Kaposi's Sarcoma in a Renal Transplant Patient Treated with Cyclosporine A

M.		Messina ^a
G.P.		Segoloni ^a
G.		Triolo ^a
B.		Malfi ^a
G.		Squicciarro ^a
M.		Rossetti ^a
M.G.		Bernengo ^b
A.		Vercellone ^b

^aDepartment of Nephrology, Dialysis and Kidney Transplant Unit, Institute of Nephrology; ^bDermatologic Clinic, University of Turin, Italy

Dr. M. Messina, Divisione Nefrologie e Dialisi, Ospedale S. Giovanni-Molinette, Corso Bramante 90, I-10126 Torino (Italy)

Dear Sir,

We wish to report a case of a renal transplant patient who developed a Kaposi's sarcoma while on treatment with cyclosporine A (CsA) and prednisone.

To our knowledge, few cases on this regimen are reported, and only 1 is described in detail [1], while at least 40 transplanted patients, assuming prednisone and aza-thioprine or other immunosuppressants are recorded. The patient, an Italian male, aged 50 years, underwent his renal transplantation from a cadaver donor in July 1984. The patient, whose typing for DR locus was 5, previously transfused and without cytotoxic antibodies detectable in his serum, received a zero DR, two AB mismatched kidney. The therapeutic schedule was: prednisone 0.4 mg/kg/day, gradually reduced to 10 mg/day at 1 year, and CsA 6 mg/kg/day intravenously for 6 days, and then orally, initially at a dose of 14 mg/kg/day, tapered off on the basis of trough plasma levels (Sandoz RIA assay), in order to maintain them between a range of 50–200 ng/ml.

Antirejection treatment consisted of methylprednisolone boluses at low doses (300 mg × 3). The patient experienced post-transplant acute tubular necrosis and two rejection episodes. CsA trough levels were higher than 200 ng/ml, up to a maximum of 450 ng/ml, only during the first 3 weeks. When discharged from the hospital, the well being of the patient was fair, his serum creatinine was 2.3 mg%, HbsAg and AB were negative, cytomegalovirus (CMV) and herpes simplex serology were positive (1/64 and 1/256) without clinical illness, varicella Zoster and Epstein-Barr serology were negative; hematological and urinary routine examinations were all negative. At the 4th month of follow-up, some infiltrating skin lesions were noted on his left arm, adjacent to a preexisting a-v fistula; this raised the suspicion of a Kaposi's sarcoma, which was histologically confirmed. At that time, no abnormality in routine examination, nor in serum creatinine was noted. Anti-CMV antibodies were slightly reduced, no CMV infection was detected; the clinical status was unchanged. A study of lymphocyte subpopulations was carried out, both on blood and on tissue specimens: we found a deep depression of circulating T4

lymphocytes (OKT4/OKT8 ratio of 0.37) and an increased number of T8 suppressor lymphocytes in the lesioned skin.

Our therapeutic procedure consisted in the reduction of the immunosuppressive regimen, as for CsA from 10 to 5 mg/kg/day and as for prednisone from 30 to 15 mg/day. In the following months no rejection episode nor any abnormality in blood and urinary checks was ever noted. At the 7th month, seroconversion for CMV was recorded, without clinical illness; at the 8th month, OKT4/OKT8 ratio became normal. The serology for human T-lymphotropic virus was negative (Abbott-Elisa) and no abnormality of white blood cells or platelets, nor of serum electrophoresis was recorded. The cumulative dose of CsA assumed by the patient at the 4th month was of 74 g; (body weight of 70 kg); at 1 year of 200 g. Until now, with a follow-up of 15 months, the well being of the patient is unchanged, no sign of visceral involvement was noted and the nodular cutaneous lesions, which never spread out, are in persistent partial regression.

The strategy we adopted is based on the well-known observation that cancer, and particularly malignant lymphomas and Kaposi's sarcoma, are closely associated with the immunosuppression level [2–6], as the increased morbidity and mortality owing to the tumor, either in transplanted patients, or in AIDS patients, demonstrate. Our therapeutic procedure was quite an intriguing one. As a matter of fact, no reliable data are as yet available in favor of a major oncogenetic effect of CsA in comparison with the other immunosuppressants commonly used in transplantation, even if we believe a longer follow-up is

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necessary to investigate its effects, mainly in lympho-proliferative diseases. Since literature could not act as a guideline as for the case of our patient, we decided not to switch to azathioprine, in order to minimize the risk of a superimposed rejection episode, with a consequent need for an increasing dose of the immunosuppressive drugs.

Besides, periodic determination of CsA trough plasma levels can afford, in our opinion, a monitoring of the immunosuppression rate, and the possibility of quickly recognizing overimmunosuppression.

Even if a longer follow-up is required in order to draw precise conclusions, in our patient, as in the few others recorded in the literature [1, 7], a drastic reduction of the immunosuppressive pharmacology allowed no further evolution of the tumor, without loss of graft function.

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