RENAL TRANSPLANTATION IN A PATIENT WITH RECESSIVE DYSTROPHIC EPIDERMOLYSIS BULLOSA: A CASE REPORT

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Abstract

Recessive dystrophic epidermolysis bullosa (RDEB) is a rare genodermatosis characterized by abnormalities in the anchoring fibrils which attach the basal cell layer of the epidermis to the underlying structures. A characteristic feature of this disorder is the presence of recurrent blistering or erosions, the result of even minor traction to these tissues. Patients with RDEB frequently develop chronic renal failure, and require renal replacement therapy being a major cause of morbidity and mortality. The role of renal transplantation in these patients is scarcely known.

We present the case of an end-stage renal disease patient with RDEB treated by renal transplantation and his follow-up during a period of 83 months after the transplant.In this period, the frequency of serious infections was very low, there was also absence of skin tumors. Renal transplantation could be an alternative to renal replacement therapy in epidermolysis bullosa patients with end-stage renal disease, reducing the comorbidities associated with this treatment.

KEYWORDS: Epidermolysis Bullosa, Epidermolysis Bullosa Dystrophica, Kidney Transplantation.

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Recessive dystrophic epidermolysis bullosa (RDEB) is a rare genodermatosis characterized by abnormalities in the anchoring fibrils which attach the basal cell layer of the epidermis to the underlying structures. A characteristic feature of this disorder is the presence of recurrent blistering or erosions, the result of even minor traction to these tissues. Patients with RDEB frequently develop chronic renal failure, and require renal replacement therapy being a major cause of morbidity and mortality. The role of renal transplantation in these patients is scarcely known.

We present the case of an end-stage renal disease patient with RDEB treated by renal transplantation and his follow-up during a period of 83 months after the transplant. In this period, there were very low frequency of serious infections as well as the absence of skin tumors.

Renal transplantation could be an alternative to renal replacement therapy in epidermolysis bullosa patients with end-stage renal disease, reducing the comorbidities associated with this treatment.

Keywords: epidermolysis bullosa; epidermolysis bullosa dystrophica; kidney transplantation.

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Introduction

The hereditary epidermolysis bullosa (EB) is an extremely infrequent genodermatosis characterized by abnormalities in the dermo-epidermal junction that favors the happening of blisters in the skin and mucous after the minimum trauma [1]. According to the level in which the above mentioned abnormality occurs, it is possible to distinguish 4 main types of EB: Simple EB (basal cell layer of the epidermis), Junction EB (basal membrane), Dystrophic EB(anchoring fibrils which attach the basal cell layer of the epidermis to the dermis) and the recently added Kindler Syndrome (simultaneous abnormalities in different levels)[2]. The dystrophic epidermolysis bullosa (DEB) can be autosomal dominant or recessive[2], being characteristic in its pervasive forms by the presence of skin injuries in places exposed to repetitive trauma and injuries in the mucous level. The mucous affectation in the digestive tract can lead to malabsorption and resulting protein-caloric malnutrition. These patients also show a higher predisposition to the development of invasive squamous cell carcinoma when compared to the general population, being also more aggressive[3]. Chronic Kidney Disease (CKD) is very frequent in this group of patients, being usually secondary to hydronephrosi, poststreptococcal glomerulonephritis or amyloidosis[4]. As a result, many of these patients have to start renal replacement therapy (RRT), either by starting hemodialysis or peritoneal dialysis. Nonetheless, the role of kidney transplantation in patients with DEB is scarcely known[5].

We will present the case of a patient with recessive dystrophic epidermolysis bullosa (RDEB) with terminal CKD, who was treated with kidney transplantation, and the following after his transplant. We have obtained informed consent from the patient.

Clinical Case

Male patient, diagnosed during birth with RDEB. Throughout his life he had skin and mucous blistering which healed leaving unappealing scars. He developed esophageal stricture, linked to chronic caloric-protein malnutrition. When he was 9 years old, he was diagnosed with CKD of indefinite etiology causing him to start RRT at the age of 16. At the beginning, he had peritoneal dialysis during 3 years, followed by hemodialysis during 3 months. During that period, the patient had recurring urinary tract infections and bacterial peritonitis, both related to the peritoneal dialysis. At the age of 19, his health professional team made an interdisciplinary assessment with the patient and his family and decided to perform a kidney transplantation. That procedure took place on June, 2008. We choose a relative living donor, who had a HLA match of 2/1/1 respectively and a recipients cross match of 5%. The surgical procedure was performed without complications, the patient presented good progress during the immediate post-operative with the graft spontaneously working and not requiring RRT. The initial immunosuppressant scheme included azathioprine, cyclosporine and steroids, receiving as induction human gamma globulins. As antibiotic prophylaxis, we used trimethoprim-sulfamethoxazole during the first year and aciclovir as chronic treatment.

The patient continued to develop favorably in the months following the transplant (creatinine levels three months after the transplant: 0,85mg/dL and proteinuria/creatinine relation: 0,74). There were no significant changes in the shape and evolution of blistering scars if compared to the period prior to the transplant. 28 month after the transplant, the patient showed a progressive deterioration of the kidney function and increase of proteinuria (creatinine of 1,7mg/dL and proteinuria/creatinine relation of 1,90). We performed a kidney biopsy: anatomic pathology informed 2 degree chronic allograft nephropathy following Banff's classification, negative C4d. He continued with stable renal function, without requiring dialysis renal replacement therapy.

The first significant infection event was a minor cellulitis picture without systemic symptom, 40 months after the transplant. As a result, we changed the immunosuppressant scheme, replacing azathioprine with mycophenolate sodium and continuing with cyclosporine and corticosteroids. Among other significant events, we emphasize an aseptic meningitis event (51 months after the transplant), a community-acquired pneumonia and a localized skin infectious event (60 months after the transplant). We incidentally found an asymptomatic uncomplicated saccular-shaped aneurysm in carotid siphon (62 months after the transplant). The patient needed some esophageal dilations procedures as consequence of the base disease.

75 months after the transplant, the patient presented severe pneumonia associated to health care, requiring a hospitalization in the intensive care unit and treatment with broad-spectrum antibiotic and amphotericin B due to suspicion of fungal infection. In this context, the patient presented a significant

deterioration of renal function, requiring RRT with hemodialysis on a permanent basis. The patient evolved favorably after being provided the above mentioned antimicrobial treatment. After this event, the patient did not develop new complications or infections until the 83th month after the transplant. Throughout the entire following period, the patient was frequently controlled by the dermatology department and the nephrology department of our hospital. Furthermore, during the same period we did not find signs of injuries suspicious for malignancy.

Discussion

This case was very challenging because we were attempting to decrease the mortality and morbidity of CKD with RRT in a patient suffering RDEB. Kidney transplantation is a known strategy for such cases, but using immunosuppressors can be associated to multiple infectious and neoplastic adverse events. Patients with EB show a baseline of multifactorial immunosuppression caused by the existence of alterations in the skin-mucous barrier and by the decrease in the populations of helper CD4 and NK T lymphocytes, secondary to malnutrition[6]. Also, about 50-80% of patients with RDEB develop through their lives squamous-cell skin cancer (particularly after they are 20 years old)[3].

Developing CKD is one of the most frequent complications in patients with EB, being the cause of 12% of the death of such patients[7]. Patients with RDEB and terminal CKD are generally treated with hemodialysis or peritoneal dialysis like RRT, being hardly known the role of kidney transplantation in such patients[5]. Kidney transplantation, in general, is the best option for patients with terminal CKD; however, the prolonged use of immunosuppressors may be associated to an increase of infections and skin-mucous malignancies. We have observed in different reports that nearly 60 to 90% of the kidney transplantation patients show some type of skin injure associated to the immunosuppressive treatment[8]. The most commonly described injuries have an infectious cause (mostly during the first 60 months after the transplant), followed by adverse reactions to immunosuppressive drugs and lastly malignant and pre-malignant injuries (usually after the 60 months following the transplant). Verrucous viral infections and dermatofitosis are the most frequent causes of skin infections in this group of patients, while bacterial infections have low prevalence[9]. In this context, the usage of azathioprine may produce a decrease of Langerhans' cells in the epidermis, which may explain the higher rates of fungal infection[10].

A few studies have reported that the usage of immunosuppressive therapy in patients with kidney transplantation increases the happening of malignancies, mostly in the skin. Wimmer et al reported in a study done in Germany the cumulative incidence of non-melanocyte skin cancer in patients with kidney transplantation is nearly 20.5% [11], while Kasiske et al, in USA, have documented a cumulative incidence of 7% after 3 years of immunosuppression[12]. Regarding studies produced in Latin America, Dufrechou et al have reported in Uruguay that 60% of the patients with kidney transplantation presented at least 1 cutaneous manifestation, of which 14.4% were malignant and pre-malignant injuries[9]. Among the immunosuppressors, they observed that azathioprine is associated to the happening of multiple squamous-cell skin cancer. This is probably related to the immunosuppressive effect and the photo activation of its aromatic nucleus with ultraviolet lights[13].

There is scarce evidence on the application of immunosuppressive therapy in patients with epidermolysis bullosa. There is only one reported case of kidney transplantation in a patient with EB that describes a favorable evolution during the first 5 months after the transplant: he is a 33-year-old Chinese patient with junctional non-Herlitz EB[5]. Another type of transplants that have been reported in this type of patients are allogeneic skin transplant for reconstructive purposes[14], and allogeneic bone marrow transplant for the therapeutic purpose of achieving the production of collagen VII in the dense layer in order to improve the evolution of the disease[15].

Conclusions

This case is important to describe the long-term evolution of a patient with RDEB who has received kidney transplantation. After following of the case for 83 months post-transplant, we observed a low frequency of infectious events (of which all were mild, except for a severe pneumonia), and lack of cutaneous malignancies. However, 75 months after the transplant, the patient had to start RRT again because of deterioration of the implanted kidney function. This case could encourage future research so as to consider kidney transplantation as an alternative to lessen the comorbidities associated to RRT in patients with EB and terminal CKD.

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