Kaposi's Sarcoma in a Heart Transplant Patient

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The increased use of organ transplantation has resulted in a higher incidence of neoplasms in organ transplant recipients than in the general population. The reduced immunologic surveillance resulting from the administration of immunosuppressive therapy to prevent rejection is considered responsible for this higher incidence. It seems that transplant patient incurs an 'iatrogenic immunodeficiency syndrome'. It is worth noting that in transplant patients there is an increased incidence of lymphomas and Kaposi's sarcoma (KS), both of which are common in AIDS patients but rarely found in the general population. KS has been reported especially in kidney transplants, but it is becoming an issue in heart transplant patients too. It has been observed that the incidence of KS in heart transplantation ranges from 0.4% to 2% (1–3), corresponding to 2.7% of all neoplasms. In transplant patients, the time span from surgery to occurrence of KS seems to be shorter than that between operation and occurrence of other types of neoplasms. In most cases KS occurs within 24 months of surgery (1–8); however, cases have been reported in which it occurred only after 2–3 months (3, 5). The data on organ transplantation, irrespective of the type of transplanted organ, suggest a racial–genetic predisposition towards the development of KS (Mediterranean, Arabic and Jewish ancestry). These data also show a correlation with the histocompatibility antigens HLA-B5, HLA-B8, HLA-B18, and HLA-DR5 (9).

The tissues in which KS most commonly arises are the skin and the mucosa of the first aerodigestive tract. However, cases have been reported in which unusual sites were involved such as liver, bone, lung and cervix (6–8). In this paper, the case of a heart transplant patient who developed a mucocutaneous KS is presented. In this patient, the use of a non-toxic and non-invasive local treatment and the reduction of the immunosuppressive therapy resulted in control of the neoplastic disease until death occurred 22 months later. In particular, we focus on the difficulties in the therapeutic approach to heart transplant patients with KS.

Case report. D.A., a 39-year-old Italian male, of Mediterranean ancestry, underwent an orthotopic heart transplant for a severe, dilated myocardiopathy in January 1992. After organ transplantation, the patient received immunosuppressive therapy. The daily maintenance dose was: azathioprine 50 mg, cyclosporine 120 mg, and prednisone 2.5 mg. The cyclosporine serum level was maintained at 200 μg/ml. Eleven months after transplantation a red, soft, vegetating lesion of 3 cm in diameter was detectable in the hard palate. The lesion was laser-resected and the histology revealed a KS. The resection was 'radical' since the surgical margins were free of disease. After only 3 weeks, some small vegetating lesions, which were consistent with local recurrence of KS, were detectable along the margins of the previously resected area. The biopsy was positive for KS recurrence. At the same time, a solitary KS cutaneous lesion of 5 mm in diameter was resected from the right shoulder. A bronchoscopy and an oesophagogastroscopy, carried out to exclude the presence of multiple localizations in the aerodigestive tract, were negative. Because of these findings, the administration of azathioprine was suspended and the patient was started on a course of radiation therapy to the oral cavity. Radiation therapy was delivered with a 6 MV linear accelerator to a total dose of 30 Gy in 15 fractions using two latero–lateral fields. The patient tolerated the treatment well and by the end of radiation the oral lesion had disappeared. From then until death occurred 22 months later, the patient did not show any sign of acute rejection and remained clinically free of KS recurrences. The patient died of chronic rejection, which is a late complication of organ transplantation, caused by graft atherosclerosis.

Discussion. It has been observed that immunosuppressive therapy, administered in several pathologies as well as after organ transplantation, is implicated as a predisposing factor in the onset of KS. This finding suggests that chronic immunodepression is a crucial condition for the development of this neoplasm (10–12). The great incidence of KS in patients with AIDS is an additional proof to this hypothesis. In pharmacological immunodepressed patients with KS, the most reasonable therapeutic approach seems to be either the reduction or the suspension of the immunosuppressive therapy to restore the level of immunologic surveillance. The restoration of immunologic surveillance might either prevent tumor development or even induce KS regression. For this reason, the reduction of the immunosuppressive therapy, either alone or in combination with locoregional treatments (surgical resection, laser-resection, radiotherapy) or with systemic treatments (chemotherapy), is the most common approach (1, 3, 5–7, 13). Although making no distinction between heart and kidney transplant patients, Penn reported a complete remission of KS in 83 out of 180 patients (46%) with cutaneous or mucocutaneous disease. Twenty-six (31%) out of the 83 patients who achieved a complete remission had either a reduction or a suspension of immunosuppressive therapy as the only treatment (14). However, discontinuation or reduction of the immunosuppressive therapy increases the risk of acute organ rejection, a risk that diminishes

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after the perioperative period. Gallo et al. (6) reported a total of 186 deaths in 1054 heart transplant patients. Of these, only 4 (2%) were due to acute rejection and occurred within 3 months of surgery. In contrast, Frances et al. (3) reported that 3 out of 4 heart transplant patients who developed KS and consequently underwent a reduction of the immunosuppressive therapy died of acute rejection.

The clinical course of KS arising during the immunodepression period may vary considerably from patient to patient and KS may also take a benign course. Klepp et al. (12), in a study of 6 drug-immunosuppressed non-transplanted patients with KS, observed that in 2 patients the tumor had a very slow growth and in 1 there was evidence of a spontaneous tumor regression, although the administration of the immunosuppressive therapy had not been altered.

Acute rejection in a heart transplant patient is obviously a more serious event than in a kidney transplant patient; the latter may at least benefit from haemodialysis and eventually undergo a further kidney transplantation. In an organ transplant patient with KS a major problem is the choice between an aggressive treatment aiming at curing KS, with a consequent increased risk of rejection, and a treatment aiming at keeping the tumor in a state of chronicity with a lower risk of death by organ rejection.

We suggest that the latter procedure should be carefully evaluated. However, in this case, radiotherapy may be used for the treatment of KS with the significant advantage of a low-risk, moderate cost, and good responses as well.

To date, in this rare disease, the clinical features on which to decide the best therapeutic procedure for each patient have not been clearly determined. In our opinion, it is reasonable to identify two groups of patients. The first group comprises patients with clinically aggressive KS (occurrence within a few months of organ transplantation, rapid growth, diffuse mucocutaneous and/or visceral spreading); in these patients the immunosuppressive therapy should be reduced while contemporarily monitoring the risk of rejection with myocardial biopsies. In some cases, the use of local and/or systemic therapies may be required. The second group includes patients with clinically indolent KS (occurrence after several months or years of organ transplantation, slow growth, limited cutaneous spreading); in these patients local treatments, such as radiotherapy, should be used as well as a minimal tailoring of the immunosuppressive therapy, if needed. The aim, in this latter group, is to keep KS in a state of chronicity.

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