

Cutaneous Kaposi Sarcoma Which Developed in a Patient with Aplastic Anaemia Using Immunosuppressive Therapy – Description of the First Adult Case

Dear Editor,

In its classic form, Kaposi's sarcoma (KS) is a multifocal lympho-angioproliferative disease seen in elderly subjects of Mediterranean origin.¹ It might also be diagnosed in organ transplant recipients who use azathioprine, prednisolone and especially cyclosporine.² All subtypes of KS are associated with infection by human herpes virus (HHV-8).^{1,2} Here, we present a HIV-negative patient with aplastic anaemia who used cyclosporine and prednisolone, who developed cutaneous KS, and whose KS disappeared completely after cessation of cyclosporine and the administration of vincristine.

A 60-year-old male patient was hospitalised in our department with fatigue, dizziness, petechiae, and ecchymoses. On physical examination; he had pallor, petechiae and ecchymoses. He had no lymphadenopathy and hepatosplenomegaly. Haemoglobin was 9.3 g/dl; haematocrit, 27.5%; leukocytes, 3300/mm³; and platelets, 3000/mm³. The corrected reticulocyte count was 0.1%. Bone marrow biopsy yielded a decreased cell/fat ratio with 5% cellularity. The patient was diagnosed with aplastic anaemia and given methylprednisolone 250 mg (thrice) with cyclosporine at a dosage of 5 mg/kg/day. As there was no response at the end of 1 month, the dosage of cyclosporine was increased to 7.5 mg/kg/day. Fifty days after cyclosporine therapy, periankle oedema and purplish – initially macular, later nodular – tumours appeared on the soles. Later, they eroded the skin forming fungiform tumours. The patient developed similar lesions over his hands. The histopathological examination of the skin lesions showed small vessels with extravasated erythrocytes and spindle cells. Serological tests for HHV-8 could not be performed. In addition, *in situ* hybridisation and PCR to detect HHV-8 in neither the bone marrow biopsy nor the skin biopsy could be performed. Anti-HIV test was negative. The patient did not give permission for esophagogastro-duodenoscopy. We discontinued cyclosporine and administered 2 mg vincristine *i.v.* 6 times with 1-week intervals. Beginning with the first dose of vincristine, KS lesions began to regress. Five years after initial diagnosis, the patient has no KS lesions and his whole blood count is normal.

Classically, KS was thought to be a rare neoplasm which affected older subjects.³ In addition to the classic subtype, the disease has other main subtypes: the endemic subtype

seen in black Africans; the epidemic subtype in HIV-infected patients; and the iatrogenic subtype in patients administered immunosuppressive drugs.³ While iatrogenic KS was often attributed to immunosuppressive therapy in organ transplant recipients, it has also been reported in patients on immunosuppressive therapy for other conditions – Wegener's granulomatosis,⁴ ulcerative colitis,⁵ bullous pemphigoid.^{6,7}

Skin lesions in KS have dark blue or purplish colour which initially are macular and later form nodular and fungiform tumours. Their main localisation is the legs; but, they may occur on the trunk and on the arms. Leg oedema might be observed before the skin lesions.³ Our patient initially had leg oedema, later KS lesions over his feet and then on his arms. These tumours became infiltrated with time and formed fungiform tumours. KS might also involve the lymph nodes, the gastrointestinal tract and the lungs. Oral involvement might be associated with the involvement of the gastrointestinal tract.² Our patient had involvement of none of these sites.

Molecular and epidemiological studies indicate that development of KS is closely related to infection with the HHV-8.⁸ In patients with KS, there is immune dysregulation characterised by CD8+ T cell activation and the production of Th1-type cytokines that induce activation of endothelial cells leading to adhesion and tissue extravasation of lymphomonocytes, spindle cell formation and angiogenesis.⁹ In one study, HHV-8-specific DNA sequences were detected in 100% of KS skin lesions, in 85% of perilesional healthy skin, and in 60% of peripheral blood mononuclear cell samples by PCR.¹ In our patient, we did not have the opportunity to search for the presence of HHV-8 in peripheral blood, and in either the skin or the bone marrow biopsy samples.

The incidence of KS is higher in organ transplant recipients treated with cyclosporine as compared with those treated with azathioprine and prednisone (10% vs 3% of all neoplasms).^{2,3} In a study by Ecker et al.,² 17 cases of KS were diagnosed among 557 renal transplant recipients (3%) and KS was the most common post-transplant malignancy, having a frequency of 68%.

In iatrogenic KS, lowering the dose of immunosuppressive drugs might be sufficient to cause disappearance of KS lesions in most cases. Other specific treatment modalities are cryotherapy, cryosurgery, laser or surgical removal of the tumours, intralesional chemotherapy and radiotherapy.

The most commonly used chemotherapeutic agents are adriamycin, bleomycin, vincristine, vinblastine – either singly or in combination.³

Intestinal KS was reported to develop in a HIV-negative patient associated with immunosuppressive therapy for severe aplastic anaemia.¹⁰ Our patient was the first adult patient who developed cutaneous KS after using immunosuppressives for his aplastic anaemia. Withdrawal of immunosuppression and the institution of vincristine therapy led to resolution of his KS and also the blood count parameters. Physicians should be aware of the possibility of KS in suspicious skin lesions of non-organ transplant recipients on immunosuppressive therapy. Withdrawal of immunosuppressive therapy should be considered.

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