rarest. Septic arthritis has been regarded as exceptional in HIV-seronegative haemophiliacs, with only five cases documented in the English literature [3] before the onset of the epidemic. Several features of the septic arthritis were recognized in the HIV-seropositive haemophilic cases reported during the past decade. The most typical infectious agent, Staphylococcus aureus is also common in HIV-infected non-haemophilic patients [19, 20], as well as in HIV-seronegative cases [21, 22]. Septic arthritis due to streptococci is also frequent in all these groups. Although Salmonella is rarely the pathogenic agent in general, especially in HIV-seronegative cases [23, 24], it is quite prevalent among the HIV-infected haemophiliacs.
the only moderately lowered CD4 counts in many of the patients at the time of the septic arthritis.

In conclusion, septic arthritis has some typical features in HIV-infected haemophiliacs, such as localization to one or two major extremity joints with pre-existing haemophilic arthropathy, a limited spectrum of bacterial pathogens, partly different from that described in other groups of patients, usually the absence of peripheral leucocytosis, challenging the differential diagnosis from haemarthrosis, relatively good short-term prognosis with adequate systemic antibiotic therapy without surgical drainage, but poor medium- to long-term prognosis as regards survival. It should, however, be recognized that these conclusions are only based on level V or, at best, level IV evidence. A multicentre prospective review of all cases with haemophilia and septic arthritis is therefore needed.

References