ORTHOPAEDIC COMPLICATIONS OF RENAL TRANSPLANTATION

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Summary

One hundred and eighty-one patients who underwent renal transplantation between 1973 and 1979 have been reviewed. Thirty of these developed one or more orthopaedic complications. The commonest and most serious was avascular necrosis of bone and the treatment of 14 patients with this condition is described. Transplant recipients who developed this complication received twice the total dose of steroids in the six months after transplantation than a control group with no avascular necrosis. The management and pathology of patients with avascular necrosis is discussed.

Introduction

With improvements in renal transplantation the number of long term survivors who develop major musculoskeletal complications has increased. These complications have been described as one of the most serious long term problems of patients with successful renal allografts [1]. In this study we describe the management and pathology of patients with avascular necrosis of bone.

Patients and Methods

There were 114 males and 67 females. The average age was 37 years (range 16 to 66). The patients in this series were examined clinically and when indicated radiographs and a technetium diprophonate ($^{99}$Tc MDP) bone scan were performed. Serum calcium, phosphate and alkaline phosphatase were measured and the total dose of corticosteroids received by the patient in the first six months recorded.

The immunosuppressive regime used in this unit is 300mg prednisolone halving every third day to a maintenance dosage of 15 mg daily. Rejection episodes were treated by reinstiution of this regimen. Azathioprine is given at
2.5mg/kg body weight indefinitely.

Results

Thirty patients (16.5%), 19 males and 11 females, developed orthopaedic complications: the commonest being avascular necrosis of bone which occurred in 14 (7.5%) patients at an average age of 37 years (range 20–61). Nine were treated conservatively and 5 surgically. Two patients who developed this complication were excluded from the study, one because of coexistent rheumatoid arthritis; the other had Still's disease. The incidence and type of orthopaedic complications are shown in Table I. Some patients developed more than one complication.

<table>
<thead>
<tr>
<th>Orthopaedic Complications</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperparathyroidism</td>
<td>13</td>
</tr>
<tr>
<td>Renal osteodystrophy</td>
<td>4</td>
</tr>
<tr>
<td>Avascular necrosis of femoral head</td>
<td>9</td>
</tr>
<tr>
<td>Avascular necrosis of femoral condyle</td>
<td>3</td>
</tr>
<tr>
<td>Avascular necrosis of humeral head</td>
<td>1</td>
</tr>
<tr>
<td>Avascular necrosis of metatarsal head</td>
<td>1</td>
</tr>
<tr>
<td>Joint effusion</td>
<td>1</td>
</tr>
<tr>
<td>Spontaneous rupture of tendo achilles</td>
<td>1</td>
</tr>
<tr>
<td>Spontaneous fracture of thoracic spine and ribs</td>
<td>1</td>
</tr>
<tr>
<td>Web space infection</td>
<td>1</td>
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</tbody>
</table>

Nine patients developed avascular necrosis of the femoral head. In 3 it was unilateral and in 6 it was bilateral, giving a total of 15 avascular hip joints. One patient was asymptomatic and the condition was discovered on a routine intravenous urogram.

In 2 patients with avascular necrosis of the femoral condyle the condition was unilateral, in one it was bilateral. One patient developed avascular necrosis of one humeral head and another had the condition in the second metatarsal head.

Patients usually presented with severe pain and limitation of movement. When a weight bearing joint was affected pain was often sufficient to prevent ambulation. Symptoms usually progressed rapidly.

The average interval between transplantation and development of avascular necrosis was 30 months (range 12 to 67).

Early radiographic changes are a linear subchondral fracture [2] with patchy porosis and sclerosis followed in the later stages (Figure 1) by collapse of the femoral head, loss of joint space and a tendency for lateral subluxation. None of our patients had dislocation of the hip, but one developed a stress fracture of the femoral neck following avascular necrosis of the head.

$^{99m}$Tc technetium diphasphonate bone scans demonstrated increased activity before radiological changes could be seen, therefore suggesting increased vascularity in the femoral head in response to bone destruction.
Five patients with avascular necrosis of the femoral head were treated conservatively: in 4 the condition was bilateral and bed rest, traction and analgesics were required; in one asymptomatic patient no specific therapy was indicated. Two patients with unilateral femoral head involvement were treated with total hip replacement and 2 patients with bilateral femoral head disease were treated with bilateral total hip joint replacement. Surgery was performed under systemic prophylactic antibiotic cover: the bone was found to be soft but this did not cause any technical difficulties. The patients were mobilised on the fourth and fifth day.

One patient with unilateral avascular necrosis died of uncontrollable diabetes shortly after surgery. The other patients regained a useful range of pain-free movement. In a single instance the prostheses loosened due to infection, and 2 months after insertion the joint was removed and a Girdlestone excision arthroplasty performed; the patient remains painfree and mobile.

A Charnley knee arthrodesis was performed for one patient with avascular necrosis of the femoral condyles but resulted in a fibrous union, which was sufficiently stable for the patient to remain painfree and ambulant. The other patients with avascular necrosis of the femoral condyles, humeral head and second metatarsal head were treated conservatively with analgesics, physiotherapy and restriction of load bearing where appropriate.
Pathology

Macroscopically there was softening of the femoral head with detachment of the articular cartilage along a line of necrotic subchondral bone. The cartilage remained viable but became irregular and covered in places with a layer of fibrous tissue. There was replacement of bony trabeculae in the head by fatty tissue, fibrous tissue and fibrocartilage (Figure 2).

Figure 2. Microscopic appearance of avascular necrosis of bone showing the replacement of subchondral bony trabeculae by fibrous and fatty tissue. (Haematoxylin and Eosin preparation x 40) (Reduced for publication)
Discussion

Previous authors have reported the incidence of avascular necrosis of bone in transplanted patients between 4.2% [3] and 14% [4,5]: in this series the incidence was 7.5%. Pierides [4] found the incidence increased with the length of stay in hospital and the number of complications.

In a retrospective sequential study Murray [5] showed that by decreasing the dose of steroids from 2,900mg to 1,200mg in the first three months, the incidence of avascular necrosis of bone fell from 34% to 10%.

In our series the 9 patients with avascular necrosis of bone were compared with 9 patients matched for age, sex and date of transplantation who did not develop avascular necrosis of bone. The patients who developed avascular necrosis had on average 4 rejection episodes compared with an average of 1 rejection episode in the controls. Also the total doses of steroids received by the patients in the first one month, three months and six months after transplantation were found to be twice as high in the patients with avascular necrosis as compared with the control patients (Figure 3).

![Graph showing average total dose of steroids against time after transplantation in 9 patients with avascular necrosis of bone compared with 9 controls](image)

- Closed circle = patients with avascular necrosis
- Open circle = patients with no avascular necrosis

Figure 3. Average total dose of steroids against time after transplantation in 9 patients with avascular necrosis of bone compared with 9 controls

In conclusion, avascular necrosis of the femoral head in renal transplant patients appears to be closely related to the cumulative steroid dose and can, when indicated, be treated successfully by total hip replacement. There was no increased incidence of operative or postoperative complications and we there-
fore believe that total joint replacement is justifiable when performed early.

References


Open Discussion

UITTENBOGAART (Los Angeles) We studied the incidence of ASN in children. We did not find a relation between the total steroid dose in the first year post-transplant. Did you look at pre-existing bone disease and PTH levels in your patients?

NIXON We did, and I could not find any correlation between bone changes and PTH levels posttransplantation and the of avascular necrosis subsequently.

PER ERLANSON (Linköping) Is the incidence of orthopaedic complications of this type influenced by the time on dialysis before transplantation?

NIXON I have not looked at that in my study. From other reported studies I recall that there is not a relationship.

CHATTERJEE (California) I have two comments. Our incidence of avascular necrosis is like yours i.e. 7%. Five had their hips replaced and in only one patient was this infected. Five years after surgery, due to proven infection manifested by pain alone, we removed the prosthesis. I do not agree with your conclusion that in all cases prednisone is responsible. We have shown earlier that this is not true and the real reason is hypercalcaemia due to persistent secondary hyperparathyroidism. We have all seen cases of avascular necrosis in patients on dialysis who are not on prednisone.

NIXON There are many criticisms of my study. I think parathyroid hormone itself regardless of transplantation is related to avascular necrosis of bone. Even without steroid treatment some pre-existing conditions can give rise to avascular necrosis.

VRIESMAN (Maastricht) The first question is: do you see aseptic necrosis after transplantation in patients who have had the parathyroid glands removed (or subtotal removal) during dialysis because of secondary hyperparathyroidism? The second question: do patients with aseptic necrosis differ from those without necrosis in terms of corticosteroid receptor density?
NIXON Many of these patients had a total or subtotal parathyroidectomy.

VRIESMAN Do they get aseptic necrosis?

NIXON Yes, we have patients who have aseptic necrosis, who have had parathyroidectomy.

VRIESMAN I think that is important to know. And the next question was whether aseptic necrosis could be related to the prednisone receptor density. If it is related to the prednisone I would try to get patients separated into groups of high and low steroid receptor density.