Sickle cell nephropathy, a complication not to be ignored, through a Moroccan case

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Abstract

Nephropathy is a major complication of sickle cell disease. Indeed, the kidneys are particularly sensitive organs to this disease.

We report a case of a patient with a major sickle cell syndrome; she was hospitalized in the nephrology department of Mohammed V Military Training Hospital, for end-stage renal failure. The family investigation revealed a composite S/O-Arab heterozygosity responsible for the severity of the clinical disorder.

Introduction

Sickle cell nephropathy (SCN) is a major complication of sickle cell disease. It manifest's in various forms, including glomerulopathy, proteinuria, hematuria, and Renal tubular disorders, and frequently results in end-stage renal disease (ESRD). Hemolysis and vascular occlusion are the main factors promoting the manifestations of this disease. Dialysis and renal transplantation are the last resort for patient with SCN [1].

Through the case of a patient with a major sickle cell syndrome S/O-Arab complicated by end-stage renal failure, we will explain the pathophysiological mechanisms of this complication and emphasize the importance of biological monitoring.

Case report

The patient was 24 years old and was admitted to the nephrology department of the Mohammed V Military Training Hospital for incidental renal failure in the context of an impure nephrotic syndrome revealing sickle cell nephropathy. In his history, we retained a follow-up since the age of 5 years in another hospital structure for a hemoglobinosis S treated by iterative transfusions with notion of acute renal failure during sickle cell crises.

The biological result showed an anemia at 7.7 g/dL, corrected serum calcium at 82 mg/L, serum phosphorus at 64 mg/L, intact parathyroid hormone 1-84 at 543 pg/L, Alkaline Phosphatase at 201 U/L.

Hemoglobin electrophoresis was ordered to this patient, but due to repeated transfusions, her electrophoretic profile remains uninterpretable (Figure 1). Therefore, hemoglobin electrophoresis (HBE) was performed in the parents as part of the hemoglobin phenotypic study. The HBE of both parents is performed on Capillarys (Sebia®) at alkaline pH followed by electrophoresis on Hydrasys (Sebia®) which showed a heterozygous Hb O-Arab variant in the mother (Figure 2) and a heterozygous hemoglobinosis S (A/S) in
Referring to the phenotypic study of Hb performed in the parents, it is concluded that the patient has a composite heterozygosity S/O-Arab explaining the severity of the renal manifestations.

The evolution was marked by the absence of improvement of her renal function and the aggravation of the uremic syndrome motivating her setting in peritoneal dialysis. The patient was treated with erythropoietin ARANESP 30µg/ per 2 weeks with a blood transfusion of 2 packed red blood cells on average every two months.

The patient died at the age of 26 years before benefiting from either a hemoglobin genotyping study or a renal transplant.

Discussion

Sickle cell disease is the most common hereditary hemoglobinopathy in the world. An estimated 300,000 children are born with this disease each year, three quarters of whom are born in sub-Saharan Africa [2]. It is characterized by extreme variability in terms of clinical manifestations, the most serious of which are renal manifestations.

The association S/O Arab is responsible for a major sickle cell syndrome, as in the case of our patient. Indeed, Hb O Arab stabilizes the intracellular polymerization of Hb S.
and leads to an irreversible sickle cell disease of red blood cells, thus expressing by a more severe clinical disorder. The clinical and biological manifestation of this association is similar to homozygous sickle cell disease and the association Hb S / Hb D Punjab. The onset is usually early, in infancy, and is marked by the classic triad of chronic hemolysis: anemia, jaundice and splenomegaly. Anemia is usually moderate outside of hemolytic attacks (Hb = 7 - 10 g/dL). The evolution is often marked by sickle cell complications. Osteoarticular complications are the most frequent, such as vaso-occlusive crises, septic arthritis and osteoporosis. Pneumonia, leg ulcers and vesicular lithiasis are also reported [3].

Sickle cell nephropathy is a major complication of sickle cell disease. The kidneys are particularly sensitive organs to the disease. Sickle cell disease substantially alters the structure and function of the kidneys and is the cause of several renal diseases and syndromes. Renal damage is more severe in SS homozygous patients than in other major sickle cell syndromes [4]. Approximately 5-18% of patients have SCN, thus increasing the risk of morbidity and mortality of the disease [5].

A number of studies have focused on this pathology, its evolution includes several stages; it starts with hyperfiltration, then the occurrence of microalbinuria, then macroalbinuria and finally the progression to renal failure. The prevalence of these complications increases with the age of the patients but can also be seen from a young age.

Two models have been proposed to explain the pathophysiology of SCN. Becker et al. showed that prostaglandin release following ischemic injury causes an increase in glomerular filtration rate (GFR). This increase leads to glomerular injury and eventually manifests as proteinuria and glomerulosclerosis [6]. Alternatively, Nath and Katusic [7] classified the manifestations of SCN into two different phenotypes: the hemolysis-endothelial dysfunction phenotype and the viscosity-vaso-occlusive phenotype. The hemolysis-endothelial dysfunction phenotype affects the renal cortex and leads to hyperfiltration and glomerulopathy; heme released due to intravascular hemolysis predisposes to proteinuria through its accumulation on the glomerular filtration barrier, which disrupts membrane selectivity by exerting cytotoxic effects on podocytes and endothelial cells [8]. On the other hand, the viscosity-vaso-occlusive phenotype is responsible for hematuria, papillary necrosis, and tubular acidosis [9].

Microalbuminuria, reflecting the early stages of renal damage, should be routinely sought in the follow-up assessment in this category of patients.

Decreased GFR, which suggests loss of kidney function, occurs with the progression of sickle cell disease and may be a sign of uncontrolled disease. Sickle cell patients have a higher risk of developing chronic kidney disease compared to the general population.

Specific treatment with an angiotensin-converting enzyme inhibitor or an angiotensin II receptor antagonist should be considered in these patients in order to slow the progression of the renal disease. The prevention of microthrombosis and thus of renal damage requires the maintenance of a hemoglobin A level of more than 50% by regular blood transfusion as soon as sickle cell disease is diagnosed. The role of hydroxyurea in the prevention and/or treatment of renal function abnormalities in sickle cell disease remains to be studied [10].

**Conclusion**

Sickle cell nephropathy is a major complication of sickle cell disease. It must be systematically and early sought in all sickle cell patients to reduce the risk of morbidity and mortality of this disease.

The development of new biomarkers has become increasingly essential for the early detection of sickle cell disease in order to improve the survival of patients with sickle cell disease.

**Declaration of interest**

The authors declare no conflict of interest.

**References**