RITUXIMAB AND mTOR INHIBITORS IN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER. IS PROGNOSIS CHANGING?

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AIMS:

Post-transplant lymphoproliferative disorder (PTLD) is the cancer with the highest frequency, excluding skin cancers, in kidney transplant recipients. In previously reported series[1], incidence of PTLD is higher in the first year post transplantation, it is related to donor and recipient EBV serological status and to the degree of immunosuppression and it is associated with high mortality rates. Five-year cumulative incidence is 1%-3% and most of PTLD are related with EBV.

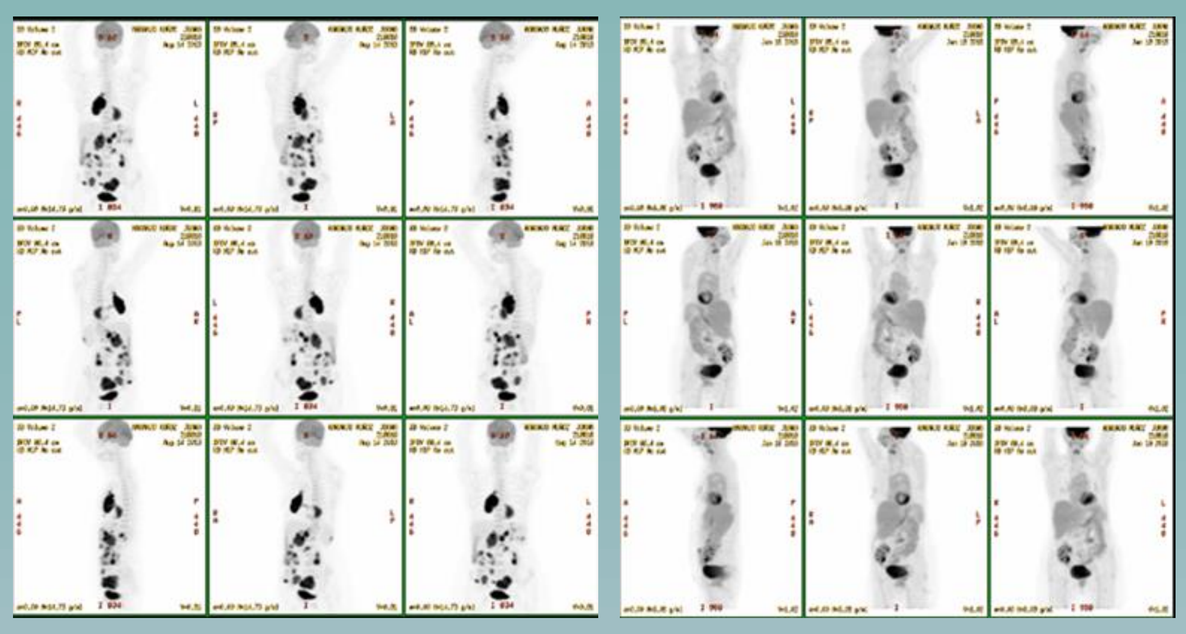
METHODS:

We review retrospectively PTLD patients diagnosed from 2005 to January 2017 in Hospital 12 de octubre Madrid (Spain) and Hospital General Ciudad Real (Spain), respectively, 417 and 1776 kidney transplant recipients. Histological variant, EBV status in lymphoma, immunosuppresion before(ISb) and after (ISa) PTLD diagnosis(D), specific lymphoma treatment (Tr) and graft and overall survival were analyzed.

RESULTS:

Patients (case,gender,age(yr))	Time IS (months)	Histology	EBV	Treatment	IS b	IS a	AR	Outcome PTLD	Renal survival	End follow up
1. M, 63	92,81	Burkitt		Burkimab	CSA-MMF-Pd	EVE-Pd	+	CR	+	+
2. M, 38	139,99	Burkitt	-	R-Rt	ATG-AZA-Pd	AZA-Pd→SRL	+	CR	+	+
3. F, 49	157,04	Polymorphous	-	mTOR conversion	FK-MMF-Pd	EVE	-	CR	+	+
4. F, 66	99,45	DLBCL	+	R-CHOP	SIMULECT-FK-MMF-Pd	EVE-Pd	-	CR	+	+
5. F, 61	76,02	DLBCL	-	R-CHOP	FK-MMF-Pd	SRL	-	CR	+	+
6. M, 56	35,58	Plasmoblastic	+	mTOR conversion	FK-MMF-Pd	EVE-MMF	-	CR	+	-
7. M, 41	51,02	Burkitt	-	Burkimab	TG-FK-MMF-Pd	FK	-	CR	+	+
8. M, 68	220,55	DLBCL	-	R-CHOP	ATG-CSA-MMF-Pd	CSA-EVE	-	In treatment	+	+
9. M, 68	20,86	Burkitt	+	Burkimab	SIMULECT-FK-MMF-Pd	FK-Pd	+	In treatment	+	-
10. F, 68	245,55	DLBCL		R-CHOP	CSA-Pd	CSA-Pd	-	In treatment	+	+
11. M, 61	134,01	Burkitt	+	Burkimab	FK-MMF-Pd	EVE	-	Refractary	+	-
12. F, 53	145,22	DLBCL	+	MTX-R ESHAP	TG-FK-MMF-Pd	SRL	-	In treatment	+	+
13. M, 58	258,69	Polymorphous	+	RX8	CSA-Pd	SRL	-	CR	-	+
14. F, 73	213,91	DLBCL		R-CHOP	ATG-CSA-AZA-Pd	CSA-MMF-Pd	-	CR	+	+
15. M, 54	231,56	DLBCL	+	R-CHOP	CSA-AZA-Pd	SRL	+	CR	+	+
16. M, 19	47,11	Plymorphous	-	RX4	FK-MMF-Pd	SRL	-	CR	+	+
17. F, 63	79,74	Polymorphous		RX8	FK-MMF-Pd→EVE-MMF	EVE	-	CR	-	+
18. F, 58	80,72	DLBCL	+	R-CHOP	TG-FK-MMF-Pd	SRL	-	CR	+	+
19. M, 24	113,91	Polymorphous	-	RX8	ATG-CSA-AZA-Pd	EVE-MMF-Pd	-	DLBCL transformation	+	-
20. M, 82	173,4	DLBCL	+	R-CHOP+Rt+Surgery	CSA-MMF-Pd→EVE-MMF	EVE-MMF	-	CR	+	+
21. M. 52	69,45	Burkitt	+	R-HyperCVAD-ARAC-MTX	BASILIXIMAB-FK-MMF-Pd	EVE	+	CR	+	-

21 patient (8women;13men),median age 55,9 SD:15,3 (R:19-82)were diagnosed of PTLD. Incidence rate 9,6 cases/10^4 kidney transplant/year. Median time IS is 127,9 months SD:72,9 (R:20,8-237).
DLBCL 9 patients(7/9 primary extranodal localization), DLBCL and polymorphous in 1 patient, polymorphous lymphoma 4 patients, Burkitt lymphoma 6 patients and plasmoblastic lymphoma, 1 patient.
A median follow up of 49,9 months SD:48,1 (R:4,2-148,1): 16/21 patients are alive and in complete response(CR).
1-year overall survival is 83% and 3-year survival is 60%.
5 patients died. Causes of death: DLBCL refractory progression in 1 patient and sepsis-infection in 4 patients.
Renal function median: Cr 1,4 SD:0,67(R:0,5-2,3), median proteinuria: 0,4g SD:0,4 (R:0,07-1,7).
5 year graft survival: 85%. A patient received a second kidney transplantation and another patient is in haemodyalisis.



DLBCL at diagnosis and after treatment (complete response)

CONCLUSIONS:

In these cohorts PTLD has a very low incidence , a late onset and a better outcome in comparison with previously reported series.

In our experience , Rituximab is an effective therapy in PTLD treatment.

MTOR inhibitors are safe to remove calcineurin inhibitors and avoid graft rejection.

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