The challenges facing the orthopaedic surgeon today in managing femoral neck fractures in HIV-positive patients

SS Mukansi, MBChB
Registrar, Orthopaedic Department, University of Limpopo, Medunsa Campus
BE Ramasuvha, MMed(Orth)
Consultant, University of Limpopo (Medunsa)

Reprint requests:
Dr SS Mukansi
Department of Orthopaedics
University of Limpopo, Medunsa Campus
PO Box 25
Medunsa 0204
Tel: 012 521 4049
Fax: 012 521 4029
Email: mukansi@webmail.co.za / Leonie.Strauss@ul.ac.za

Abstract
The use of highly active anti-retroviral therapy (HAART) in treating HIV-positive patients has led to a reversal of complications such as HIV-related mortality and morbidity. The lifespan of HIV-positive patients on HAART especially if started early (CD4 ± 350 cells per microlitre) as is done in developed countries, is as good as is in non-reactive cohorts. However age-related complications such as decreased bone mineral density (BMD) are emerging early, resulting in fragility fractures. We present a case of bilateral neck femur fractures in a 53-year-old female patient on HAART.

Key words: HAART, BMD, internal fixation, fatigue fractures

Case study
This 53-year-old female patient presented to Dr George Mukhari hospital (DGM) with bilateral neck of femur fractures. Before admission to our orthopaedic unit she had complained of bilateral hip pains (impending femur neck fractures) and was treated with non-steroidal anti-inflammatory drugs (NSAIDs) and steroids by her general practitioner (GP). (During her ordeal with bilateral hip pains she was diagnosed as HIV-positive and HAART was then started.) Pulmonary tuberculosis (PTB) was also diagnosed and a course of anti-TB therapy was given for a period of 9 months. During most of this time she was bedridden and she was put off sick. Her occupation was that of a cleaner in one of the peripheral hospitals. The initial plain X-rays done at the referring hospital showed no fractures of either femoral neck (Figure 1); however, follow-up plain X-rays showed bilateral tension sided incomplete fractures (Figure 2).

The patient has been erroneously discharged on elbow crutches and pain medication by a junior orthopaedic registrar. After discovery of this error a home visit was arranged and a full discussion of her condition was done with her. The risk of progression of the fracture to the stage of complete fracture and fracture displacement was also highlighted. The patient agreed to a hospital admission and a course of tetracycline was started so as to include histomorphometric studies in determining the cause of her bone fragility. Bloods for metabolic biochemical screening as well as markers of osteoblastic and osteoclastic activities were taken. Scintigraphic study was also done to exclude avascular necrosis (AVN). After a course of three cycles of a four-day tetracycline separated by ten days of tetracycline-free periods, a bicortical trucut biopsy from the iliac crest was done for histology. At the same time, the left femoral neck fracture was pinned with multiple cannulated screws under fluoroscopic guidance, on a traction table in theatre under general anaesthesia.

Results
The results are given in Tables I and II.
Histology

Histomorphometric features of adynamic bone with close to zero resorptive and mineralisation activities were found. There was extreme reduction of cortical bone width which could be indicative of additional hormonal factor; gonadotrophin hormone leading to reduced bone cortices.

Literature review

The entry point to healthcare of an HIV-positive patient is testing of blood for HIV status. Dr Wayne Towers of the Northwest University (Potchefstroom campus) stated in his paper that since the unravelling of the human genome there has been a major paradigm shift in the manner in which human disease is being investigated and treated. He uses the ‘omics’ – sciences to improve health with nutrition. One of the fields in which these new approaches are making great inroads is that of nutritional sciences. There is a field of genomics which can be used for gene sequencing. The field of transcriptomics, the field of proteomics and the field of metabolomics are some of the tools used to analyse the nutritional status of a patient.

Dr Theo van den Handel also describes the evolution of HIV counselling and testing. Initially the approach was to use voluntary counselling and testing (VCT). This was followed by HIV counselling and testing (HIV CT), which was followed by advice, consent, testing and support (ACTS). This in turn was followed by provider-initiated counselling and testing (PICT) and of late home test kit (HTK).

Femur neck fractures in HIV-positive patients are reported to be more prevalent in the literature; but there is no consensus as to exactly what the cause of the fracture is. Some authors say that the viral load may be associated with BMD; others say CD4 count is the cause; and others propose that HAART, vitamin D deficiency or poor absorption from the gut may lead to fragility of bone. There is no gold standard on the method of surgical intervention. Many studies have been done on trauma cases to look at infection rate on HIV-positive patients and the results are conflicting. Arthroplasty has been performed on haemophilic HIV-positive patients. In 2012 the protocol for management of patients with bilateral femur neck fractures was unclear. After meta-analysis of several papers, there is no evidence-based orthopaedic approach to this problem which affects all citizens whether infected by HIV virus or not. Infected individuals have to reassess their life goals, and their needs must be reflected in the treatment options offered to them.
Cierny and Mader classified the patient (host) according to the physiological capacity to withstand the infection post surgery. It is known that fragility fractures and BMD vary across regions. The BMD in HIV-positive patients decreases. However controversy surrounds the cause of this decrease. Some authors believe that the viral load of more than 400 copies is associated with fragility fractures. Other authors believe that a low CD4 count is associated with fragility fractures. Still others believe that HAART may be the cause of a low BMD. Chronic immune activation and upregulation of inflammatory cytokines may play a role in the pathogenesis of bone mineral loss in HIV-positive patients.

Bone demineralisation and resultant fragility fractures are an emerging clinical problem affecting an increasingly ageing HIV-infected population. Some studies have found that bone fracture risk is reduced in patients exposed to statins, while other studies found no difference.

Bisphosphonates are the clinically important class of antiresorptive agents available to treat diseases characterised by osteoclast-mediated bone resorption.

The spectrum of fragility fractures is the same in the non-HIV-infected osteoporotic population (vertebral bodies 25%, neck of femur 21%, wrist 18%).

Management of HIV-positive patients is dependent on the entry point at which you first meet your patients. However, prevention, nutrition, medical and surgical approaches are all options of management.

### Discussion

My first encounter at DGM hospital with an HIV-positive patient was in 1986, while doing my internship. In the medical department we were challenged by a patient who was referred to us from Namibia with symptoms and signs of AIDS, but it took us almost a month to make a diagnosis which we managed to do with the help of histology. The patient was booked on the next flight and flown out of the country back to Namibia. Today 26 years later after that first encounter with an HIV-positive patient at DGM hospital, the orthopaedic surgeon is still being challenged by the care of an HIV-positive patient.

### Table I: Laboratory investigations

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>June</th>
<th>Sep</th>
<th>Oct</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/L)</td>
<td>142</td>
<td>139</td>
<td>140</td>
<td>136–145</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.9</td>
<td>3.9</td>
<td>3.9L</td>
<td>3.5–5.1</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>111H</td>
<td>110H</td>
<td>108H</td>
<td>9.8–107</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>24</td>
<td>21L</td>
<td>23</td>
<td>23–29</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>-</td>
<td>2.19</td>
<td>2.11L</td>
<td>2.15–2.55</td>
</tr>
<tr>
<td>Phosphate (mg/dl)</td>
<td>-</td>
<td>1.03</td>
<td>0.71</td>
<td>0.78–1.42</td>
</tr>
<tr>
<td>Alk phosphatase (u/L)</td>
<td>-</td>
<td>-</td>
<td>243H</td>
<td>42–98</td>
</tr>
<tr>
<td>25(OH) Vit D (ng/mL)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>130H</td>
<td>94H</td>
<td>-</td>
<td>49–90</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>5.3</td>
<td>7.4H</td>
<td>-</td>
<td>2.1–7.1</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>9.1L</td>
<td>11.0</td>
<td>-</td>
<td>12.1–16.3</td>
</tr>
<tr>
<td>Wcc</td>
<td>7.11</td>
<td>7.10</td>
<td>-</td>
<td>4.00–10.00</td>
</tr>
<tr>
<td>Platelet</td>
<td>373</td>
<td>-</td>
<td>-</td>
<td>150–400</td>
</tr>
<tr>
<td>Albumen (g/L)</td>
<td>-</td>
<td>34L</td>
<td>36</td>
<td>35–52</td>
</tr>
<tr>
<td>Magnesium (mmol/L)</td>
<td>-</td>
<td>0.84</td>
<td>0.96</td>
<td>0.63–1.05</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>0–10</td>
</tr>
<tr>
<td>HIV (Ag/Ab) combination assay</td>
<td>(reactive)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 count</td>
<td>346</td>
<td>-</td>
<td>379.90</td>
<td>500–2010</td>
</tr>
</tbody>
</table>

H=high, L=low. (HIV positive, CD4 count trend going up, Alk phosphatase is high)

### Table II: HAART drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspen stavudine (NRTI)</td>
<td>30 mg bd</td>
<td>p.o</td>
</tr>
<tr>
<td>Ciplo efavirenz (NNRTI)</td>
<td>600 mg nocte</td>
<td>p.o</td>
</tr>
<tr>
<td>Aspen lamivudine</td>
<td>150 mg bd</td>
<td>p.o</td>
</tr>
<tr>
<td>Erige</td>
<td>600 mg daily</td>
<td>p.o</td>
</tr>
<tr>
<td>Tryriten</td>
<td>200/300 mg daily</td>
<td>p.o (stopped)</td>
</tr>
</tbody>
</table>

Stopped drugs due to kidney failure. NRTI=Nucleoside reverse transcriptase inhibitor. NNRTI=Non-nucleoside reverse transcriptase inhibitor.
The approach to HIV-positive patients is to use PICT approach in dealing with the patient. A one-size-fits all approach does not work. A personalised approach is advised. Team work may be the solution, involving the 'omics' of the dietician, a psychologist, a physiotherapist, occupational therapist, family support, spiritual support and a surgeon as a co-ordinator. Other tools needed in managing these patients are laboratory and imaging facilities; chemotherapy and surgical intervention; and centres of excellence.

Although our patient had bilateral femoral neck fractures, these are rare, especially in young patients. We started our patient on a course of tetracycline antibiotics in preparation for a bone biopsy for histomorphometric studies. She received three cycles of a four-day course of tetracycline with intervals of ten days of no treatment in-between. While on the theatre table fluoroscopic pictures showed a united femoral neck fracture of the right hip and as a result an intra-operative decision was taken to treat the right hip conservatively. A traction table was used in theatre to position the patient. Manipulation of the left hip failed to reduce the femoral neck fracture and as a result the fracture was fixed with cannulated screws in a triangular fashion (Figure 4). X-rays taken six months post-operatively show the fractures uniting (Figure 5). The patient is now mobilising on elbow crutches.
Managing HIV-positive patients is an expensive exercise both in fiscal and emotional terms. Drugs used by the patient may have deleterious side effects such as BMD, Fanconi syndrome, diabetes mellitus and cardiac disease (lipodystrophy).

Limitation to our management

We have not used the ‘omics’ sciences to workup the nutritional requirements of our patient. We have not started our patient on bisphosphonates, nor have we been aggressive enough in our surgical management. We have not given hormone replacement therapy (HRT) and the team work has been in name only but not jointly involved with a common purpose.

To our knowledge there is no similar case report in our South African or continental journals.

Conclusion

The management of HIV-positive patients has become not only challenging over the years, but also costly and needs centres of high excellence and a team spirit in dealing with affected populations. More research and understanding of the entire complex problem of HIV is required. The patient must understand the magnitude of the problem and note that the success of the management programme depends on him/her.

No benefits of any form have been or will be received from a commercial party related directly or indirectly to the subject of this article. The content of this article is the sole work of the authors.

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