

New Onset diabetes after kidney transplantation.

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ABSTRACT: *Introduction. The occurrence of the new-onset diabetes after kidney transplantation is common and represents a risk factor for decreased survival of the graft and the patient.*

Case presentations. We report 6 cases of diabetes appeared in post renal transplantation. Treatment after kidney transplantation was based on corticosteroids associated with immunosuppressive therapy in all cases. Diabetes appeared after renal transplantation in 30% of cases, it was discovered during a systematic examination. The treatment consisted of insulin therapy for 3 patients, oral anti-diabetic for a patient and 2 patients had normalized their blood glucose levels after discontinuation of corticosteroids and immunosuppressive therapy adjustment.

Conclusion. Immunosuppressive therapy associated with multiple risk factors presented by patients favor the occurrence of this diabetes.

KEYWORDS: *diabetes, renal transplantation, immunosuppressive therapy, corticosteroids.*

I. INTRODUCTION.

The occurrence of secondary diabetes is common after renal transplantation. This complication is due to immunosuppressive therapy and would be supported by multiple risk factors.

The aim of our study was to determine the incidence and to describe the clinical, biological and therapeutic characteristics of patients with diabetes appeared after kidney transplantation and to detail the pathophysiological mechanisms of its appearance.

II. CASE PRESENTATIONS :

It is a descriptive study of 6 patients with diabetes appeared after renal transplantation, collected from 20 renal transplant patients followed in nephrology department of the Hassan II University Hospital in Fez. It corresponds to a frequency of 30%.

The average age of our patients was 49 years. Our patients had received a kidney transplant from a living donor in all cases.

After kidney transplantation treatment was based on corticosteroids at a dose of 1mg/kg/day, in combination with immunosuppressive therapy in all cases.

Figure 1: Treatment given after kidney transplantation.

Fasting glucose levels before transplantation was normal for all patients. Diabetes appeared after renal transplantation, the time of its appearance was on average 5 months (between 1 and 9 months). Diabetes was found in our patients in a systematic examination.

Table 1: Characteristics of the population.

The treatment consisted of insulin therapy for 3 patients, oral anti-diabetics for a patient and 2 patients had normalized their blood glucose levels after discontinuation of corticosteroids and immunosuppressive therapy adjustment.

The average hemoglobin A1C of our diabetic patients under treatment was 7.5%.

III. DISCUSSION:

The fear after organ transplantation is the acute or chronic graft rejection. This complication is getting better controlled by improved immunosuppressive treatment. However, we should remain vigilant to the risk of complications of immunosuppressive therapy, notably the occurrence of a secondary diabetes which can quickly become life-threatening. Indeed, the immunosuppressive therapy associated with multiple risk factors presented by patients, favor the occurrence of this type of diabetes. [1]

The incidence of appearance of a diabetes after renal transplantation varies between 2% to 53% depending on the series; it occurs, usually within 6 months after transplantation, a period when immunosuppressive therapy are at high doses, which emphasizes the importance of diabetes screening measures before and after kidney transplantation, especially in patients at risk. [2,3,4]

The risk factors for the occurrence of a diabetes after kidney transplantation are : age greater than 45 years, high body mass index, African or Hispanic ethnicity, family history of type 2 diabetes, history of gestational diabetes, presence of metabolic syndrome, positive serology of hepatitis C, variant-T of the gene TCF7L2 (transcription factor 7-like 2) and finally hypomagnesemia. [1,5]

In 67% of cases our patients were older than 45 years at the discovery of diabetes, diabetic heredity was found in 50% of cases and 67% of our patients were overweight.

Immunosuppressive drugs, by inducing a defect in insulin secretion (toxicity to β Langerhans cells) and an insulin resistance, probably act as triggers for abnormalities of glucose metabolism in patients at risk. [2]

Several meta-analyzes have shown that the risk of diabetes was significantly higher for patients on tacrolimus versus cyclosporine and a complete remission or significant improvement of diabetes is seen after the passage from tacrolimus to cyclosporine in renal transplant patients.[1]

Tacrolimus has been prescribed for 4 of our patients, while one patient was put under rapamycin and one patient was put under cyclosporine. After installation of diabetes, tacrolimus was replaced by cyclosporine for two patients with good evolution of the glycemic control.

The latest recommendations for screening the diabetes after kidney transplantation are the dosage of fasting blood glucose at least weekly for 4 weeks and then every 3 months for one year and then annually. [1,3]

The criteria for diagnosis of diabetes after a renal transplantation are those issued by the *American Diabetes Association (ADA)* in 2003. The hemoglobin A1C test is not recommended for the diagnosis but must be used for monitoring diabetes. The goal of A1C is 7%. A1C should be interpreted with caution for patients with anemia. [3,6,7]

The choice of immunosuppressive treatment must first consider the immunologic risk of patients to prevent the acute rejection. The scheme of adjustment of immunosuppressive treatment proposed by the ADA in 2012, to reduce the risk of developing diabetes and to improve diabetes already installed, is: [1]

- For patients with a high immunological risk, treatment by tacrolimus is preferred.
- For patients who developed diabetes, a progressive reduction of immunosuppressive therapy should be done carefully and progressively.
- For tacrolimus-treated patients whose diabetes is difficult to control a passage to cyclosporine may be considered in cases of high immunologic risk, while the transition to belatacept could also be considered in cases of low immunological risk.

Data from various studies indicate that new-onset diabetes after kidney transplantation affects medium and long-term morbidity and mortality of transplant patients, by the risk of serious infections, especially in the first 6 months, and the risk of developing or worsening of cardiovascular pathologies. However, these data suggest that the risk is less if good glycemic control is maintained. [8,9,10]

Regarding the pharmacological treatment of hyperglycemia, it is considered that patients with an A1C assay higher than 6.5% should start a hypoglycemic treatment. As for type 2 diabetes, a progressive approach should be adopted. The first step includes lifestyle measures (weight reduction, balanced diet and exercise). The second step is the start of monotherapy. [1]

Almost all oral anti-diabetics can be used, with the exception of first generation sulphonylureas given the risk of hypoglycemia and biguanides given the risk of lactic acidosis. Biguanides should be avoided if the glomerular filtration rate is less than 60ml/min. The Gliquidone, is the most prescribed agent for renal transplant patients: it is efficient, well tolerated and did not interact with immunosuppressive therapy. The third step is a combination of oral agents with different mechanisms of action and the last step is the administration of insulin with or without oral agents. [1,11,12,13].

IV. CONCLUSION:

The application of a good monitoring helps to anticipate and optimize the management of renal transplant patients. Therapeutic adjustments of immunosuppressive therapy to reduce the risk of diabetes while avoiding the risk of rejection, are proposed.

Competing interests :

We declare that we have no competing interests.

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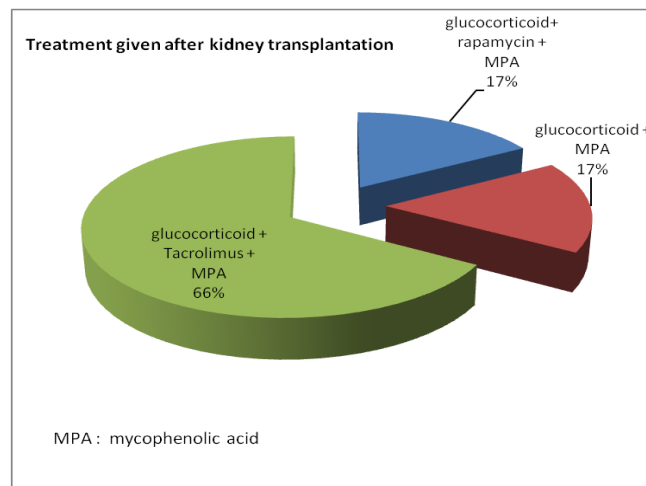


Figure 1: Treatment given after kidney transplantation.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	45 years	50 years	61 years	59 years	31 years	48 years
Sexe	Male	Male	Male	Male	Male	Male
Diabetic heredity	no	no	yes	no	yes	yes
BMI	25	27	24	23	26	26
fasting blood glucose	0,98	1,20	1,10	1,43	1,35	1,66
hemoglobin A1C	5,4%	7,5%	6%	7,1%	6,9%	8,5%

Table 1: Characteristics of the population.