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Case Report

Renal Replacement Therapy in a Haemophilic Patient: a Case Report

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Abstract

Life expectancy and quality of patients affected by haemophilia have dramatically improved during the last years.

Different important clinical problems arise from this change in the natural history of haemophilic patients. In particular, aging-related diseases, such as diabetes, hypertension, cancer and chronic infections are emerging as new challenges in this patient population. Among chronic illness, renal diseases are of particular interest, since they implicate some issues of difficult clinical management. Here, we present a case of a patient affected by a severe form of haemophilia A, who presented advanced renal disease requiring the initiation of renal replacement therapy. This case offers us the possibility to examine the major issues regarding the management of dialysis treatment in haemophilic patients.

Key words: RRT; Haemophilia A; Recombinant FVIII; Haemodialysis; Peritoneal dialysis; Bleeding risk

Abbreviations

RRT: Renal Replacement Therapy; ESRD: End-stage Renal Disease; AVF: Artero-venous Fistula; HIV: Human Immunodeficiency Virus; HCV: Hepatitic C Virus; PD: Peritoneal Dialysis; HD: Haemodialysis

Introduction

Haemophilia A and B are genetic X-linked bleeding disorders, caused by mutations in genes encoding factor VIII and IX, respectively [1]. Clinical manifestations of haemophilia are spontaneous haemorrhage or acute bleeding caused by minor trauma, resulting in severe functional consequences that can culminate in a debilitating arthropathy [2].

Life expectancy and quality of life of haemophilic patients have dramatically improved over the last years, mainly for new therapeutic options and the awareness to the risk of HCV and HIV infections [3,4].

Different important clinical problems arise from this change in the natural history of haemophilic patients. In particular, aging-related diseases, such as diabetes, hypertension, cancer and chronic infections are emerging as new challenges in this patient population [5]. Among chronic illness, renal diseases are of particular interest, since they implicate some issues of difficult clinical management [6].

Here we present a case of a patient affected by a severe form of haemophilia A, who presented advanced renal disease requiring the initiation of renal replacement therapy (RRT). This case offers us the possibility to discuss the major concerns regarding the dialysis treatment of haemophilic patients.

Case Presentation

We describe the case of a 63 years old male patient affected by severe haemophilia A (residual Factor VIII activity <1%), who was treated at our Nephrology Unit, because of progressive end-stage renal disease (ESRD), requiring initiation of RRT.

Haemophilia A was diagnosed when he was a 6-month-old baby because of the onset of haematomas and bruises. In his childhood the patient was treated with red blood and plasma transfusions, and then from the 70's with non-virus inactivated Factor VIII concentrates. In 1990 a HCV infection was diagnosed, attributed to the infusions of coagulation factor concentrates. Thereafter, he was treated with virus inactivated Factor VIII concentrates until 1995, when he began to receive recombinant FVIII administrations (at the dose of 3000 IU of recombinant factor VIII three-time weekly, i.e. 28-30 IU/kg for a patient's weight of about 100 Kg).

In his medical history he presented many episodes of haemarthrosis involving above all of the joints, in particular hip and the knees. Because of severe functional limitations and pain, total knee and hip replacements were needed. The latter intervention was complicated by cutaneous cellulitis with blood culture positive for Staphylococcus Aureus, treated firstly with cotrimoxazole and chinolonics, and then with teicoplanin and meropenem. Contextually, he underwent a surgical evacuation of an iliopsoas abscess.

In addition, he also had a medical history of chronic HCV hepatopathy not responsive to IFN, type 2 diabetes, arterial hypertension, sigma diverticular disease and gastric angiodysplasia.

His renal function began to decline in 1989, when he underwent left nephrectomy for papillary urothelial carcinoma of the left renal pelvis (at that time, serum creatinine was 1.3 mg/dl).

In the following years, he presented some other urological problems, including bladder papillomatosis and right renal pelvis Papilloma, which required surgical excision.

In the meanwhile, renal function progressively worsened being

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associated to the onset of nephrotic proteinuria (4-5 g/24h).

In July 2011, he was admitted to our nephrology department because of asthenia, nausea, melena and anemization (Hb 6.8 g/dl) with serum creatinine levels of 8.53 mg/dl and blood urea nitrogen of 242 mg/dl. Hydrating therapy and blood transfusions were started, allowing the improvement of the renal function up to serum creatinine level of 4 mg/dl. Subsequently, the patient was discharged and strictly followed-up for some months in our outpatients' clinic until initiation of RRT was considered necessary. The decisions regarding the choice of dialysis modality, the placement of vascular access and the scheduling of dialysis sessions were particularly challenging, also because there are few data available on these issues.

So, considering the severity of haemophilia (with stable Factor VIII activity <1%), patient history, comorbidities and psychological factors we opted for haemodialysis by artero-venous fistula (AVF). Therefore, subject to prophylactic recombinant factor VIII administration (50 IU/kg Factor VIII one hour before surgery and 28 IU/kg every 12h day for three days after the procedure, followed by once-daily administration for the next two days); the patient underwent surgical intervention for AVF placement in the left forearm between the cephalic vein and the radial artery. There were no complications during surgery, preoperative PTT was 70 seconds while postoperative value was of 38 seconds and no postoperative bleeding occurred. Then, RRT was started, performing 4h of HD treatment two times per week with replacement of recombinant Factor VIII (3000 UI) after each procedure, that was associated to PTT levels of about 45-50 seconds.

In the following months the patient was substantially stable, presenting only occasional minimal bleeding after the removal of the dialysis needles. Currently he is in good clinical conditions and under evaluation to be placed on waiting list for kidney transplantation.

Discussion

Early reports showed that renal failure was a rare complication of hereditary clotting disorders [7], but this tendency has changed in the time and the potential number of haemophilic patients requiring RRT is now increased.

In fact, more recent investigations highlighted that haemophilic patients present an increased risk of renal disease [8]. The reasons for this change could be found in the prolonged life expectancy and the consequent ageing of haemophilic patients, high rate of survival among patients affected by human immunodeficiency virus (HIV) and Hepatitic C virus (HCV), as well in the progressive inclusion of high-risk patients in dialysis and kidney transplantation programs [9].

Hypertension was the main determinant of chronic renal disease, followed by viral infections, older age, non-white race and diabetes [10].

However, the role of viral infections in the pathogenesis of renal disease is particularly remarkable.

It should be considered that many haemophilic patients were infected by HCV and/or HIV transmitted through clotting factor concentrates used before the mid-1980s [11]. These infections have led, in the majority of cases, to chronic disease involving liver, immune system and kidneys.

Indeed, both HIV and HCV are associated with a number of renal syndromes, including HIV-associated nephropathy and immune-complex glomerulonephritis, characterized by the presence of high-grade proteinuria and progressive renal failure [12,13]. Moreover, viral infections may influence renal function also because of the nephrotoxic effects of the drugs used to treat the infections [14].

In our patient, different conditions- nephrectomy, diabetes, hypertension, HCV infection, use of nephrotoxic drugs (antibiotics) and proteinuric nephritis (not characterized by renal biopsy)- coexisted, making him particularly susceptible to the development of chronic kidney disease.

Then, despite attempts to slow chronic kidney disease progression, renal failure progressed to ESRD requiring RRT initiation. In this regard, the choice of RRT modality and the placement of vascular access are critical issues. Both peritoneal (PD) and extra-corporeal haemodialysis (HD) have been reported in haemophilic patients [15,16].

Because of the reduced risk of bleeding and not requirement of coagulation factor infusions after any treatment, PD should be considered the treatment of choice in patients affected by coagulatopathy [17].

However, PD seems not to be suitable for every haemophilic patient, mainly in presence of decompensated liver failure.

Alternatively, HD offers the advantage to be performed in a hospital setting; so expert nurses and physicians supervise it. Moreover, use of AVF as vascular access may significantly reduce the risk of infections. As counterpart, HD exposes the haemophilic patient to an increased risk of bleeding.

In our patient, considering the previous history of major abdominal surgery (which is one of the most important contraindication to PD), infections and his limited mobility, due to severe haemarthrosis, we opted for HD. After the treatment has been chosen, placement of dialysis access is mandatory.

While venous catheter, which is a potential source of infection, should be considered only a temporary access, in the long-term AVF is thought to be the optimal permanent access [18].

However, AVF placement implies a surgical intervention, which should be carefully planned in haemophilic patients [19].

In our case, in agreement with the local haemophilia treatment center and according to the international guidelines, recombinant Factor VIII was administrated before and for 5 days after the surgery for AVF preparation (see dosage above) and the patient did not present bleeding complications.

Finally, it should be also considered that in the course of HD treatment anticoagulation is required to prevent clot formation in the extracorporeal circuits. Obviously, this needing exposes the haemophilic patients to increased bleeding risk and different approaches have been developed to overcome this problem, including regional heparinization and use of citrate [20,22].

In our case, the patient suffered from a severe form of haemophilia

A and, at the time of RRT initiation, he was receiving 3000 IU of recombinant factor VIII (28 IU/kg for a patient's weight of 106 Kg) three-time weekly, so we decided to continue prophylactic treatment avoiding heparin and scheduling factor VIII administration twice a week at the end of each HD session, through the arterial line of the dialysis machine.

This treatment was successful and the patient did not experience any significant clinical complication.

In conclusion, management of renal diseases and RRT in haemophilia is complex and requires a full expertise, including haemophilia centers, infectivologists, surgeons and nephrologists.

However, our experience, together with those previously reported, demonstrates that, although challenging, RRT in haemophilic patients is possible and is manageable also in the daily clinical practice [6].

Moreover, even if the experience in the kidney transplantation is very limited, we think that this possibility has not to be denied to patients suffering from haemophilia [23].

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