

NEW-ONSET DIABETES AFTER RENAL TRANSPLANTATION (NODAT) AND NODULAR GLOMERULOSCLEROSIS OF THE RENAL ALLOGRAFT

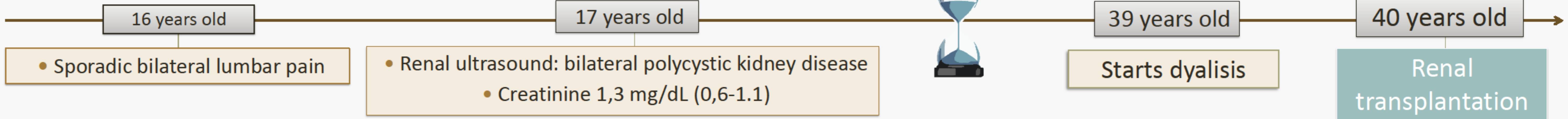
D Martins¹, C Baptista¹, M Bastos¹, J Pratas², R Alves², C Romãozinho², L Cardoso¹, C Marinho³, D Oliveira¹, N Vicente¹, D Guelho¹, C Moreno¹, J Saraiva¹, R Dantas⁴, M Balsa⁴, A Mota⁵, F Carrilho¹

¹Endocrinology, Diabetes and Metabolism Department of Coimbra Hospital and University Centre, Portugal
²Nephrology Department of Coimbra Hospital and University Centre, Portugal
³Pathological Anatomy Department of Coimbra Hospital and University Centre, Portugal
⁴Endocrinology, Diabetes and Nutrition Department of Baixo Vouga Hospital Centre, Portugal
⁵Urology and Renal Transplantation Department of Coimbra Hospital and University Centre, Portugal

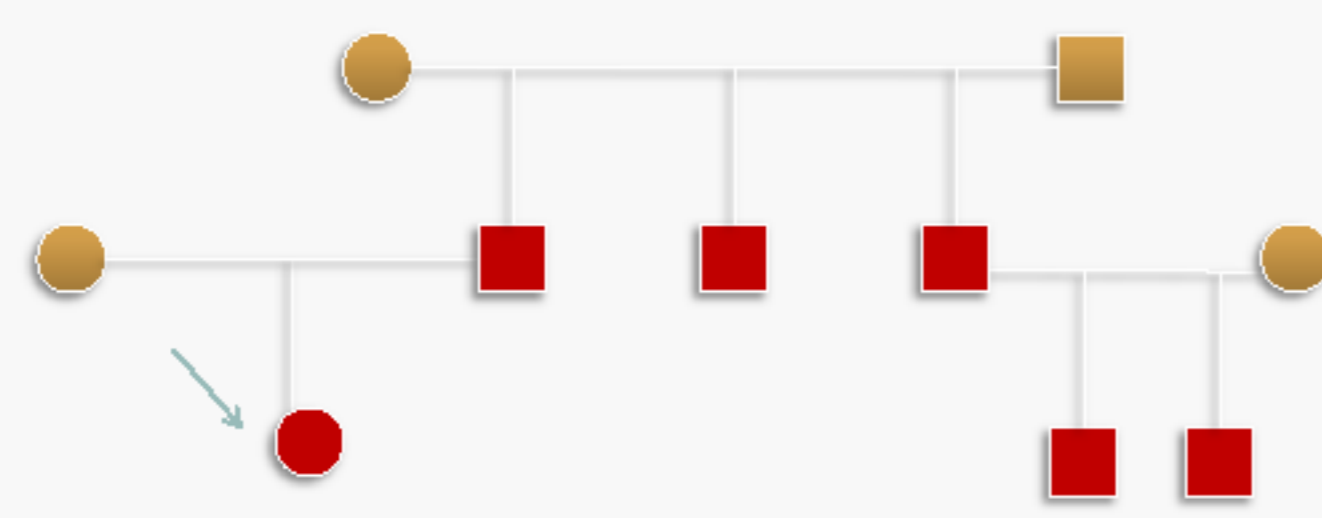
INTRODUCTION: Diabetes mellitus is a common metabolic complication after kidney transplantation, occurring with a frequency of 15-30% in the first year¹. However, despite the high incidence, there are described few cases of diabetic nephropathy with nodular glomerulosclerosis of the allograft.

CLINICAL REPORT:

- Female, 49 years old
- History of present illness:



PERSONAL HISTORY: Autosomal dominant polycystic kidney disease (ADPKD)



RENAL TRANSPLANTATION (CADAVER ALLOGRAFT, June 2004) → Rx Tacrolimus 5mg +4mg id; Sirolimus 3mg id; Prednisone 15mg id

EVOLUTION:

Analyte	Pre operative	Post operative	November 2004	Reference
Creatinine mg/dL	8,3	1,20	1,70	0,6-1,1
BUN mg/dL	80	25	37	7,94-20,9
Glucose mg/dL	123	102	901	60-109
Osmolality mOsm/kg	299	278	301	260-302
Na ⁺ mmol/L	137	137	124	136-146
K ⁺ mmol/L	5,1	3,6	4,6	3,5-5,1

Diabetes mellitus
Polydipsia, polyuria

ENDOCRINOLOGY, DIABETES AND METABOLISM DEPARTMENT

A1c: 6,8%
Diabetes-related autoantibodies:

	Result	RV
Islet Cell Cytoplasmic Autoantibodies	Neg	-
GAD65 (U/L)	0,00	<1,0
IA2A (U/L)	0,02	<1,0
Insulin U/mL	0,00	<0,4

Starts insulin therapy, with 3 administrations per day
0,8 units per Kg/dia

Good clinical evolution, reducing the doses of immunosuppressive agents and prednisone suspension
→ Tacrolimus 2mg id, Insulatard® 8 units id

EVOLUTION:

Analyte	June 2005	June 2006	October 2007	November 2009	June 2010	RV
Creatinine mg/dL	1,70	1,40	1,20	1,03	1,32	0,6-1,1
BUN mg/dL	27	29	26	22	33	7,94-20,9
Glucose mg/dL	106	112	184	128	110	60-109
A1C (%)	6,5	6,7	7,5	6,7	6,9	4,0-6,0
Serum Tacrolimus level ng/mL	8,2	5,6	3,8	4,5	4,5	-

Analyte	6/2011	7/2012	01/2013	11/2013	RV
Creatinine mg/dL	1,21	1,44	1,83	3,46	0,6-1,1
BUN mg/dL	34	33	49,7	67	7,94-20,9
Glucose mg/dL	103	113	89	304	60-109
A1C (%)	7,0	6,5	6,8	6,6	4,0-6,0
Osmolality mOsm/kg	284	286	290	304	260-302
Serum Tacrolimus level ng/mL	11,8	4,5	4,2	3,8	-

Progressive dysfunction of the allograft

Urology and Renal Transplantation Department

UROLOGY AND RENAL TRANSPLANTATION DEPARTMENT

Clinical presentation: nausea and vomiting

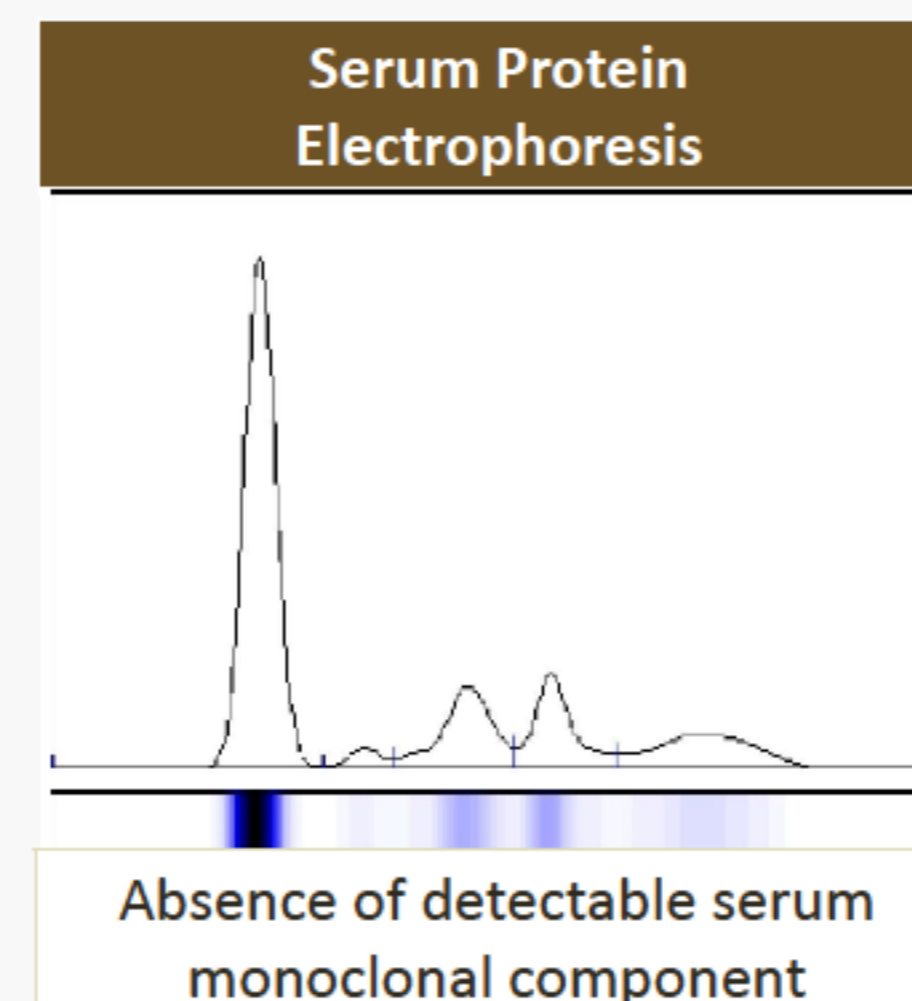
Physical examination: Apyretic, hemodynamically stable, with no other alterations

Analyte (Urine)	Result	RV
Creatinine mg/dL	34,9	-
Proteins mg/dL	185	0,0-20,0
Proteins/Creatinine mg/g	5301	<200

Rx -Mycphenolate mofetil 360 mg id
-Prednisone 5mg id
-Tacrolimus 2mg id
-Insulatard® 8 units 2id

Urinalysis	Result	RV
pH	6,0	5,0-8,0
Density	1,008	1,010-1,030
Glucose mg/dL	50,0	0,0-30,0
Proteins mg/dL	100,0	0,0-0,2
Nitrits	Neg	-
Leucocytes cel/μl	25,0	1,0-36,0
WBC /μl	0,5	0,0-0,9
RBC /μl	10,1	1,0-43,0

Serological tests	Result	RV
CMV-IgG	>250,0	POS
CMV-IgM	0,22	NEG
EBV-IgG	470,0	POS
EBV-IgM	< 10,0	NEG
EBV-EBNA	34,7	POS
Parvovirus B19	NEG	-



	Result	RV
IgG g/L	9,17	7,0-16,0
IgA	1,85	0,70-4,0
IgM	1,18	0,40-2,30
Kapa	7,36	6,66-14,65
Lambda	4,23	2,99-6,99
K/L	1,74	1,35-2,65

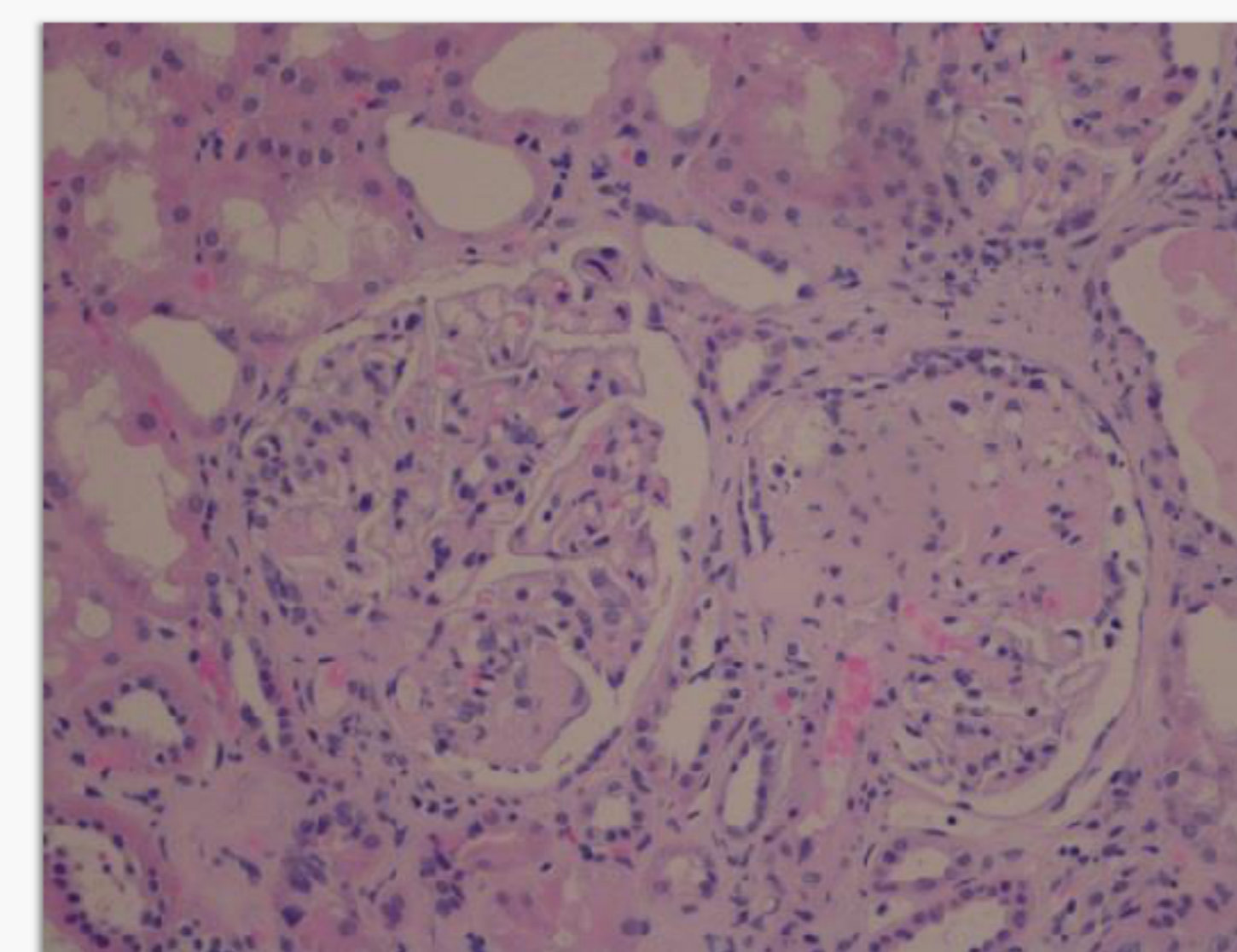
High digestive endoscopy

Unchanged esophagus, stomach and duodenum

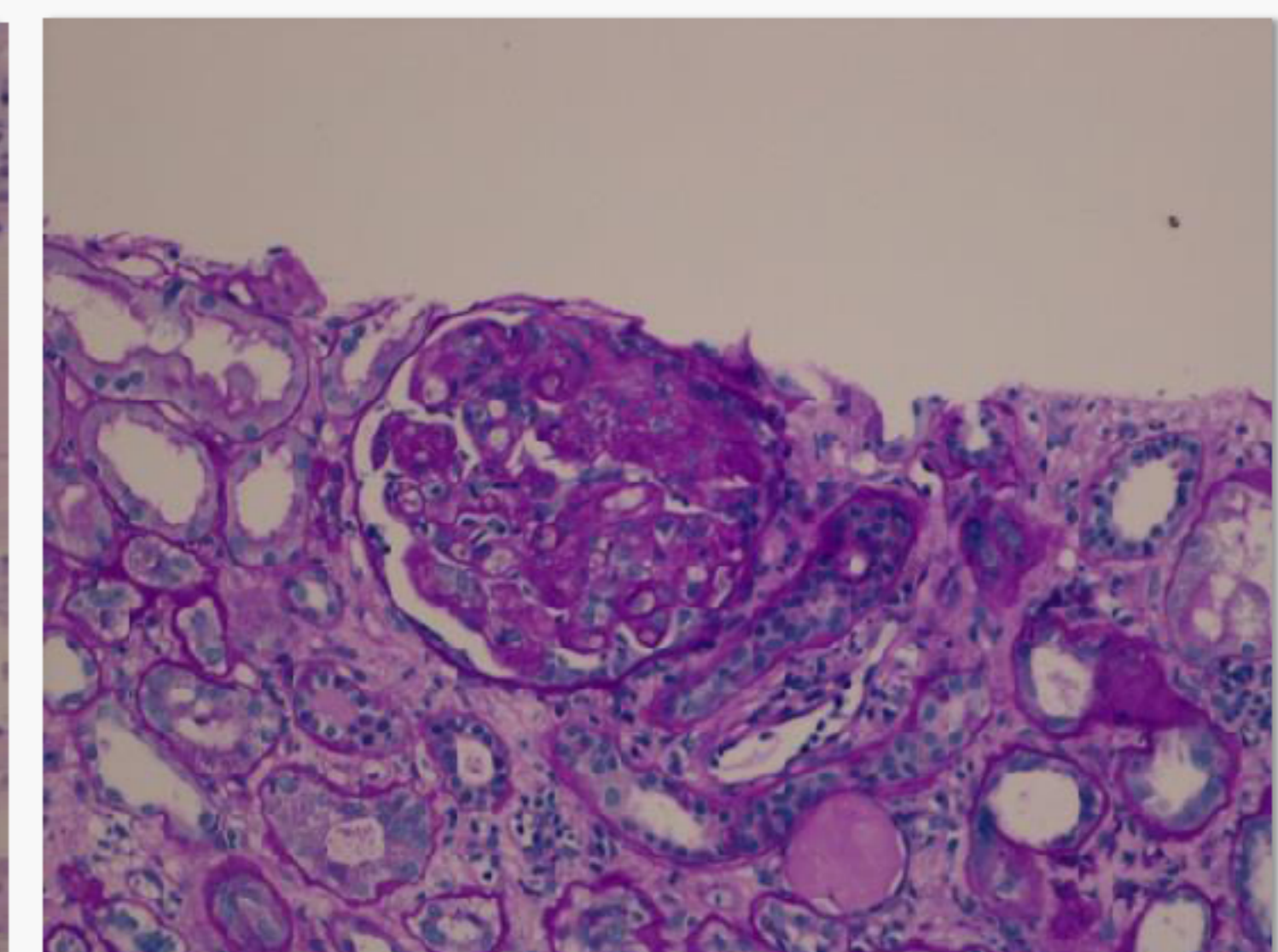
Complement system		
C3	0,78	0,90-1,80
C4	0,29	0,10-0,40

Biopsy of renal allograft –Pathologic examination

Renal biopsy predominantly with nodular glomerulosclerosis in diabetes mellitus context clinically known. There are no signs of acute rejection, observing mild chronic rejection phenomena with mild fibrosis and tubular atrophy (Ci1; Ct1). Absence of Polyoma virus infection.



Glomerulus with global and segmental glomerulosclerosis, HE (400x)



Highlighted areas with glomerulosclerosis, PAS (200x)

CONCLUSIONS: In the case described there was a progressive graft dysfunction despite good glycemic control, with lesions of nodular glomerulosclerosis compatible with diabetes mellitus identified. Thus, in the NODAT with chronic renal allograft dysfunction, it's not to exclude the possibility of association with diabetic nephropathy. This case also shows that in NODAT there are the same risk factors for the occurrence of late complications of diabetes.

Bibliography: ¹Chakkeria H. et al. Can new-onset diabetes after kidney transplant be prevented? Diabetes Care, Volume 36, May 2013; 1406-1412; Ghisdal L. et al. New-onset Diabetes after renal transplantation. Diabetes Care, Volume 35, January 2012; 181-188; Pham P-T. et al. New onset diabetes after transplantation (NODAT): an overview. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2011; 4 175-186; Owda K. Ali et al. De novo diabetes mellitus in kidney allografts: nodular sclerosis and diffuse glomerulosclerosis leading to graft failure. Nephrol Dial Transplant 1999; 14: 2004-2007

