Kaposi’s sarcoma in kidney transplant recipients: a 23-year experience

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Received 17 November 2003 and in revised form 22 December 2004

Summary

Background: Kaposi’s sarcoma (KS) is a relatively common malignancy after kidney transplantation, accounting for up to 80% of all malignancies in developing countries.

Aim: To assess the frequency of KS in renal transplant recipients, and determine the impact of demographic factors, immunosuppression and treatment options.

Design: Retrospective study in a single centre in South Africa.

Methods: Charts and pathology reports of 542 recipients of 623 kidney allografts treated at our institution between 1976 and 1999 were reviewed.

Results: After a mean follow-up of 6.4 years, 21 (3.9%) recipients had KS, representing 47.7% of all post-transplant malignancies. KS accounted for more post-transplant cancers in non-White than White patients (79.1% vs. 11.7%, p < 0.001). KS was equally common in males and females, and was not more frequent under cyclosporine.

Skin involvement was universal; visceral disease occurred in six patients (28.6%). Sixteen (94.1%) patients with limited skin disease and two (100%) with superficial nodal disease responded to withdrawal or reduction of immunosuppression. Renal function was preserved when immunosuppression was reduced instead of withdrawn (p = 0.02). Patients with vital organ involvement succumbed rapidly to KS. Post-mortem examination revealed more extensive disease than was suspected clinically.

Discussion: Ethnic differences exist in the frequency of KS in patients residing in the same geographical area. Since withdrawal results in graft loss, reducing immunosuppression should be first-line treatment for patients with disease limited to skin, and possibly for disease of the superficial lymph nodes. The malignant behaviour of KS, and extent of pathological involvement, cast doubt on the idea that KS is a hyperplasia rather than a true malignancy.

Introduction

Kaposi’s sarcoma (KS) is an enigmatic disease that has held the medical profession in awe since its original description in 1872.1 Renewed interest in KS was triggered by its association with the increasing number of patients that are immunosuppressed, either as a result of acquired immunodeficiency syndrome (AIDS)2,3 or following organ transplantation.4 KS is one of the most common malignancies to occur in patients after kidney transplantation5,6 especially in developing countries.7–9

The aetiopathogenesis of KS is complex and poorly understood, but is almost certainly dependent on human herpesvirus type 8 (HHV-8) infection10 in immunosuppressed, immunogenetically susceptible individuals.11,12 Although the treatment of KS is controversial it should, ideally, address these pathogenic issues.9,13 The current guideline...
is reduction of immunosuppression as first-line treatment, but these recommendations are based on anecdotal experience or uncontrolled studies.\textsuperscript{13,14} Perhaps the most fundamental controversy that has implications for all aspects of the disease surrounds the nature of KS: i.e. whether it is a true malignancy or reversible hyperplasia.\textsuperscript{15,16}

In this study, we document our experience with KS in a cohort of kidney transplant recipients and make some observations that may influence understanding and management of this disease.

**Methods**

**Patient population**

We studied 542 patients who received 623 kidney transplants at our institution between April 1976 and March 1999. Patients were then followed for a further 2 years. All Renal Transplant Unit records, hospital records, computerized renal transplant database and South African Dialysis and Transplant Registry records, as well as pathology and post-mortem reports, were reviewed to identify malignancies, including KS. All cases of KS were pathologically confirmed. The details of patients with other confirmed malignancies were also recorded. Data included demographics, donor source (cadaveric or living-related), primary renal disease, type of immunosuppression, number of transplants, human leukocyte antigen (HLA) profile, human immunodeficiency virus (HIV) status, duration of graft survival, and reason for graft loss.

**Immunosuppression**

Between April 1976 and October 1983, 123 patients primarily received conventional immunosuppression, including methylprednisolone and azathioprine. From October 1983, 419 patients received cyclosporine as part of triple therapy. Cyclosporine blood levels were regularly monitored. Acute rejection was treated initially with pulse methylprednisolone, and severe or steroid-resistant rejection with polyclonal antibodies and/or monoclonal antibody OKT3. Patient 2 was initially treated with azathioprine for 18 years; azathioprine was then replaced with cyclosporine to permit introduction of allopurinol for treatment of gout. He developed KS 10 months later. This patient was excluded from analyses of interval from transplantation to development of KS. Patient 21 received a combination of cyclosporine and mycophenolate mofetil (MMF) during a clinical drug trial; with diagnosis of KS, only MMF was withdrawn.

**Treatment**

In patients with KS limited to skin, treatment until 1989 was discontinuation of all immunosuppression. Thereafter, our protocol required withdrawal only of the most potent immunosuppressive agent, which was usually cyclosporine. The progression of skin lesions and renal function were carefully monitored. If patients had visceral involvement (excluding superficial nodes) all immunosuppression was immediately discontinued. Two patients with inguinal lymphadenopathy were also managed with reduction, rather than discontinuation of immunosuppression.

**Statistics**

For purposes of analyses, as well defining years of follow-up, patients were censored at the time of death or diagnosis of malignancy, but not when returning to dialysis. Although some patients were followed up at peripheral hospitals and private physicians, regular contact was maintained with the study centre. Continuous data were compared by Student’s t-test and non-parametric data by Mann-Whitney U test. Categorical data were analysed using the \( \chi^2 \) or Fisher’s exact test. Graft survival was determined using the actuarial method of Kaplan and Meier, and comparisons were made with log-rank analysis. A \( \text{p} \) value <0.05 was considered statistically significant. Statistical analysis was performed using Statistica for Windows (Release 6.1, 2003; Stat Soft).

**Results**

**Frequency and demographics of KS**

The 542 patients transplanted during the study period accumulated a total of 3450 person-years, with a mean follow-up of 6.4 years. Twenty-one (3.9%) recipients developed KS. If 75 patients who received immunosuppression for <28 days, and who therefore were at no significant risk of KS are excluded, the proportion with KS rises to 4.5%. Of 41 patients with post-transplant malignancies, KS occurred in 21 (51.2%), accounting for 47.7% of all malignancies (Table 1).

Details of patients with KS are shown in Table 2. Demographic details are summarized in Table 3. When corrected for the slightly greater transplant rate in males, KS was equally common in males and females. Of 17 White patients with malignancies, KS occurred in two (11.7%) compared with 19/24 (79.1%) non-White (Black and Coloured) patients with post-transplant cancers.
Clinical aspects

There was no significant increase in the number of KS patients under cyclosporine compared to azathioprine (Table 3) or in the interval to development of KS. Skin involvement was universal and visceral involvement occurred in six (28.6%) patients. The interval to development of KS was significantly shorter with visceral forms of the disease, compared with KS limited to skin (Figure 1). The sites of cutaneous involvement were lower extremities in 12 (63%), followed by upper-limb involvement in six (32%) patients. In total, KS lesions occurred on extremities in 17 (89%) patients, trunk in five (26%) and hard palate in two (10%) patients.

The range of organ involvement in three patients who underwent post-mortem examination is shown (Table 4). Of note, KS affected the liver, lungs and deep lymph nodes in all three patients. Patient 17, diagnosed at post-mortem, had extensive disease, including, unusually, renal allograft, splenic and bone involvement. Table 5 summarizes our overall experience of visceral KS. With exception of lung disease and two patients with superficial nodes, all other visceral involvement was diagnosed post-mortem. Routine gastroscopy was performed in only five patients, none of whom had upper gastrointestinal disease. Computerized axial tomography (CT) scanning for deep lymph nodes was not routinely performed.

Outcome of treatment

In 16 (94.1%) of 17 patients, KS skin lesions improved with therapy (excluded are four patients who died soon after KS diagnosis or with post-mortem diagnosis). KS healed over several months with residual pigmented or hyperkeratotic lesions. Lesions improved whether or not patients received additional local radiotherapy or chemotherapy. Patients received additional therapy arbitrarily if, in the opinion of the treating clinician, lesions were not improving. Of three patients treated before 1989, two received adjunctive radiotherapy compared with only 1/12 treated subsequently. KS skin lesions responded to treatment irrespective of size and type (macule-patch, papule-plaque or nodule), although improvement occurred over several months (Figure 2). Only patient 2 had progressive skin lesions, which formed exophytic friable tumours that became secondarily infected and ultimately proved fatal. The lesions seen in our patients were generally multifocal, consisting of mostly papules/nodules that varied in size from <1 cm to some that were >5 cm. Macular lesions were not very common, occurring in only 2 (9.5%) patients, and were usually seen in early stages of KS or when the lesion was regressing. In some of our patients, lesions had marked overlying hyperkeratosis, superficially resembling psoriasis (Figure 2).

Vital visceral involvement at presentation was an important determinant of patient outcome. Three patients presenting with lung disease died within days of diagnosis, while the diagnosis was confirmed in patient 17 at post-mortem. Patients 19 and 21 had bilateralinguinal lymphadenopathy but no other apparent visceral involvement. Both responded well to reduction in immunosuppression, although the former required local irradiation after 3 months for painful lymph nodes. The nodes in both patients regressed over months without any further intervention (Figure 3). Patient 19 had recurrence of KS affecting both legs 2 years after the initial diagnosis, associated with local necrotizing infection affecting both legs. The patient eventually succumbed to disseminated KS.

Renal outcome

The renal prognosis of patients who did not succumb to disseminated disease was related to the management of immunosuppression. All three patients in whom immunosuppression was discontinued had functioning grafts when KS was diagnosed, but all grafts were acutely rejected. Dialysis was re-instituted in these patients a mean of 5 weeks.
### Table 2: Details of the cohort of kidney transplant recipients with Kaposi’s sarcoma

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Treatment</th>
<th>Distribution of lesions</th>
<th>Latency (months)</th>
<th>Treatment of KS</th>
<th>Outcome: patient/lesions</th>
<th>Outcome: renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>M</td>
<td>White</td>
<td>Azathioprine</td>
<td>Visceral</td>
<td>8.4</td>
<td>IS withdrawn</td>
<td>Died of disseminated disease</td>
<td></td>
</tr>
<tr>
<td>2*</td>
<td>45</td>
<td>M</td>
<td>Coloured</td>
<td>Azathioprine</td>
<td>Cutaneous</td>
<td>228.3</td>
<td>CsA withdrawn</td>
<td>Patient died of sepsis/Lesions infected</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>M</td>
<td>Coloured</td>
<td>Azathioprine</td>
<td>Cutaneous</td>
<td>24.0</td>
<td>IS withdrawn</td>
<td>Lesions improved</td>
<td>Graft loss</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>21.2</td>
<td>IS withdrawn + DXR + Chemo</td>
<td>Lesions improved</td>
<td>Graft loss</td>
</tr>
<tr>
<td>5†</td>
<td>39</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Visceral</td>
<td>11.2</td>
<td>IS withdrawn</td>
<td>Died of disseminated disease</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>29</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>2.9</td>
<td>IS withdrawn</td>
<td>Lesions improved</td>
<td>Graft loss</td>
</tr>
<tr>
<td>7</td>
<td>54</td>
<td>M</td>
<td>Black</td>
<td>Cyclosporine</td>
<td>Mucocutaneous</td>
<td>56.3</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>M</td>
<td>Black</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>26.8</td>
<td>CsA withdrawn + DXR</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>64.1</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>10</td>
<td>31</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>34.4</td>
<td>Cyclosporine + DXR</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>11</td>
<td>35</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Mucocutaneous</td>
<td>22.2</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>12</td>
<td>27</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>4.1</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>13</td>
<td>41</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>17.5</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>14</td>
<td>43</td>
<td>F</td>
<td>White</td>
<td>Cyclosporine</td>
<td>Visceral</td>
<td>4.1</td>
<td>CsA withdrawn + Chemo</td>
<td>Lesions improved</td>
<td>Graft loss</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
<td>F</td>
<td>Black</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>8.9</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>(advanced renal failure)</td>
</tr>
<tr>
<td>16</td>
<td>53</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>61.4</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>17</td>
<td>40</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Visceral</td>
<td>8.3</td>
<td>Nil</td>
<td>Died of disseminated disease</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>48</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>13.9</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>(advanced renal failure)</td>
</tr>
<tr>
<td>19</td>
<td>36</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Nodal</td>
<td>13.3</td>
<td>CsA withdrawn + DXR (after 3 mo.)</td>
<td>Lesions improved, relapse after 2 years</td>
<td>Maintained</td>
</tr>
<tr>
<td>20</td>
<td>44</td>
<td>F</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Cutaneous</td>
<td>31.5</td>
<td>CsA withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
<tr>
<td>21†</td>
<td>37</td>
<td>M</td>
<td>Coloured</td>
<td>Cyclosporine</td>
<td>Nodal</td>
<td>10.6</td>
<td>MMF withdrawn</td>
<td>Lesions improved</td>
<td>Maintained</td>
</tr>
</tbody>
</table>

*Cyclosporine substituted for azathioprine after 18 years because allopurinol started for gout.*

*Patient with clinical KS organ involvement. Autopsy examination not performed.*

*Patient under MMF instead of azathioprine. Latency, interval from transplantation to the development of KS; IS, all immunosuppression; CsA, cyclosporine; DXR, radiotherapy; Chemo, chemotherapy; MMF, mycophenolate mofetil.*
after discontinuation of all immunosuppression. In contrast, the only patients to lose their grafts with withdrawal of cyclosporine only were patients 15 and 18, who already had advanced renal failure (plasma creatinine values >800 μmol/l) when KS was diagnosed. The difference in renal outcomes of these two management strategies (discontinuation vs. reduction of immunosuppression) was significant ($p=0.022$). In the latter group, none of 12 patients developed acute rejection; at one year 11/12 patients who had plasma creatinine values <800 μmol/l had survived and had functioning allografts. One year following reduction of immunosuppression, mean plasma creatinine values were lower, although not significantly so (165.2 μmol/l, 95%CI 80.7–249.7 vs. 142.2 μmol/l, 95%CI 84.8–199.6; $p=0.25$). Actuarial graft survival was not compromised by reduction of immunosuppression (Figure 4). Of patients with limited disease, two died of septicaemia, at 9 months and 5 years, respectively, and one of heart failure at 5 years.

### HLA profiles

The HLA antigen frequencies in renal transplant patients with and without KS were compared. Partial antigen profiling was available for 518 (98.9%) patients and full profiling (including DR antigens) was available for 457 (84.3%). The HLA antigen profile was available for 19 (90.5%) of the 21 KS patients. No single HLA antigen occurred with significantly increased frequency in KS patients compared to the rest of the cohort. The HLA-A2 antigen occurred in 5/21 (26.3%) patients with KS and in 149 (28.8%) of the transplant patients. HLA-DR2 was the most frequent class II antigen and occurred in 121 (28.9%) patients, and it was
Table 4  Post-mortem findings in patients with disseminated Kaposi’s sarcoma

<table>
<thead>
<tr>
<th>Patient</th>
<th>Stomach</th>
<th>Liver</th>
<th>Spleen</th>
<th>Lung</th>
<th>Renal allograft</th>
<th>Bone marrow</th>
<th>Lymph nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Mesenteric</td>
</tr>
<tr>
<td>14</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Hilar</td>
</tr>
<tr>
<td>17</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Mesenteric, mediastinal</td>
</tr>
</tbody>
</table>

Yes/No, involvement/no involvement.

Table 5  Visceral involvement in patients with Kaposi’s sarcoma (n = 21)

<table>
<thead>
<tr>
<th>Visceral organ</th>
<th>n (%)</th>
<th>Clinical features</th>
<th>Diagnosed antemortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>5 (23.8)</td>
<td>Lymphadenopathy</td>
<td>2</td>
</tr>
<tr>
<td>Superficial</td>
<td>2</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Deep</td>
<td>3</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
<tr>
<td>Lung</td>
<td>4 (19.0)</td>
<td>Hypoxaemia, reticulonodular pattern</td>
<td>3</td>
</tr>
<tr>
<td>Abdomen*</td>
<td>3 (14.3)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Liver</td>
<td>3</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
<tr>
<td>Stomach</td>
<td>2</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
<tr>
<td>Bone†</td>
<td>1 (4.7)</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
<tr>
<td>Spleen†</td>
<td>1 (4.7)</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
<tr>
<td>Renal allograft†</td>
<td>1 (4.7)</td>
<td>Asymptomatic</td>
<td>0</td>
</tr>
</tbody>
</table>

*See Table 4. Two patients with stomach disease also had liver involvement. †All these lesions occurred in a single patient (patient 17).

Figure 2. Improvement of skin lesions over time.
present in 4/15 (26.6%) KS patients who had full HLA-antigen typing available.

Discussion

Ethnic variations in frequency

The proportion of non-White renal transplant patients in the present study who developed KS (5.3%) is among the highest in the world, matching that reported from Saudi Arabia. Comparisons of the absolute incidence of KS in other developing countries is confounded by differing periods of follow-up. However, KS was the most common malignancy in non-White patients, in whom it accounted for >79% of all cancers. In reports from other developing countries, KS is consistently the most common cancer after kidney transplantation. In developed countries, the risk of KS is increased several-fold, and KS accounts for 0–10% of all post-transplant cancers, an experience commensurate with the 11% noted in White patients in this study. George Oettle first noted profound racial differences in susceptibility to endemic KS: Black patients were considerably more prone to KS than the White, Coloured and Indian patients living alongside them. Importantly, Oettle reported that KS was rare in the Coloured group in South Africa, who form the bulk of the Western Cape population.

Genetic variation may explain racial differences in the incidence of post-transplant KS. In Saudi Arabia, HLA-A2 was significantly more common in patients with post-transplant KS compared to controls. In the present study of a more heterogeneous population, we were unable to identify a distinct HLA pattern in post-transplant KS patients. The role of genetics in the aetiology of post-transplant KS remains uncertain, and requires further investigation. Ethnic variation may arise from differences in the prevalence of HHV-8 infection, an important factor in the aetiology of KS. Several cross-sectional epidemiological studies have found that HHV-8 is more prevalent in regions where there is a higher prevalence of KS. The seroprevalence of HHV-8 antibodies in subjects from developing countries (especially sub-Saharan Africa) is much higher than in the general population of Europe and the US. In South Africa, standardized prevalence of HHV-8 antibodies was substantially greater among Black blood donors than among White blood donors from the same area (20% vs. 5%), the prevalence rose to 39% in the general black population. A recent South African study confirmed that renal transplant recipients had relatively higher levels of anti-HHV-8 antibodies, and also that marked racial differences existed in the prevalence of antibodies, with the lowest being in Whites (1.8%) and highest in Coloured patients (12.5%) in South Africa. As with post-transplant KS, the prevalence of anti-HHV-8 antibodies in White patients in our cohort mirrors that of developed countries, while that in non-White patients is similar to that reported from developing countries.

Gender and age differences

In the present study, KS was equally common in males and females, once correction was made for the differential transplant rates. The male to female
ratio of post-transplant KS reportedly ranges between 3:1 and 1.5:1, but in developing countries, up to 93% of renal allograft recipients may be male. If correction is made for this discrepancy, then the gender ratio approaches unity. In all other forms of KS, the disease is much more common in males. Post-transplant KS, like the epidemic form, tends to occur in younger patients and is less strongly correlated with onset of disease than with duration of immunosuppression.

Clinical aspects

Skin involvement may be universal, as in the current study, but has been reported in between 73% and 93%. The legs are affected twice as commonly as the arms. In post-transplant KS, the course of skin disease is generally benign, but reports from the Arabian peninsula describe an aggressive pattern in over one quarter of renal transplant patients, characterized by rapid growth within a few weeks and widespread dissemination, often with visceral involvement. This aggressive cutaneous form of post-transplant KS seems to be confined to Saudi Arabia.

There is a dearth of published information on post-mortem findings in post-transplant KS; post-mortem findings of the present study, although relatively small, suggest that subclinical disease is more common than suspected. The experience in other forms of KS supports our tentative suggestion that the internal organs are more commonly affected than is clinically appreciated: estimates of KS patients with internal organ involvement range from 10 to 70%. This may be because the disease is indeed silent, and that the clinical manifestations of visceral disease are unusual. This is supported by the observation that in a large number of patients with KS who have routine endoscopic examinations, there are lesions in the gastrointestinal tract that are clinically occult. Alternatively, patients with more extensive and aggressive KS disease succumb and undergo post-mortem examinations. This is supported by observations in the present study that patients with extracutaneous disease have a shorter time to development of KS. Visceral involvement has been reported clinically in 45% of post-transplant KS. Extracutaneous involvement most commonly involves lymph nodes followed by gut and lungs. The involvement of bone and renal allograft noted here are both unusual, and stress the value of post-mortem examination.

Treatment

Based on our own observations we would concur that the mainstay of treatment of post-transplant KS is reduction of immunosuppression. In the present study, reduction of immunosuppression in patients with limited disease resulted in remission of KS in all but one patient; in addition, renal function remained preserved. This suggests that discontinuation of immunosuppressives is unnecessary as the primary therapeutic option in patients with disease limited to the skin. Although KS usually regresses after manipulation of immunosuppression, patients may pay a heavy price: almost one-half of the patients in whom immunosuppression is withdrawn or reduced lose their grafts. Qunibi and colleagues have suggested a management algorithm based on progressive reduction and ultimate cessation of immunosuppression. At least 50% of their patients died or returned to dialysis when immunosuppression was discontinued. In other reports, varying degrees of success have been achieved, but patients with visceral KS universally have a grim prognosis. The current recommendation for disease of the superficial nodes is discontinuation of immunosuppression. Experience in the present study suggests that these nodes regress if immunosuppression is reduced, and the loss of a graft could potentially be avoided. This approach needs to be corroborated and until such time, we would urge great caution, with the patient carefully monitored for improvement.

Which immunosuppressive agent is withdrawn or reduced appears to be immaterial. In most reported studies azathioprine was discontinued, with or without a reduction in the dose of cyclosporine. Our own bias was to withdraw the most potent immunosuppressive agent, namely cyclosporine, because it may have direct oncogenic potential. An added benefit to withdrawing cyclosporine, besides cost savings, was reduction in plasma creatinine levels in the majority of patients.

A problem with many published reports is that no time-frames are given within which initial treatment outcomes are judged, before resorting to other modalities of treatment. In a recent report, patients were managed with reduction of immunosuppression for a minimum of one month only before other forms of therapy were introduced. We have shown that extensive local lesions may take several months to regress, an experience shared by others, and may in fact show initial deterioration before improvement becomes manifest. From our experience, for isolated skin lesions
we would tentatively recommend an observation period of 2–4 months before implementing more potent therapies. Serial photographs of lesions provide a useful objective tool for evaluation of the number, size and colour of lesions. Regression can also be monitored by serial assessment of the size of lesions.45

This retrospective case-series has inherent limitations and therefore our observations, interesting as they appear, need to be corroborated and our recommendations treated with due caution. Although the follow-up of our patients is quite complete, the number of cases reported is relatively small, and controls are historical. Because of the rarity of post-transplant KS, it is very unlikely that randomized control studies will ever be performed to compare the merits of certain aspects of treatment over others (for example, reduction of immunosuppression vs. discontinuation). Perhaps meta-analysis of reported series will go some way to providing evidence of the superiority of one form of treatment over the other.

The true nature of KS remains a matter of contention, with some authors arguing that the disease is probably a reversible hyperplasia.15 Certainly, the benign clinical course followed by the majority of our patients in response to treatment supports this contention. However, the extent of metastatic involvement of KS in the remaining one-quarter of patients, combined with the very aggressive course of the disease, culminating in a fatal outcome, exceeds the malignant nature of most other cancers. We would therefore urge caution in labelling iatrogenic KS a benign disease based on its pathology, because of its potential to follow a very malignant clinical course.

In summary, post-transplant KS is a disease predominantly of non-White renal transplant recipients that affects males and females equally. Mucocutaneous disease responds very well to withdrawal of cyclosporine (as compared to discontinuation of immunosuppression), but visceral disease has a poor prognosis. Worryingly, post-mortem examination can reveal the presence of clinically unsuspected disease.

Acknowledgements

This study was supported by grants from the National Kidney Foundation of South Africa, the Harry Crossley Foundation and the Hendrik Verwoerd Trust. Thanks are due to Professor Johann Schneider and Professor Faffa Jordaan for reviewing the pathological specimens, and Professor Jane Gralla for reviewing the manuscript.

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