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Multiple Myeloma Secondary to HIV Infection, Revealed by Renal Failure: About a Case

Mbengue Mansour[1], Cissé Mouhamadou Moustapha[1], Faye Maria[2], Lemrabott Tall Ahmed[2], Fall Khodia[2], Keita Alex[2], Faye Moustapha[2], Ba Bakary[2], Diagne Seynabou[2], Keita Niakhaleen[2], Ba Mamadou Aw[2], Dieng Ameth[2], Niang Abdou[2], Ka El Hadji Fary[2], Diouf Boucar[2]

[1]Department of Nephrology, Regional Hospital, Thies, Senegal
[2]Department of Nephrology, Aristide Le Dantec University Hospital, Dakar, Senegal
Email: mansourmbengue92@gmail.com

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Abstract

Multiple myeloma is on the list of neoplasia that may be associated with human immunodeficiency virus infection. It is an affection that aggravates the prognosis in these particular patients. We present the case of a patient with multiple myeloma and HIV infection, revealed by renal failure. This was a 59-year-old patient who was received to the Department of nephrology for renal failure associated with severe aregenerative pancytopenia. In etiological investigations, multiple myeloma associated with HIV1 infection was found. The evolution was unfavorable, marked by the death of the patient caused by digestive haemorrhage before the start of antiretroviral treatment and chemotherapy.

Keywords

Multiple Myeloma, HIV, Renal Failure

1. Introduction

Multiple myeloma (MM) is included in the list of neoplasia that may be associated with human immunodeficiency virus (HIV) infection [1] [2]. It is an affection that aggravates the prognosis in these particular patients. In this article, we present the case of a patient with multiple myeloma and HIV infection, revealed by renal failure. We then propose an updated review of the mechanisms that may explain the link between HIV infection and MM, as well as the particular clinical manifestations and therapeutic implications of this association.

2. Case Report

Mr N.D, a 59 years old senegalese patient, with no particular pathological ante-

cedent with a notion of taking herbal medicine. He was admitted on 03/10/2018 in the nephrology department of the regional hospital of Thies for renal failure in a context of deterioration of the general state (DGS). Upon admission, the interrogation found nausea accompanied by vomiting evolving for 2 months. The general examination found a DGS with weight loss and physical asthenia. Arterial pressure was 129/82 mmHg and diuresis was 1700 cc/day. The physical examination found a silky trichopathy. The rest of the clinical examination was normal. At the paraclinical explorations, the hemogram showed aregenerative pancytopenia with anemia at 8.7 g/dl, thrombocytopenia at 37,000/mm^3, leucopenia at 1800/mm^3 and a reticulocyte count at 1.9%. The medullogram showed a plasmocyte infiltration at 20% (**Figure 1**). The serum creatinine was 375 mg/l and blood urea was 2.2 g/l. The serum calcium was 91 mg/l and the phosphatemia was 117 mg/l. Serum proteins electrophoresis found polyclonal hypergammaglobulinaemia, hypoalbuminemia at 18 g/l and hypoproteinemia at 57 g/l. The proteinuria was 0.45 g/24 h. The account of Addis found a leukocyturia at 110,000/mn without hematuria. The X-ray of the skull showed no geode. The renal biopsy puncture was not performed because of severe thrombocytopenia. The HIV serology was positive for HIV1. The viral load of HIV1 was 7152 copies/ml. The diagnosis of multiple myeloma associated with HIV was retained. Hemodialysis was performed in our patient every 48 hours. The evolution was unfavorable, marked by the death of the patient caused by digestive haemorrhage, two weeks after admission, before the start of antiretroviral treatment and chemotherapy.

3. Discussion

The association of multiple myeloma and HIV infection gives rise to three reflections. The first is to see if HIV infection is a contributing factor to multiple myeloma. It is also to highlight the specific clinical and paraclinical manifestations of this association, finally to see the implications for this different therapeutic modalities in this association.

The exact mechanisms of plasma cell disorders in HIV patients are unclear. Two main mechanisms probably contribute to the development of plasma cell disorders in this population of patients: antigenic stimulation and immunodeficiency [3].

It is generally accepted that chronic antigenic stimulation is important step in the process. Indeed, HIV antigens and/or other bacterial or viral antigens can act as super-antigens [4] [5] [6] [7] [8] and stimulate B-cell proliferation and immunoglobulin secretion without the help of T cells. However, very little is known about the nature of the antigen(s) and the published data has been controversial. It was stipulated that a viral infection or HIV, Epstein-Barr virus, human herpes virus 8, herpes simplex virus and hepatitis B and C viruses antigens could play an important role in the development of B cells [8].

HIV viruses can cause T-cell dysfunction and dysfunctional T cells can induce B cell activation without the need for antigenic stimulation [8]. In addition, HIV

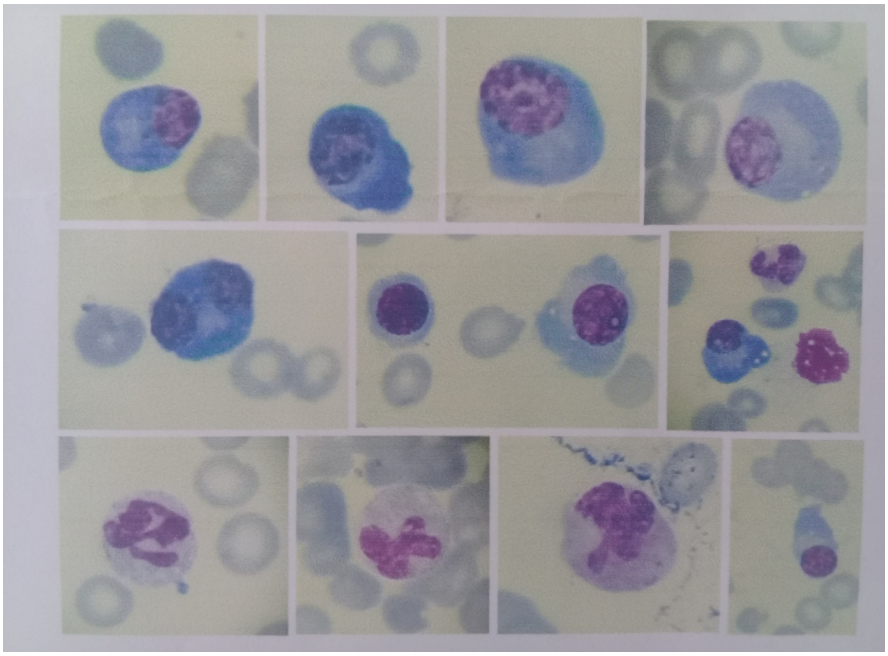

Figure 1. Medullogram showing plasmocyte proliferation.

infection depletes T cells, resulting in profound immune deficiency. Grulich *et al.* recently conducted a meta-analysis to study the role of immunodeficiency in the development of MM. The authors compared the incidence of cancers, including MM, in HIV/AIDS patients and kidney transplant patients on immunosuppressive drugs [9]. The authors found that the standardized incidence ratio (SIR) of MM in HIV-infected patients was 2.71, which was quite similar to that of MM in renal transplant patients (SIR: 3.12). These data suggest that T-cell depletion and immune deficiency may act an important role in increasing the incidence of MM in HIV patients.

Several epidemiological studies conducted in the United States, Italy and Australia have shown a 2- to 5-fold increase in the risk of developing MM in HIV-infected patients [10]. In this patient population, MM has particular characteristics. In the general population, MM is a disease that mainly affects the older patients: the median age of diagnosis is 66 years and only 2% of patients are under 40 years of age [11] [12]. However, in HIV-infected patients, MM appears much earlier: the mean age of patients varying in the quarantine [12]. In our patient, MM was diagnosed at 59 years old. In fact, the age of onset of MM in these patients depends on that of HIV infection. MM in HIV-infected patients shows atypical clinical evolution. It tends to be associated with solitary bone plasmocytoma or extramedullary plasmacytoma [13]. These patients also tend to have a low level of M protein despite the aggressiveness of the disease. The progression of MM in HIV-infected patients is very rapid and overall survival is short. MM in HIV-infected patients has atypical histopathological characteristics, and some patients may have anaplastic cells. These anaplastic cells are negative for the common leukocyte antigen, lysozyme, and cytoplasmic immunoglo-

bulins [14] [15]. The interval between HIV infection and the diagnosis of MM remains to be determined. In some reported cases, MM was the first manifestation of HIV/AIDS infection [14]. In our patient, the diagnosis of MM and that of HIV infection were concomitant. It appears that MM occurs at different stages of HIV infection: some patients develop MM at the beginning of the infection, while others develop it several decades later.

Highly active antiretroviral therapy (HAART) treatment acts an important role in the management of plasma cell disorders in patients with HIV infection. Limited data suggests that a good response to HAART may lead to a reduction in M protein in some HIV-infected patients with monoclonal gammopathy [16]. Amara *et al.* reported 9 on 25 patients who presented a decrease in serum M protein levels during HAART [17]. It was reported that HAART could achieve complete remission of multiple myeloma [18]. The exact effect of antiretroviral therapy on myeloma is poorly documented, contrary to the implication of these therapeutics in the regression of certain tumoral pathologies such as Kaposi's sarcoma and certain types of non-Hodgkin's malignant lymphoma, which is a phenomenon already well described [1] [3]. It is also not known how long patients need to take antiretroviral therapy before the start of chemotherapy.

It was recently reported that protease inhibitors such as ritonavir, saquinavir and nelfinavir (but not indinavir) induce growth cell arrest and apoptosis in several MM cell lines. These protease inhibitors down-regulate the antiapoptotic protein Mcl-1, block interleukin-6-stimulated phosphorylation of STAT3, and inhibit production of vascular endothelial growth factor [19]. Nelfinavir has synergistic effects with bortezomib on the proteotoxic death of MM cells [20]. The chemotherapy regimens for MM in HIV-infected patients are the same as for seronegative HIV-infected MM and usually consist of 2 to 3 drug combinations including thalidomide, lenalidomide, bortezomib, and dexamethasone [21].

4. Conclusion

The development of MM during HIV infection implicates various molecular mechanisms and pathways, and the understanding of these pathways has important implications in the treatment of MM in general. Antiretrovirals undoubtedly have other targets than viral enzymes. The discovery of these pathways offers new perspectives especially in the MM.

Ethical Statement

The informed consent of the patient's family was obtained.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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