CASE REPORT

Waldenström Disease in a Renal Transplant: a Case Report and Review of the Literature

El Mostafa Chachi\textsuperscript{1,2}, Intissar Ajhoun\textsuperscript{1}, Mounya Bouabdellah\textsuperscript{1,3}, Laila Benchekroun\textsuperscript{1,3}

\textsuperscript{1}Laboratory of Biochemistry, Ibn Sina Hospital in Rabat, Morocco
\textsuperscript{2}Faculty of Medicine and Pharmacy, Ibn Zohr University, Agadir, Morocco
\textsuperscript{3}Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco

SUMMARY

\textbf{Background:} We report through this case, the exceptional occurrence of Waldenström's macroglobulinemia in a renal transplant.

\textbf{Methods:} A 65-year-old diabetic man, who had a kidney transplant in 2008, presented to the hospital in 2020 for ketoacid decompensation. The blood ionogram showed hyperproteinemia at 102 g/L. Electrophoresis and immunofixation of serum proteins revealed a monoclonal immunoglobulin of IgM Kappa isotype numbered at 46 g/L. Confirmation of Waldenström's disease was made by myelogram and immunophenotyping of tumor cells.

\textbf{Results:} The diagnosis adopted for our case is Waldenström's disease which occurred 12 years after the kidney transplantation.

\textbf{Conclusions:} Post-transplant lymphoproliferative syndromes are secondary to immunosuppressive therapy, the main concern in this case is the involvement of the graft with the risk of losing its function, hence the interest of monitoring and identifying any hyperproteinemia.


KEYWORDS

transplanted Waldenström, renal immunoglobulin, monoclonal immunosuppressive electrophoresis

INTRODUCTION

Waldenström's macroglobulinemia (MW) is a chronic lymphoproliferative syndrome characterized by lymphoplasmocytic infiltration of the bone marrow and IgM-type serum monoclonal immunoglobulin [1]. Waldenström's macroglobulinemia is a very rare disease with an estimated annual incidence of 3.4 cases per million people [2]. Through this clinical case, we report the rare occurrence of MW in a renal transplant 12 years after transplantation.

CASE PRESENTATION

A 65-year-old man, who has had a renal transplant since 2008 for chronic end-stage renal disease on indetermi-
nate nephropathy, presented to the hospital in February 2020 for an inaugural ketoacid decompensation following the change in immunosuppressive treatment (replacement of cyclosporine with tacrolimus). At admission, biologically, in addition to hyperglycemia and acidosis, the patient had hyperproteinemia at 102 g/L, persistent even after correction of blood glucose and electrolyte disorders. This required proteinuria electrolytaphoresis (capillary electrophoresis on Helena Nexus V8®) which showed a monoclonal peak in the beta-2-globulin band of 46 g/L, with a hypoalbuminemia of 25.57 g/L (Figure 1). Immunofixation of serum proteins on agarose gel (Helena SAS®) led to the identification of a monoclonal immunoglobulin of the IgM kappa isotype (Figure 2). The weighted doses of IgM and IgG on Architect c16000® (Abbott) were 55.31 g/L and 7 g/L, respectively. The doses of serum free light chains kappa and lambda (nephelometry on SPAplus®) were 362.97 mg/L and 19.35 mg/L, respectively, and the kappa/lambda ratio was 18.75.

The 24-hour proteinuria was 5.58 g/24 hours and the Bence Jones protein was positive with presence of kappa isotype monoclonal free light chain. Following the discovery of this IgM kappa isotype monoclonal immunoglobulin, a clinical reassessment and a set of confirmatory and complementary studies were carried out, the main points of which we report.

Clinically: the patient is completely asymptomatic, and the clinical examination is unremarkable except for the background examination which found signs of hyperviscosity.

Biologically the hemogram showed normochromic normocytic regenerative anemia at 10.5 g/dL, and on the myelogram a medullary infiltration made of small lymphocytes and lymphoplasmocytes at 29% in favor of a cytological aspect of MW.

Immunophenotyping of tumor cells on flow cytometer (CytoFlex®) found in 100% of the population the expression of CD19 and CD20 with a high fluorescence intensity and in 60% of CD5-, CD23- and CD10-B cells. CD22 expression is low and also the absence of a CD138+ and CD 38+ population.

The creatinine level remained stable and the osteomedullary biopsy was negative. The sedimentation rate at the first hour accelerated to 120 mm. The dosage of beta2-microglobulin was 3.79 mg/L to around 12 mg/L. However, a biopsy puncture of the graft showed a membranoproliferative glomerulonephritis with secondary cryoglobulinemia. The serologies of hepatitis C and B viruses, Epstein virus (EBV), and cytomegalovirus (CMV) were negative.

On the basis of all these clinico-biological elements, the diagnosis is Waldenström disease after kidney transplantation. The patient was treated with rituximab and bendamustine; however, no data on disease progression are available.

**DISCUSSION**

MW is a mature B-cell chronic lymphoproliferative syndrome occurring preferentially in males and is considered lymphoplasmacytic lymphoma (LPL) in the World Health Organization (WHO) classification [3]. Most cases of PLL are MW, and less than 5% of cases are associated with IgG. IgA monoclonal immunoglobulin or are non-secreting. The median age of onset is 68 years. An accurate estimate of the prevalence of MW is difficult, because diagnostic criteria have long remained poorly defined and also because of the existence of asymptomatic forms. The clinical presentation is protean due to the physicochemical properties or antibody activity of monoclonal IgM. Its annual incidence is estimated at 3.4 cases per million people [2]. According to a study carried out in the eastern region of Morocco over a period of 5 years, its prevalence was estimated at 0.8% of all hematological malignancies [4], making it a rare pathology in our country. Its discovery is often fortuitous in the face of the demonstration of a monoclonal immunoglobulin at IgM [2] and its diagnosis is confirmed by the presence of bone marrow infiltration by clonal lymphoplasmatocytic cells greater than 10% [5].

Chronic renal failure (CRF) is characterized by a gradual decrease in glomerular filtration rate (GFR). When the GFR falls below 15 mL/minute, it is called terminal CRF. It is at this stage of the disease that renal replacement therapy becomes necessary: hemodialysis in the center or at home, peritoneal dialysis (at home), and kidney transplantation. Currently, kidney transplantation is the best replacement treatment for kidney function because compared to dialysis, it is associated with increased survival, improved quality of life, and lower cost to the health system [6].

Rejection of kidney transplantation has become rare due to the development of immunosuppressive treatments; however, immunosuppressive treatment has adverse effects as it exposes recipients to cardiovascular and infectious risks and especially to increased post-transplant lymphoproliferative syndromes (PTLD) that require close monitoring [6].

Our case met all the criteria in favor of MW. He is male, 65 years old, with an IgM monoclonal peak associated with 29% lymphoplasmacytic infiltration on the myelogram and tumor cell phenotype agrees with that defined during the second MW workshop: IgM+, CD5-/+, C10-, CD19+, CD20+, CD22+, CD23-, CD25+, CD27+, FMC7+, CD103- [7].

Hyperviscosity syndrome and glomerulonephritis are complementary to the clinical and biological picture. The latter is rare in Waldenström's disease and is secondary to cryoglobulinemia. If the medical observation of our patient is typical of a MW, its occurrence 12 years after the kidney transplant gives it a very special character. Indeed, post-transplant lymphoproliferative diseases (PTLD) represent a significant complication in solid organ transplant recipients with an incidence of 0.8 to 2.5% in the case of kidney transplantation [8].
Figure 1. Serum protein electrophoresis showing a monoclonal peak in the beta-2 globulin zone quantified at 46 g/L, associated with hypoalbuminemia.

Figure 2. Serum immunofixation result showing IgM kappa monoclonal immunoglobulin.
MW post-transplant is a very rare entity. After reviewing the literature, we found one case whose tumor clone was located at the level of the kidney transplant [9] and another case of hyperviscosity syndrome evoking MW in a liver transplanted child secondary to post-transplant lymphocyte proliferation but the diagnostic criteria were insufficient [10].

CONCLUSION

Waldenström’s disease is a rare malignant hemopathy, which can occur in patients with special conditions, such as our kidney transplant case. The main concern in this case is graft damage with the risk of loss of function; hence, the importance of monitoring and identifying any hyperproteinemia.

Acknowledgment:
We would like to express our full gratitude to the whole team. Thank you for the important contribution and availability.

Declaration of Interest:
The authors do not declare any conflict of interest.

References: