Arthroscopic anterior cruciate ligament (ACL) reconstruction has been successfully used for restoring knee stability after ACL injury. The incidence of septic arthritis after this procedure by use of an autograft is rare and has been reported to be between 0.14% and 1.7%.1-6 A systematic search of literature in the English language did not yield any reported case of septic arthritis due to Mycobacterium tuberculosis (MTB) after ACL reconstruction.

The prevalence rate of MTB in all age groups in India is as high as 40%,7 and, hence, we decided to investigate our patients with septic arthritis of the knee after ACL reconstruction with repeated negative bacterial cultures to assess for the presence of this organism. We hypothesized MTB as a possible cause of septic arthritis in these patients. In this report, we review our experience with postoperative MTB infections after ACL reconstruction and describe our treatment approach and results.
METHODS

This is a retrospective review of all arthroscopic ACL reconstructions performed between January 1998 and May 2007 at our institute. Cases with only isolated tubercular infection were considered in this study. Septic arthritis due to MTB was defined if material from the joint yielded a positive stain for acid-fast bacilli (AFB), a positive culture on Löwenstein-Jensen medium, characteristic histopathology, or a positive polymerase chain reaction (PCR). Characteristic histopathology was defined when there was an epithelioid granuloma with or without central caseation and Langhans-type giant cells.8 PCR was done for the presence of the mpt64 gene of MTB at our institute as described previously in the literature.9 The patient records were reviewed to identify the operative procedure, type of graft fixation, presentation, and treatment. Preoperatively, a thorough history for past tubercular infection or for any history of contact with a patient with tubercular infection was routinely taken in all cases. Hemogram and chest and knee radiographs were obtained in all patients. The arthroscopic ACL reconstruction was done as described in standard textbooks.10 Every case of septic arthritis was subjected to arthroscopic lavage and debridement, and the synovial tissue and pus collected were submitted for culture for MTB, histopathology, and PCR for MTB (except in the initial 2 cases), in addition to routine bacteriology workup. Patients were followed up for at least 2 years after the initial diagnosis of MTB infection. The strategies for medical and surgical therapy of MTB infection after ACL reconstruction are not standardized, and management decisions were made by treating surgeons. The details of the patients are given in Tables 1 and 2. At follow-up, patients underwent a detailed physical examination and the Lysholm score was determined.11

RESULTS

Between January 1998 and May 2007, 1,152 ACL reconstructions were performed; septic arthritis devel-

### Table 1. Patient Demographics and Follow-up

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr)/Sex</th>
<th>Graft Used</th>
<th>Additional Procedures</th>
<th>Time to Presentation from Index Procedure (d)</th>
<th>Time From AD and Lavage to Start of ATT (d)</th>
<th>Follow-up (mo)</th>
<th>Pain</th>
<th>Instability</th>
<th>Range of Motion (°)</th>
<th>Lysholm Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30/M</td>
<td>BPTB</td>
<td>None</td>
<td>35</td>
<td>22</td>
<td>72</td>
<td>None</td>
<td>No</td>
<td>0-130</td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td>41/M</td>
<td>STG</td>
<td>PMM</td>
<td>43</td>
<td>15</td>
<td>61</td>
<td>Minimal</td>
<td>No</td>
<td>0-120</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>35/M</td>
<td>STG</td>
<td>None</td>
<td>92</td>
<td>22</td>
<td>32</td>
<td>None</td>
<td>No</td>
<td>0-135</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>46/F</td>
<td>STG</td>
<td>None</td>
<td>152</td>
<td>9</td>
<td>30</td>
<td>None</td>
<td>No</td>
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<td>86</td>
</tr>
<tr>
<td>5</td>
<td>26/F</td>
<td>STG</td>
<td>PMM</td>
<td>23</td>
<td>27</td>
<td>48</td>
<td>None</td>
<td>No</td>
<td>0-130</td>
<td>84</td>
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<tr>
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<td>23/M</td>
<td>STG</td>
<td>PCL</td>
<td>72</td>
<td>8</td>
<td>44</td>
<td>Minimal</td>
<td>No</td>
<td>0-125</td>
<td>72</td>
</tr>
<tr>
<td>7</td>
<td>31/M</td>
<td>STG</td>
<td>None</td>
<td>61</td>
<td>5</td>
<td>37</td>
<td>None</td>
<td>No</td>
<td>0-130</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>40/F</td>
<td>STG</td>
<td>None</td>
<td>37</td>
<td>9</td>
<td>25</td>
<td>None</td>
<td>No</td>
<td>0-130</td>
<td>80</td>
</tr>
</tbody>
</table>

Abbreviations: AD, arthroscopic debridement; BPTB, bone–patellar tendon–bone; STG, semitendinosus-gracilis; PMM, partial medial meniscectomy; PCL, posterior cruciate ligament reconstruction.

### Table 2. Management

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Clinical Features</th>
<th>ESR (mm)</th>
<th>CRP (mg/dL)</th>
<th>Bacterial Cultures</th>
<th>Aspirate Stain (AFB)</th>
<th>Aspirate Culture (AFB)</th>
<th>Biopsy Culture (AFB)</th>
<th>Histology</th>
<th>DNA-PCR</th>
<th>Debridement</th>
<th>Graft Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E/W/F</td>
<td>60</td>
<td>58</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>NA</td>
<td>AD (2), S</td>
<td>Rt</td>
</tr>
<tr>
<td>2</td>
<td>E/W</td>
<td>32</td>
<td>52</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>NA</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
<tr>
<td>3</td>
<td>E/W</td>
<td>34</td>
<td>36</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
<tr>
<td>4</td>
<td>E/P</td>
<td>48</td>
<td>67</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+, AFB</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
<tr>
<td>5</td>
<td>E/P/F</td>
<td>40</td>
<td>56</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>AD, S</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
<tr>
<td>6</td>
<td>E</td>
<td>54</td>
<td>75</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
<tr>
<td>7</td>
<td>E</td>
<td>41</td>
<td>84</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+9</td>
<td>+</td>
<td>AD (2), S</td>
<td>Rt</td>
</tr>
<tr>
<td>8</td>
<td>E</td>
<td>52</td>
<td>48</td>
<td>–</td>
<td>–</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>AD, S</td>
<td>Rt</td>
</tr>
</tbody>
</table>

Abbreviations: E, effusion; W, warmth; F, low-grade fever; –, negative; +, positive; NA, not available; AD, arthroscopic debridement; S, synovectomy; Rt, graft retained; P, pain; ±, positive but not typical.
oped after the procedure in 26 patients (2.25%). Of these 26 patients, 8 (30%) had isolated tubercular infection (i.e., an incidence of 0.69% in our study). Other organisms isolated were *Staphylococcus aureus* in 10 patients, *Staphylococcus epidermidis* in 4 patients, *Peptostreptococcus* in 2 patients, *S aureus* and MTB in 1 patient, and *Enterobacter* in 1 patient. There were 4 male and 4 female patients with a mean age of 34 years (range, 23 to 46 years). None of our patients showed evidence of an active form of tubercular infection either in the past or in the present or had a history of contact with actively infected patients. None of them were diabetic, and all were negative for human immunodeficiency virus during preanesthetic check. None of our patients had undergone any prior operative procedure. After aspiration, all patients received intravenous infusion of cloxacillin, 1 g 4 times a day, until culture sensitivity reports were obtained or until antitubercular chemotherapy (ATT) was started. Gentamicin, 80 mg twice a day, was given for 10 days after aspiration. All cases were performed with the use of a tourniquet. Bone–patellar tendon–bone graft and quadrupled hamstring graft were used in 1 case and 7 cases, respectively. Bone–patellar tendon–bone graft was fixed with titanium interference screws (Arthrex, Naples, FL) at both the femoral and tibial ends. Quadrupled hamstring graft was fixed with closed-loop EndoButton (Smith & Nephew Endoscopy, Andover, MA) in 5 cases and Bio-Transfix (Arthrex) in 2 cases on the femoral side, whereas on the tibial side, titanium interference screws (Arthrex) were used in 5 cases and Bio-Interference screws (Arthrex) were used in 2 cases. Of the patients, 3 had concomitant procedures, with partial medial meniscectomy in 2 and posterior cruciate ligament reconstruction in 1. Two staff surgeons were involved either as a main surgeon or as a supervising surgeon when the surgery was performed by the residents. The same team of staff surgeons was involved in the 1,152 cases reviewed.

Postoperative infections are classified as acute (<2 weeks), subacute (2 weeks to 2 months), or late (>2 months). The mean time to presentation after ACL reconstruction was 64.4 days (range, 23 to 152 days). The mean time to start of chemotherapy from arthroscopic debridement was 14.6 days (range, 5 to 27 days). Four patients had a subacute onset, whereas four had a late onset. Swelling was present in all cases, whereas warmth was present in 3 cases, low-grade fever in 2, and pain in 2. Laboratory data showed that the mean erythrocyte sedimentation rate (ESR) was 45 mm in the first hour (range, 32 to 60 mm in the first hour) and the mean C-reactive protein (CRP) level was 59.5 mg/dL (range, 36 to 84 mg/dL). Peripheral leukocyte counts were normal, and blood cultures were negative. Radiographs obtained showed rarefaction of the femur and tibia in 2 cases. Aspiration of intra-articular fluid was turbid yellow in color, with an elevated leukocyte count. The aspirate did not show any organism with Gram’s stain or AFB.

All patients underwent arthroscopic debridement and lavage with at least 10 L of normal saline solution by use of standard anterolateral and anteromedial knee portals. Synovial hypertrophy and intra-articular adhesions were present in all cases, and arthroscopic partial synovectomy was done in all cases. Graft tension was normal and graft was retained in all cases. One additional arthroscopic debridement was done in cases 1 and 7. Synovial tissue obtained was submitted for culture for pyogenic and tubercular organisms and histopathology. Culture of tissue biopsy specimens for MTB was positive in 3 patients. Histopathology showed the presence of typical epithelioid granulomas with or without caseation in 5 cases and poorly formed granulomas in 2 cases. AFB was seen in biopsy specimens of 2 cases; DNA–PCR was performed in 6 cases, and all showed a positive result. Case 3 did not show either a positive culture or positive histopathology but had a positive PCR, which was repeated twice on 2 tissue specimens and responded to treatment.

ATT was started and later continued on an outpatient basis in all 8 cases with 4 drugs—isoniazid (5 mg/kg), rifampin (10 mg/kg), ethambutol (15 mg/kg), and pyrazinamide (25 mg/kg)—daily for 4 months, followed by isoniazid and rifampin for 8 months. Laboratory parameters such as ESR and CRP level returned to normal by the fifth month of ATT. After arthroscopic debridement, the knee was splinted in a knee brace until 3 weeks of ATT. Toe-touch weight bearing on the operated limb with crutches was allowed from the first postoperative day until all wounds healed clinically. The patient was then gradually allowed to increase to full weight-bearing status. A physical therapy program with active-assisted range of motion was instituted for all patients 4 times a day from the first postoperative day and gradually increased as wounds healed. This was followed by a graded knee-strengthening program.

Patients were followed up for a mean of 43.6 months (range, 25 to 72 months); 6 patients had no pain on performing daily activities and sporting activities, whereas 2 had pain on performing sporting activities. One patient was involved in competitive sports and returned to his previous level of activity,
Clostridium perfringens, Propionibacteriaceae, pathiae mantbacilli in a previously exposed individual. 16 of a latent distant focus or local reactivation of dor-
implant site by hematogenous spread from activation probably for life.15,16 Any event causing an altered immunocompetent persons there are no clinical man-
mention.13 presence of chronic inflammation may cause reactiva-
derangements, a foreign-body reaction, or even the tissue and may lead to breakdown of old tubercular granuloma and hence to reactivation in susceptible individuals.19 In fact, factors such as local vascular injury to surrounding tissues, and this possibly causes mechanical grinding of synovial tissue and may lead to breakdown of old tubercular granuloma and hence to reactivation in susceptible individuals.19 In fact, factors such as local vascular derangements, a foreign-body reaction, or even the presence of chronic inflammation may cause reactiva-
tion.13

The prevalence rate of TB in all age groups in India is around 40%, and the prevalence of all forms of TB disease is approximately 400 million.7 Thus, with such a large number of patients exposed to and infected with MTB, it is unlikely that the lesions in our patients were due to implantation of MTB into the wound at the time of surgery; they were probably a result of decreased immunity after surgical trauma leading to either hematogenous spread from a distant focus or local reactivation. For the diagnosis of tubercular infection during screening, the tuberculin test is practically the only tool currently available.20 Its use-
fulness depends on the clinical situation and population. Tuberculin testing is a nonspecific measure of prior mycobacterial sensitization.20 It may be positive in individuals who have had prior bacille Calmette Guerin (BCG) vaccination. BCG vaccination is given to infants at birth in India under the national immu-
nization program. A false-positive test also commonly results from cross-reacting sensitivity to nontubercu-
losous mycobacterial antigens, which are very common in tropical and subtropical climates.20 Thus, with such a high prevalence rate of infection, as well as routine BCG immunization, we do not recommend routine tuberculin testing in our population.

From these 8 cases, several features emerge. All patients were apparently healthy and were subjected to surgical trauma. The interval of time from the index procedure to presentation was subacute or late, ranging from 23 days to 5 months. The most common symptom was swelling, followed by warmth and pain. Fever was rarely seen and was of low grade. ESR and CRP level, though increased, were not very specific, nor were radiologic findings. Comparison of ESR and CRP values with cases of infection after ACL reconstruction in published studies showed similar trends.1-5 Repeated cultures of the aspirate were negative, and the diagnosis was established only after testing of tissue obtained at debridement.

Biopsy samples have been used extensively in the diagnosis of TB.21 Positive MTB culture and/or char-
acteristic histopathology have been the main criteria for definitive diagnosis. In contrast to many other bacterial infections, MTB is often not easy to culture, and false-negative results are very common.21 In our study synovial fluid aspirates were negative for stain-
ing and culture in all cases; biopsy culture was pos-
tive in 44.5% of cases. This may be because of the low bacterial load in skeletal TB. The literature, however, reports sensitivities of 77% for synovial fluid cultures and 90% for synovial tissue cultures.21 In terms of histopathology diagnosis, TB can be diagnosed only as “a chronic granulomatous inflammation, suggestive of TB” on a routine surgical pathology report.8 How-
ever, histopathology features of chronic granuloma-
tous inflammation can be found in various conditions and diseases other than TB, such as foreign-body reaction, fungal infection, sarcoidosis, cut scratch disease, leprosy, and brucellosis.22 Therefore AFB stain, TB tissue culture, and TB-PCR should be performed to enable a definitive diagnosis of TB.8 Histopathol-
ogy was positive in 87.5% of our cases with a gran-

DISCUSSION

Organisms commonly reported in the literature in patients with septic arthritis after ACL reconstruction include S aureus, S epidermidis, Peptostreptococcus, and Enterobacter.1-6 Others have reported methicillin-resistant Staphylococcus aureus, Erysipelothrix rhusio-
pathiae, Propionibacteriaceae, Veillonella parvula, and Clostridium perfringens.6,12-14 This report describes 8 cases of isolated MTB infection after ACL reconstruc-
tion in immunocompetent patients.

Tubercular bacilli have a tendency to remain dor-
mant in remote parts of the body after initial dissemina-
tion from a primary complex.15 In fact, in 90% of immunocompetent persons there are no clinical man-
ifestations, but the infection remains for many years, probably for life.15,16 Any event causing an altered immunologic response may lead to clinical manifesta-
tions of tuberculosis (TB).15 MTB can involve an implant site by hematogenous spread from activation of a latent distant focus or local reactivation of dor-
mant bacilli in a previously exposed individual.16 Major trauma can cause a lowering of humoral and cellular immunity in its initial stages.17,18 Surgical trauma also leads to injury to surrounding tissues, and this possibly causes mechanical grinding of synovial tissue and may lead to breakdown of old tubercular granuloma and hence to reactivation in susceptible individuals.19 In fact, factors such as local vascular derangements, a foreign-body reaction, or even the presence of chronic inflammation may cause reactiva-
tion.13

The prevalence rate of TB in all age groups in India is around 40%, and the prevalence of all forms of TB disease is approximately 400 million.7 Thus, with such a large number of patients exposed to and infected with MTB, it is unlikely that the lesions in our patients were due to implantation of MTB into the wound at the time of surgery; they were probably a result of decreased immunity after surgical trauma leading to either hematogenous spread from a distant focus or local reactivation. For the diagnosis of tubercular infection during screening, the tuberculin test is
ulomatus reaction with or without caseation and/or the presence of AFB. DNA-PCR of tissue biopsy samples appears promising in the early diagnosis of tubercular infection and is sensitive. All 6 cases subjected to this test in our study had a positive result. The initial 2 cases in our study were not subjected to PCR because, at that time, we did not suspect a tubercular etiology after ACL infection. A high sensitivity with PCR has been reported in the literature; however, false-positive findings are to be kept in mind. In the literature comparison between histopathology and PCR has shown that 100% of cases with the typical histopathologic features of TB (well-formed granuloma with caseous necrosis and Langhans-type giant cells) were positive by TB-PCR, 69% of cases with only poorly formed granulomas were positive by TB-PCR, and 36% of cases with chronic inflammation but without definite granulomatus lesions were positive by TB-PCR. In addition, PCR testing detected MTB in 1 day, as compared with a mean of 24.3 days required for detection by conventional Löwenstein-Jensen medium and 12.89 days by the radiometric BACTEC technique. Despite DNA-PCR results coming in early, we have a lag period of a mean of 13.3 days (range, 5 to 27 days) in our study until ATT was started because we preferred to wait for histopathology or culture confirmation before the start of ATT. In those cases with recurrent negative bacterial cultures, we recommend DNA-PCR testing coupled with histopathology as an investigation modality of choice for the diagnosis of TB.

There is no current standard regimen for the diagnosis and treatment of tubercular infection after ACL reconstruction. Swelling and warmth developing in a healthy individual over weeks to months is the initial physical finding. Low-grade fever is rarely seen. ESR, CRP, and radiology offer baseline values that serve as a guide during follow-up. In all cases of suspected septic arthritis in areas endemic for MTB, we recommend arthroscopic lavage and debridement with graft retention. Synovial material obtained should be submitted not only for bacteriologic workup but also for culture for MTB, histopathology, and DNA-PCR for MTB. One should rule out diabetes, search for any other immunocompromising factors, and improve the overall nutritional status of the patients. Locally palliative measures such as orthosis and walking aids are important. Given the high correlation between PCR and histopathology, as shown in the literature and in our study, we now start ATT after a positive PCR result is obtained and recommend the same. In endemic areas in the presence of a positive PCR result but negative histopathology and repeatedly negative bacterial and MTB cultures, we recommend clinicians to perform a synovial biopsy and repeat PCR study and, if positive, to continue ATT to its full course. Repeat debridement and graft removal can be performed if necessary. However, one should bear in mind that the results of revision ACL reconstruction are worse than those of primary ACL reconstruction.

Evaluation of knee stability by physical examination revealed results similar to those in uncomplicated cases. However, the Lysholm score was lower, and this may be because of factors such as postinfection damage to cartilage and delay in returning to physical therapy.

Our study has some limitations. It is a retrospective review of cases that presented to us, only isolated tubercular infections were included in this study, the cases have a variable presentation, and all of the various laboratory results are not consistent in all of the cases.

CONCLUSIONS

To our knowledge, tubercular infection as a complication after arthroscopic ACL reconstruction has not been previously reported. Tubercular infection as a complication after arthroscopic ACL reconstruction, though rare, should be kept in mind as a possible cause of infection in immunocompetent patients in zones endemic for TB. It should also be kept in mind in nonendemic areas, among immigrants from endemic areas, and in cases with persistent swelling and discharge, effusion with minimal inflammatory signs, and negative cultures. We recommend DNA-PCR testing for early diagnosis of TB. Arthroscopic debridement and ATT together are the mainstay of treatment.

REFERENCES


