Influencing factors of incision healing in HIV positive patients with giant cell tumor of long bone in extremities

Rui Ma  
Capital Medical University

Yao Zhang  
Capital Medical University

Qiang Zhang  (✉️ zhangqwte@sina.com )  
Capital Medical University

Article

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Abstract

Objective

To evaluate the risk factors that affect wound healing after surgery of giant cell tumor in patients with human immunodeficiency virus (HIV).

Methods

20 patients of giant cell tumor with HIV were recruited from June 2018 to June 2022, once diagnosed, 20 patients were receive timely HAART (Highly Active Antiretroviral Therapy) with China's first choice of national free HAART drug containing tenofovir disoproxil fumarate, lamivudine and efavirenz (TDF + 3TC + EFV, ) and 20 patients of giant cell tumor without HIV were enrolled as control at same time. All patients were underwent the same surgical method. Observe the incidence of infection at the surgical site and risk factors that affect wound healing were evaluated.

Results

The incidence of poor outcome of wound healing in HIV-positive group was higher than HIV-negative group (p < 0.05), but there was no significant difference in infection of the wound between two groups (p > 0.05). Multivariable regression analysis demonstrated that CD4 + T-lymphocyte count and clinical categories of HIV were independent risk factors for postoperative wound healing (p < 0.05), while age, gender, operation time, albumin, hemoglobin and combined disease, were not (p > 0.05).

Conclusion

The wound can be healed normally in most of HIV-positive patients with giant cell tumor, and the outcome of postoperative wound healing was significantly associated with CD4 + T-lymphocyte coun and HIV clinical category. At the same time, we recommended that reasonable perioperative adjuvant treatments, including nutritional support and immunomodulators, and anti-retroviral drugs should be used.

Introduction

In China, there were 12.5 hundred thousand persons infected with HIV, and the newly diagnosed cases were 0.8 hundred thousand in 2022 [1]. HIV invades human immune system, causing continuous reduction of CD4+ T lymphocytes, and leading to various opportunistic infections. At the same time, highly active antiretroviral therapy, which has been widely used and transformed HIV infection to a chronic, manageable condition, results in the increase of life expectancy of HIV/AIDS patients as well as the
number of HIV-positive patients undergoing orthopaedic surgeries. Giant cell tumor (GCT) which mononuclear cells and osteoclasts multiple nuclear cells are the main component is one of the osteolytic tumor. Local aggression and high recurrence rate are the main clinical features of GCT [2–4]. The treatments of GCT including intralesional curettage, ultrasonic scalpel and local adjuvant therapies, such as phenol or liquid nitrogen zoledronic acid, have been recommended [5–9]. At present, few literatures reported the effective treatments for GCT in patients with HIV.

So far, many clinical studies have reported the clinical outcomes of orthopedic surgeries in HIV-positive patients. Some authors suggested that HIV-positive patients had higher rate of wound infection than HIV-negative patients after internal fixation [10]. However, in a study of 42 HIV-positive patients, Hao suggested that HIV infection did not correlate with a higher rate of postoperative infection [11]. Li also advocated that the wound in HIV-positive patients could be normally healed and without infection in most of patients [12].

Moreover, in terms of the risk factors correlated with postoperative wound healing in HIV-positive patients, Abalo suggested that they were associated with HIV clinical category B, CD4+T-lymphocyte category of ≥ 200, and contaminated wounds [9]. Li advocated that multi-factors including age, constitutional index, operation time, wound contamination and emergency operation were correlated to the postoperative infection [12]. Up to now, there are different viewpoints in this regard. It is critical to carry out a study to clarify these issues.

Therefore, we retrospectively reviewed the HIV-positive patients with giant cell tumor treated surgically in our hospital from June 2018 to June 2022. The purposes of our study were to evaluate: the incidence of postoperative wound healing, and the risk factors for postoperative wound healing in HIV-positive patients.

**Methods**

A retrospective analysis of 20 patients with HIV-positive giant cell tumor treated by orthopedic surgery in beijing ditan hospital from June 2018 to June 2022 was performed. Clinical data included age, gender, albumin, hemoglobin, time to surgery, CD4+T-lymphocyte count, HIV clinical classification, and postoperative wound healing (redness, exudation, hematoma, fat liquefaction, rupture, infection, etc.). The follow-up and results were reviewed.

Inclusion criteria were as follows: (1) Giant cell tumor surgery was performed on HIV-positive patients; (2) Comprehensive clinical medical records; (3) Follow-up for at least 12 months. Her HIV status was confirmed by HIV antibody enzyme-linked immunosorbent assay and western blot. Intravenous or oral administration of amino acids, albumin injections, and thymopentin as routine nutritional supplements for nutritional improvement and hypoalbuminemia. Red blood cell suspension and/or plasma are infused as necessary. (4) The same HAART regimen and treatment time. Our exclusion criteria were: (1) patients with incomplete clinical data; (2) Previous infection; (3) Patients with diabetes, tuberculosis, liver and
kidney diseases or other diseases that may affect wound healing. At the same time, 20 HIV-negative giant
cell tumor patients in the same period were selected as the control group, whose age, gender, and surgical
method were similar to those in the HIV-positive group.

Ethics approval and consent to participate. This retrospective study was approved by the ethical
committee of Beijing Ditan Hospital, Capital Medical University and performed in accordance with the
ethical standards of the 1964 Declaration of Helsinki. And all participants signed informed consent for
publication.

To evaluate the immune system status of HIV-positive patients, CD4\(^+\) T-lymphocyte counts were measured
at < 200/ul, 200-499/ul, and ≥ 500/ul. CD4\(^+\) T-lymphocyte count < 200/uL indicates a high risk of
opportunistic infection [13]. In addition, the diagnosis of postoperative infection was based on the
Centers for Disease Control/National Health Security Network [14].

Curettage by Ultrasonic scalpel burr was performed in all patients, combined with local methotrexate
gelfoam adjuvant treatment, and then filled with allograft and/or homograft bone (Figure 1). Plain
radiographs, chest X-ray, computed tomography (CT) and/or magnetic resonance imaging (MRI) were
performed in more than one plane (Figure 2 and 3). Fine needle aspiration cytology (FNAC) and/or open
biopsy were performed in all patients (Figure 4).

Statistical analysis was performed using SPSS 25.0 software (SPSS Inc, Chicago, IL, USA). Continuous
variables were expressed as mean SD and compared by analysis of variance. Categorical variables were
compared using chi-square test. Multivariate regression analysis was used to identify independent risk
factors associated with postoperative infection. P value < 0.05 was considered to have statistical
significance.

Results

Of the 20 HIV-positive patients, 16 (80.0%) were males and 4 (20.0%) were females, and the mean age
was 35.6 years, ranging from 21 to 55 years. In the control group of 20 HIV-negative patients, 18 (90.0%)
were males and 2 (10.0%) were females, and the mean age was 33.5 years, ranging from 20 to 61 years.
The baseline characteristics of two groups are shown in Table 1, there was no significant difference in
age, gender and surgical site between the two groups (\(p>0.05\)). CD4\(^+\) T-lymphocyte count was significantly
lower in HIV-positive group than that in the control group (\(p<0.05\)).

Table 1. The baseline characteristics of patients in the two groups.
<table>
<thead>
<tr>
<th>Variables</th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>16/4</td>
<td>18/2</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Age (year)</td>
<td>35.6</td>
<td>33.5</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Surgical site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper limb</td>
<td>3</td>
<td>2</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Lower limb</td>
<td>17</td>
<td>18</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>CD4⁺ T cell count</td>
<td>356±61</td>
<td>712±87</td>
<td>P&lt;0.05</td>
</tr>
</tbody>
</table>

In 20 HIV-positive patients, incisions in 16 cases were healed normally, and poor healings were found in 4 patients, including 4 cases of incision redness, 3 cases of incision exudation, 1 case of incision dehiscence, 1 case of incision fat liquefaction, and 1 case of incision delayed healing. 2 cases got superficial infections in surgical site, and 1 was infected by Staphylococcus aureus, while bacterial culture from the other case was negative (Figure 5). The incidence of poor incision healing and infection were 20.0% and 10.0% respectively. In HIV-negative group, incisions in 19 cases were healed normally and poor healings were found in 2 cases, including 2 cases of incision redness, 1 cases of incision exudation. 1 case got superficial infections in surgical site, the incidence of poor incision healing and infection were 10.0% and 5.0% respectively. All the infections resolved after debridement, dressing change and antibiotic treatment, and no infections developed chronic osteomyelitis. The incidence of poor wound healing in HIV-positive group was higher than that in HIV-negative group (p<0.05), but there were no significant differences in wound infections between the two groups (p>0.05).

The 20 HIV-positive patients were divided into normal and poor incision healing subgroups. The comparison of age, albumin, hemoglobin, operation time, CD4⁺T-lymphocyte category, and HIV clinical category between two subgroups were listed in Table 2, and there were significant differences in above variables (p<0.05). However, multivariable regression analysis demonstrated that HIV clinical category (p<0.05) and CD4⁺T-lymphocyte category (p<0.05) were independent risk factors for postoperative wound infections, while age, gender, operation time, albumin and hemoglobin, were not (p>0.05).

**Table 2. The comparison between the two HIV positive subgroups.**
### Table 1: Comparison of Postoperative Incision Healing in Patients with HIV-GCT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Poor incision healing</th>
<th>Normal incision healing</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>41.6±6.1</td>
<td>35.5±5.7</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>128.6±14.2</td>
<td>136.8±16.5</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>37.5±12.5</td>
<td>42.3±15.8</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>185.4±45.8</td>
<td>162.8±38.1</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>CD4⁺ T cell category (n)</td>
<td></td>
<td></td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>HIV clinical category (n)</td>
<td></td>
<td></td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>A</td>
<td>2</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Postoperatively, allograft reconstruction was perfect. During the 12 months of follow-up after the operation, local recurrence of the tumor and distant metastasis were not found. All patients had good bone knitting. No physical deformities, partial collapse, fracture, obvious function obstacle and rejection was found, and there was no distant metastasis. The typical cases were showed in the **Figures 6**.

### Discussion

Acquired immunodeficiency syndrome (AIDS) is a fatal infectious disease caused by human immunodeficiency virus (HIV) infection. The cellular immune function of infected individuals is gradually reduced, which may lead to a series of complications such as opportunistic infection of cattle caused by viruses, *Mycobacterium tuberculosis*, fungi, and tumors due to the lack of immune monitoring mechanism [15,16]. Giant cell tumor (GCT) is a common bone tumor between benign and malignant tumors. In China, the incidence is relatively high, accounting for 13%–15% of all primary bone tumors. It has the characteristics of potential malignancy, large destructive power of invasion, easy recurrence and malignant transformation and metastasis after operation. The surgery was mainly performed by scraping the bone graft and reconstructing the tumor segment [17–22].

In our study, we focused on assessing the incidence of postoperative wound healing and risk factors for postoperative wound healing in patients with HIV giant cell tumor. We found a higher incidence of incision infection in the HIV-positive group but no significant difference between the two groups, suggesting that HIV infection does not significantly increase the incidence of postoperative infection. This result is consistent with Li's study [12]. Contrary to Li's study, the incidence of poor incision healing...
in HIV-positive patients is 20.0%, which is much higher than 10.0% in HIV-negative patients. However, the difference between the two groups is not statistically significant [12]. In our opinion, this is because the sample size of this study is small and large-scale studies may be required to clarify these issues in the future.

In the HIV-positive group, we found that the albumin and hemoglobin levels in patients with poor incision healing were lower than those in patients with normal incision healing, suggesting that nutritional support might play an important role in healing (Table 2). Previous studies have recommended reasonable perioperative adjuvant therapy, including nutritional support, immunomodulators, and antiretroviral drugs [23,24].

This is supported by the fact that the majority of patients in this study with normal incision healing received perioperative nutritional support. In our multivariate regression analysis, we found a significant correlation between postoperative wound healing and HIV clinical classification and CD4+T lymphocyte count, which was consistent with the conclusion of abalo [9].

Limitations of the study. First, this study is retrospective, although randomized controlled trials are difficult to conduct in this regard, and prospective studies may better explain the current problems. Second, the sample size of this study is small, and some meaningful results cannot be obtained.

Although there are some limitations, we can conclude from this study that most HIV-positive giant cell tumors have normal incision healing, and postoperative wound healing has a significant correlation with HIV clinical typing and CD4+T lymphocyte typing.

References


Figures

Figure 1

The bone cavity of the lesion was polished by ultrasonic knife after surgical focus cureting, and the inner wall of the bone cavity was burned and polished with anhydrous alcohol.
Figure 2

Preoperative X-ray show the preoperation situation.
Figure 3

Preoperative CT and MRI show the tumor decenter growth, large erosion extent, multilocular, cortical bone expansion and thinning.

Figure 4

HE staining showed a large number of giant cells and stromal cells, with a small amount of focal hemorrhage and fibrous tissue hyperplasia (20x, 40x). Immunohistochemical staining showed positive CD68 antigen (20x, 40x).
Figure 5

Postoperative wound infection, poor healing, wound healing after secondary clearance.
Figure 6

Postoperative X-ray show the bone is filed and healed well. Left the proximal tibia has no collapse or fracture at final follow-up study.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- data.xlsx
- Normalcontrolgroup.xlsx