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Myeloma Cast Nephropathy Complicating Multiple Myeloma Associated with Kaposi Sarcoma: Is This a New Victim of Human Herpes Virus Type 8? Case Report

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Abstract **Case Report**

Kaposi sarcoma (KS) is an angiogenic neoplasia characterized primarily by purplish to brownish skin lesions. Most often linked to infection by human herpes virus type 8 (HHV8), it affects men more than women and has especially been found in elderly people around the Mediterranean. Classic Kaposi sarcoma is rare and the association with multiple myeloma (or Kahler's disease) remains exceptional with a few cases sporadically described in the literature. We report a new case illustrating this association. This is a 70-year-old patient in whom classic Kaposi disease was recently diagnosed by skin biopsy with positive HHV8 serology. He was subsequently referred to the Department of Nephrology due to the fortuitous discovery of severe kidney failure with a renal biopsy in favour of myeloma light chain cast nephropathy. The hypothesis incriminating an HHV8 variant in the pathogenesis of multiple myeloma is known in the literature but not yet elucidated. It is therefore of great interest that clinicians be sensitized about this association in order to progress in research and improve treatment and prognosis.

Keywords: Kaposi sarcoma, multiple myeloma, human herpes virus type 8, myeloma cast nephropathy.

INTRODUCTION

Kaposi sarcoma is a multifocal neoplastic disease characterized by angioproliferative skin lesions [1]. The main disease associated with infection by human herpes virus type 8 (HHV8), Kaposi sarcoma affects men more than women and appears in four forms. These are the classic form sporadically present especially in elderly people in the Mediterranean basin, the endemic form common in East and Central Africa where it represents 1 to 10% of diagnosed cancers, the so-called post-transplant form found in transplant recipients (particularly kidney recipients) and the epidemic form, the most widespread encountered in patients infected with HIV [2]. The classic form is rare and the association with multiple myeloma remains exceptional, with a few cases sporadically described in the literature.

We report, to our knowledge, a 31st case of Kaposi sarcoma-multiple myeloma association revealed by a myeloma cast nephropathy. Our objective is to increase clinicians' awareness of this very exceptional association between the two cancers and thus improve their management.

CASE PRESENTATION

A 70-year-old man from North African was referred to the Department of Nephrology by a dermatologist for severe kidney failure fortuitously discovered. His history was marked by chronic hip pain for which he was followed by a rheumatologist. The recent history of the disease dated back 3 months with the onset of itchy maculopapular skin lesions on the arms and thighs in a context of deterioration in general condition. He consulted a dermatologist where a skin biopsy performed was in favor of the classic Kaposi sarcoma, with positive human herpes virus type 8 serology and discovery of renal failure at 117 mg/l for which he was transferred to the Department of Nephrology.

The clinical examination, upon admission to the Department of Nephrology, noted a blood pressure of 120mmHg, a heart rate of 88 beats/minute, a respiratory

rate of 18 cycles/minute. He had no fever and the weight was 77kg. He had no lower limb edema. Diuresis was preserved. The mucocutaneous examination revealed maculopapular lesions in clusters, purplish, on the arms and left thigh. The remainder of the examination didn't show anything particular.

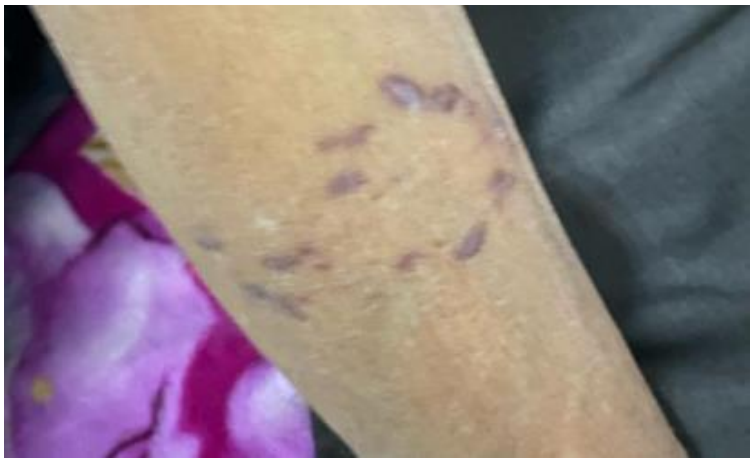

Figure 1: Purplish maculopapular skin lesions on the arm

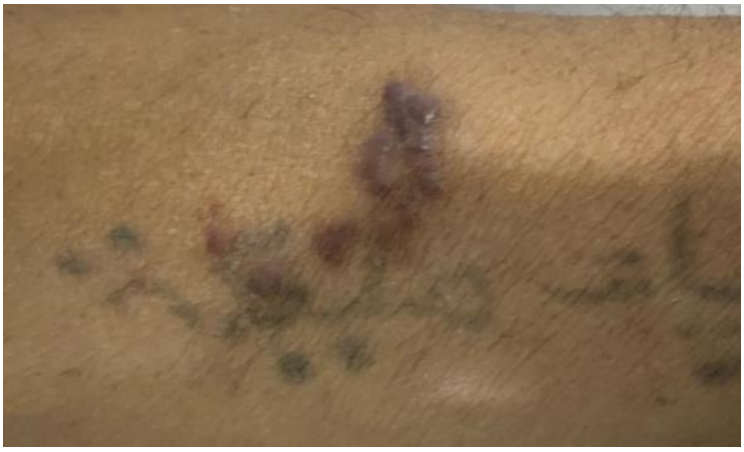

Figure 2: Purplish maculopapular lesions on the thigh

The biological checkup revealed severe renal failure of 160 mg/l with urea of 2.68 g/l requiring hemodialysis.

Blood sodium was 139mmol/l and potassium 4.4mmol/l. Proteinuria was 3.5g/24h without impact on the proteinogram with hyperproteinemia at 105g/l. The serum albumin was 32g/l. Protein electrophoresis showed a narrow band with a monoclonal appearance. The dosage of light chains and Bence Jones proteinuria had not been done. The cytobacteriological examination of urine revealed a leukocyturia of 380000/ml, without hematuria, with sterile culture. The liver and lipid profile was without abnormalities. The blood count noted anemia at 7g/dl for which the patient received a blood transfusion.

Serology for human herpes virus type 8 was positive, while the rest of the seroimmunological checkup was negative. The complement dosage was normal.

Renal ultrasound showed kidneys of limited size with good cortico-medullary differentiation, without obstruction of the urinary tract.

Faced with renal failure, anemia and chronic hip pain (3 CRAB criteria; where C= hypercalcemia; R= renal impairment; A= Anemia; B=Bone lesions), multiple myeloma was suspected. A myelogram performed was unfortunately inconclusive. A renal biopsy performed suggested a myeloma light chain (lambda) cast nephropathy, with 70% of tubular fibrosis, easing the diagnosis of multiple myeloma.

Therapeutically, the patient was treated with chemotherapy in addition to symptomatic treatment. The evolution was marked by the regression of the skin lesions. But there was no recovery of kidney function. Renal failure was classified as End-Stage Renal Disease (ESRD, requiring long-term hemodialysis.

DISCUSSION

Classic Kaposi sarcoma was first described in 1872 by Moritz Kaposi. Also called "multiple pigmented

sarcoma", according to Kaposi, it is a hemorrhagic multifocal neoplastic acroangiomatosis whose appearance is mainly cutaneous, that can be visceral and mainly affects men aged between 50 and 70 years in Eastern Europe and the surrounding areas of Mediterranean [3], which tallies with our case. The association of Kaposi's sarcoma and hematological disease is known in the literature. It is often described as associated with Castleman's disease or lymphomas. Kaposi's disease precedes hemopathy in 15% of cases, appears simultaneously in 36% of cases and in 46% of cases, it occurs subsequently [4]. In our case, it is an association between the classic Kaposi sarcoma and a secondarily diagnosed myeloma, and not a lymphoma or Castleman's disease.

The question that arises here is whether this Kaposi sarcoma-multiple myeloma association is just a coincidence or whether there is a causal link between these two cancers. Kaposi sarcoma, whatever its form, is most likely associated with a chronic viral infection with human herpes virus type 8. The serology is positive in almost 100% of cases, with a seroconversion preceding the lesions of an average of 33 months [5]. In 1994, Chang et al. detected by polymerase chain reaction (PCR) DNA sequences related to human herpes virus type 8 in Kaposi's lesions of spindle and endothelial cells [6]. This could demonstrate the involvement of the virus in Kaposi sarcoma.

On the other hand, in 1997, Retting *et al*., suggested that human herpes virus type 8 may be a causative factor in multiple myeloma. Indeed, they detected viral DNA in the dendritic cells and bone marrow mononuclear cells of all the subjects in their serie suffering from multiple myeloma and in some of the subjects with monoclonal gammopathy of undetermined significance (MGUS); human herpes virus type 8 may contribute, according to them, to the transformation of these MGUS into myeloma [7]. Human herpes virus type 8 mainly affects B lymphocytes and endothelial spindle cells, but also other cell types. It encodes a viral analogue of interleukin-6 (IL-6) known for its major role in the emergence of the plasma cell tumor clone. This inflammatory cytokine thus delivers a survival and proliferation signal to tumor plasma cells [8].

However, the involvement of the human herpes virus type 8 in the occurrence of multiple myeloma remains controversial. Indeed, many publications, such as that of Tarte *et al*., [9], have failed to confirm the generalized infection of bone marrow stromal cells of subjects suffering from multiple myeloma by the human herpes virus type 8 and emphasize that this virus is not involved in the pathophysiology of multiple myeloma. In our case, it was not possible to prove whether or not there was a causal link between human herpes virus type 8 and myeloma.

Management consists of local treatment in cases of stable and limited mucocutaneous damage. Systemic treatment is indicated in cases of extensive lesions, rapid progression, painful segmental edema or visceral involvement.

The prognosis depends on the patient's immune status, and not on the number of lesions, while visceral involvement determines the severity of the disease [10]. Our patient had active multiple myeloma complicated by severe renal damage with extensive chronic lesions. This may probably be the reason why there was no recovery of the renal function.

CONCLUSION

The Kaposi-Kahler association remains an exceptional clinical entity. To our knowledge, we have reported a 31st case. The hypothesis of an involvement of human herpes virus type 8 in the pathogenesis of multiple myeloma has already been mentioned in the literature but remains controversial. Further works are therefore necessary to progress in the research on this association and improve the treatment and prognosis.

Conflict of Interest: No conflict of interest declared by the authors.

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