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Multiple Myeloma of the Young Subject Revealed In Chronic Hemodialysis: About an Observation and Review of the Literature

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Abstract **Case Report**

Introduction*:** Multiple myeloma (MM) is a monoclonal proliferation of mature plasma cells. It usually occurs in people over 50 years of age with a peak in frequency at 65 years of age and less than 2% of patients are under 40 years of age. ***Case presentation*:** This case report is of a 38 year old black African woman with chronic kidney disease stage 5D. The IR was of glomerular origin (hypertension for 2 years, proteinuria at 4 g/24 hours, oedematous syndrome). Serum protein electrophoresis showed a beta peak at 29.7 g/l and urine protein immunoelectrophoresis showed a kappa/lambda ratio of 8.4. The myelogram showed a rich marrow with 51% plasma cells. Radiography showed multiple cystic images at the upper 1/3 of the left humeral shaft. Renal histology showed minimal glomerular damage. The diagnostic profile of IgG kappa light chain MM with CRAB criteria complicated by chronic glomerulonephritis with unorganised monoclonal immunoglobulin deposits was suggested. Management consisted of chemotherapy with bortezomib and dexamethasone for 4 cycles. The evolution under chronic dialysis was favourable after 1 year. ***Conclusion: MM in young adults (defined as 19-40 years of age) is rare, but it does exist. In young patients, this condition is initially not considered in the differential diagnosis and the occurrence of IR has a strong prognostic impact. Survival seems to be better in young adults than in elderly patients, which needs to be proven by a longer follow-up.

Keywords: Renal impairment, multiple myeloma, young subject, haemodialysis.

INTRODUCTION

Multiple myeloma (MM) is a chronic lympho-proliferative syndrome and corresponds to a monoclonal proliferation of mature plasma cells [1]. Monoclonal plasma cells are responsible for the synthesis of monoclonal immunoglobulin (Ig), which may be complete (2 heavy and light chains) or incomplete (light chain only). The disease may be responsible for lytic bone complications, hypercalcaemia, anaemia, renal impairment, repeated infections and has a poor prognosis [2].

It represents 10% of haematological malignancies and is the second most common haematological cancer after non-Hodgkin's lymphoma, accounting for 1-2% of cancer mortality. MM usually occurs in people over 50 years of age, with a peak in frequency at 65 years of age, and less than 2% of patients are under 40 years of age [2-5].

The present case report concerns a case of MM revealed by stage 5D chronic renal impairment in a 38-year-old black African woman.

CASE PRESENTATION

History:

A 38-year-old black African patient of Gabonese origin was referred to the nephrological clinic at the University Hospital of Point G (Mali) for chronic renal impairment stage 5D of probable glomerular

origin (arterial hypertension for 2 years, proteinuria at 4 g/24 hours, oedematous syndrome).

At the time of her initial admission, the interrogation revealed a notion of non-selective anorexia, physical asthenia, dizziness, and incoercible vomiting in a context of rupture of the dialysis sessions for 10 days.

Clinical and paraclinical examination:

The physical assessment showed conjunctival pallor, blood pressure 140/80 mmHg, heart rate 96 beats per minute, temperature 37°C, weight 61 kg and body mass index 21.7 kg/m2. The rest of the examination noted the presence of crackling rales in both lung fields, hepatomegaly with turgidity and hepatojugular reflux, and painless symmetrical oedema of the lower limbs guarding the bucket.

The continuation of his dialysis sessions was instituted urgently on a right jugular catheter in view of a serum creatinine of 1442 µmol/l and azotemia of 42 mmol/l.

The biological assessment showed a hypochromic microcytic anaemia at 6.8g/dl, an accelerated sedimentation rate (SV) at 99/146mm, massive proteinuria at 5.94g/24h with hypoprotidemia at 56g/l without hypoalbuminemia at 31g/l, and a normal urine sediment. The phosphocalcic assessment showed a corrected calcemia of 2.18 mmol/l, hypovitaminosis D, and hyperparathyroidism (674.3pg/l).

Serum protein electrophoresis showed a beta peak at 29.7 g/l. Urinary protein immunoelectrophoresis showed the presence of kappa free light chains at 37.8 mg/l and lambda light chains at 4.5 mg/dl with a kappa/lambda ratio of 8.4. Bence Jones proteinuria was negative.

Anti-nuclear, anti-DNA and rheumatoid factor antibodies were negative, as were serologies for hepatitis B, hepatitis C, HIV and syphilis. Serum complement fractions C3, C4 and CH50 were normal.

X-rays of the skull, femur and hip were unremarkable. However, the x-ray of the upper 1/3 of the left humeral shaft showed multiple cystic images (Figure 1). The myelogram showed a rich marrow with 51% plasma cells.

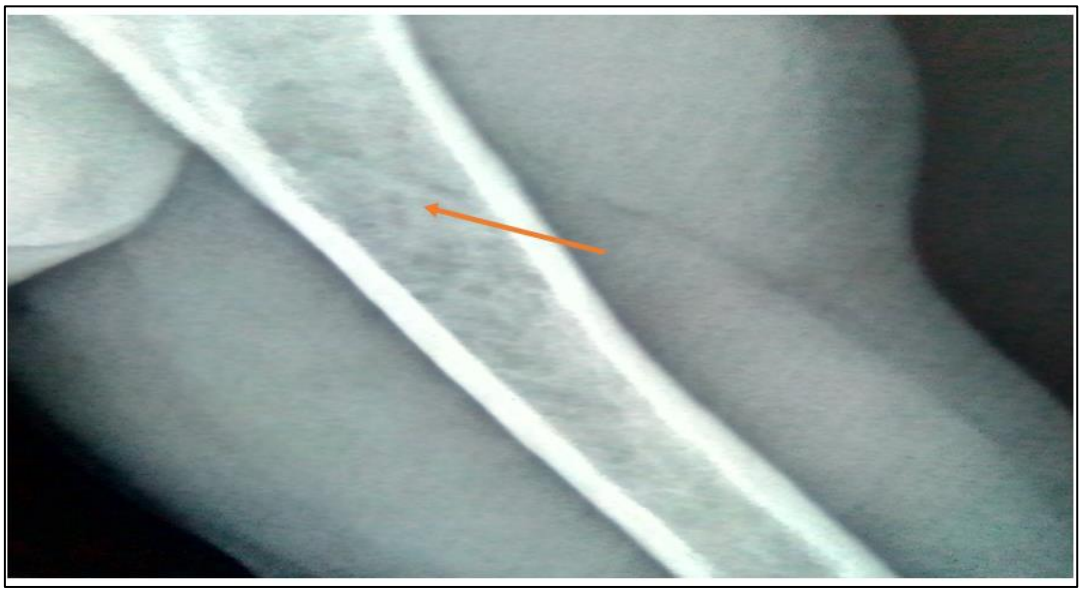

Figure 1: Die-cut lacunar images of the upper 1/3 of the humeral shaft (arrow)

Abdominal ultrasound revealed anatomically situated, normal-sized, echogenic, dedifferentiated, alithiasic kidneys without dilated pyelocalic cavities.

On the cardiac side, the frontal chest X-ray showed cardiomegaly (ICT 0.63) with discrete hilobasal alveolar condensation and the echocardiography discovered a bi-atrial dilatation with preserved left ventricular systolic function.

Histological diagnosis:

At 2 months of admission, renal biopsy was performed.

On light microscopy the renal fragment is essentially adipose with a medullary tip without glomerulus. It contains dilated tubes in epithelial necrosis with hyaline content or in atrophy (10%) with a discrete fibrosis (10%). The inflammatory infiltrate is diffuse mononuclear (10%). Vascular areas are not represented. The congo red stain is negative.

In immunofluorescence, the 3 glomeruli analysed showed mesangial sclerosis with fibrous thickening of Bowman's capsule.

In total, the diagnosis of minimal glomerular lesions is evoked.

Therapeutic management and outcome:

Management consisted of conventional chemotherapy with bortezomib (VELCADE®) and dexamethasone for 4 cycles and pamidronic acid 60mg every 4 weeks for bone involvement. Independently of this chemotherapy, the patient was dialysed twice a week for 4 hours per session and received injectable iron at the end of the dialysis, alternating with transfusion of packed red blood cells to correct the anaemia. In parallel, she also received vitamin D and calcium supplementation for the correction of phosphocalcic disorders, and sulfamethoxazole/trimethoprim for the prevention of opportunistic infections.

The evolution under chemotherapy with continuation of chronic dialysis sessions was favourable for about 18 months.

DISCUSSION

MM is a malignant bone marrow plasma cell dyscrasia related to the secretion of monoclonal Ig. It represents about 1% of all neoplasia in the white population and 2% in the black population [3]. In France, its annual incidence is 5 to 6/100,000 inhabitants, i.e. about 3,000 new cases diagnosed each year, with a discrete male predominance [4]. In the United States, 15,000 new cases are diagnosed each year, i.e. an estimated annual incidence of 4 cases per 100,000 inhabitants. This incidence appears to be higher in men than in women [6]. The average age of onset is over 60 years, although it is rare before the age of 40 [5, 7].

The case reported in this observation is a 38 year old black female subject. In Mali, according to data from a study carried out in oncology and internal medicine on the epidemiology of haematological malignancies in 264 cases, two cases of myeloma before the age of 40 were found and the frequency of this haemopathy seemed to increase significantly after the age of 60 [8]. A case of 36 years old was also reported in Morocco [9]. To our knowledge, the youngest cases have been documented in India, including a series of two female patients aged 18 and 20 years [10], and a 13-year-old boy [11].

According to the literature, the classic mode of revelation of myeloma in young people is bone involvement, such as bone pain, spinal syndrome with or without spinal cord compression and rarely sacral plasmacytoma [5, 9, 12]. Although renal impairment (RI) is common in MM, inaugural renal impairment in young patients has not been well described [13].

The initial clinical manifestations observed in our patient did not point to myeloma. The MM in the reported case was revealed by an IR in a context of massive non-nephrotic proteinuria (5.94g/24H) without any painful manifestation. The diagnostic profile was that of IgG kappa light chain MM with CRAB criteria (IR, anemia, bone involvement). In this case, there is no hyperproteinemia or accelerated SV with more frequent and severe renal involvement than in other types of MM. This IR almost inevitably progresses to terminal IR despite chemotherapy [3].

Our patient presented with hypoprotidemia, and an accelerated SV (possibly related to severe renal IR). Thus, on the basis of the renal histology results (subject to the quality of the fragment analysed by light microscopy) in addition to the clinico-biological data, chronic glomerulonephritis with non-organised non-Randall monoclonal Ig deposits was evoked in this case.

This condition presents on renal histology with consistent tubular and heterogeneous glomerular lesions. The usual appearance under light microscopy is that of membranoproliferative glomerulonephritis, or diffuse endocapillary glomerulonephritis, more rarely mesangial glomerulonephritis. On electron microscopy, the deposits are granular, discontinuous, subendothelial and mesangial. Unlike Randall's syndrome, no peritubular or vascular deposits are visible [14].

Amyloidosis had also been suggested, but seemed unlikely given the absence of Congo red staining on renal histology and the presence of a kappa monoclonal light chain on urine immunoelectrophoresis. The diagnostic criteria for myelomatous cell carcinoma (MCN) (a priori ARF, free light chain level >500 mg/L and abundant proteinuria with less than 10% albumin) were not met in the patient and the Bence-Jones proteinuria test was negative [15].

Radiologically, the presence of multiple small die-cut lacunar images of the upper 1/3 of the humeral diaphysis with no other abnormalities on the other bone structures in our case, is in line with the literature which reports the frequency of lytic bone lesions in very young patients [3, 5, 9, 11].

With regard to the management of MM, the treatment of young patients does not differ sufficiently from that of adult subjects. To date, no prospective, randomised studies have been able to establish solid recommendations for the treatment of MM complicated with IR [16]. The aim is to achieve as rapid and complete a haematological response as possible, with a preference for agents that do not require adaptation to renal function to limit haematological toxicity [17].

Several retrospective studies have shown the efficacy of chemotherapy regimens based on the

combination of bortezomib and dexamethazone in achieving a renal response, with a safety and toxicity profile comparable to normo-renal subjects [18, 19].

Apart from conventional chemotherapy (bortezomib + dexamethasone), correction of anaemia and phosphocalcic disorders, our patient underwent several sessions of haemodialysis and there was no recovery of renal function, indicating the progression to chronicity.

Intensive treatment followed by haematopoietic stem cell (HSC) autotransplantation is currently the gold standard treatment for young MM (<65 years) that can improve long-term survival. However, most randomised studies that have established the superiority of intensive therapy over conventional chemotherapy have excluded patients with proven persistent IR. However, the feasibility of intensive treatment with autotransplantation has been well demonstrated in patients with IR, including those on haemodialysis. The benefit/risk ratio of autotransplantation therefore remains uncertain and the place of intensive treatment in a situation of proven persistent IR must be rigorously evaluated. It seems legitimate to propose intensive treatment when renal function remains relatively preserved (GFR> 30 ml/min) [20].

In this case, financial constraints and the lack of technical facilities were an obstacle to the performance of HSC autotransplantation. The evolution under chronic dialysis was favourable after one year.

According to the results of several cohorts, the average survival time was longer in young subjects, i.e. about 40 months [3, 5, 11]. The renal prognosis remains poorly established, even in patients treated with modern chemotherapy protocols, and the impact of chronic end-stage renal disease on survival remains significant, with a median of nearly 32 months [21].

CONCLUSION

MM in young adults (defined as 19-40 years of age) is rare, but it does exist. It may have similar symptoms to those seen in older patients. In young patients, this condition is not initially considered in the differential diagnosis and the occurrence of IR is highly life threatening.

Histological confirmation should be considered when the clinical presentation is not typical of MCN, or when haemodialysis is required. Survival appears to be better in young adults than in older patients, which needs to be proven by longer follow-up.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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