Post-Transplant Lymphoproliferative Disorders following Alemtuzumab Induction in Kidney Transplantation

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Introduction

Post-transplant lymphoproliferative disorders [PTLD] is a well-recognised serious complication of renal transplantation and includes a spectrum from benign proliferations to malignant lymphomas. Cumulative incidence of PTLD ranges between 0.5% and 3%[1,2,3].

Alemtuzumab is used as an induction therapy in our Trust. It is associated with profound and prolonged lymphocyte depletion. We had concerns that there may be a higher incidence of PTLD and infection. In this study we report the incidence, associated risk factors, nature and outcome of PTLD post Alemtuzumab induction in our patients.

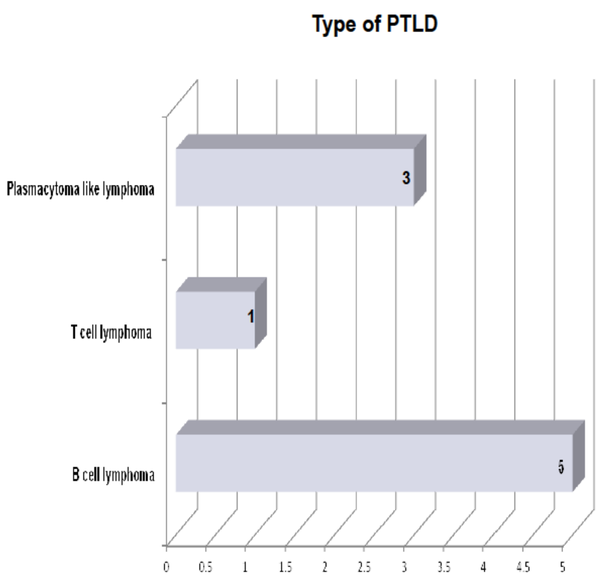
Methods

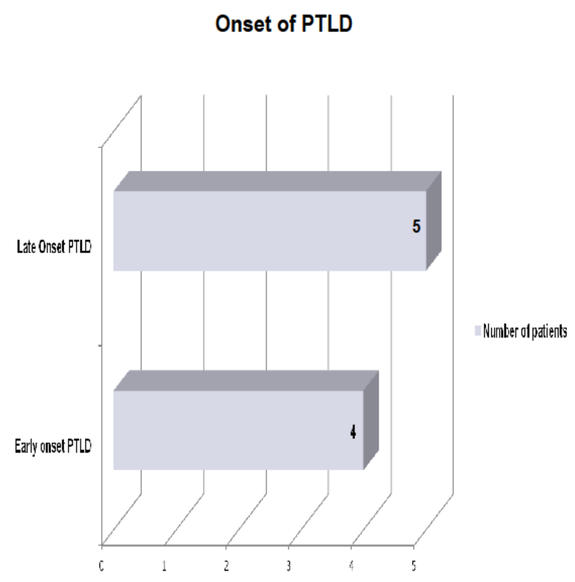
We retrospectively reviewed the medical records of all renal transplant recipients in our centre between November 2005 and January 2014 for the occurrence of histologically proven PTLD. Follow up was until January 2015. ABOi and HLAi transplants were excluded. All patients received a steroid sparing immunosuppressive regimen with Alemtuzumab and Tacrolimus [Tac] monotherapy. Steroids and Mycophenolate Mofetil [MMF] were only introduced to treat rejection. Kaplan-Meier survival analysis was performed using MedCal.

Results

Patient demographics

		All Patients N = 999	Patients with PTLD N=9
Gender	Male Female	641 358	9 0
Mean age at transplant [yrs]	Years	48.8 ±13.1	43.5 ±6.0
Ethnicity	Caucasian Asian Afro-carribean Other	486 298 110 105	3 4 1 1
RRT pre-transplantation	Pre-emptive HD PD	235 700 64	2 7 0
Graft type	Living donor kidney Deceased donor kidney	430 569	4 5
Mean follow up [yrs]		4.4±2.3	6.3 ±2.1





3/9 patients were bcl-6 positive, 7/9 were CD-20 positive, 5/9 had EBV positive serology pre transplant and 3/9 developed EBV viraemia post transplant. 3/9 patients received tacrolimus, MMF and steroids prior to the diagnosis of PTLD for treatment of rejection.

Treatment

Surgery/ chemotherapy:

Chemotherapeutic agent:

Surgical procedure	Number of patients	Type of PTLD
Hemicolectomy	1	Colonic MALT
Hemicolectomy and rituximab	1	Diffuse large B-cell lymphoma presenting with bowel obstruction

Chemotherapeutic Agent	Number of patients	Type of PTLD
Rituximab	3	Monomorphic B cell with EBV positivity GI isolated polymorphic B cell lymphoma with EBV positivity Marginal zone lymphoma [B cell]
Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone [RCHOP]	2	Diffuse large B-cell lymphoma Plasmacytoma with EBV positivity
Velcade, cyclophosphamide and dexamethasone [VCD]	1	Plasmacytoma
Etoposide, methylprednisolone, cytarabine and cisplatin [ESHAP]	1	T cell analplastic Non-Hodgkin's lymphoma
Methotrexate and gemcitibine	1	Relapse of T cell anaplastic Non-Hodgkin's lymphoma

One patient with a T-cell anaplastic lymphoma had an autologous stem cell transplant. Tac dosage was reduced to run levels 3-5 ug/l and MMF was stopped if patients were on it.

Outcomes

Kaplan-Meier survival:

	No PTLD	PTLD
Patient survival [%]		
1 year	97.8	100
5 years	89.9	100
End of study	85.4	83.3
Graft survival [%]		
1 year	95.6	100
5 years	86.6	100
End of study	80.7	100

Patient and graft survival [censored for patient death with functioning graft] at 5 years were 89.9% and 86.6% respectively. 1 patient died and there were no graft failures in recipients with PTLD.

None of the patients developed rejection post the diagnosis. 2 patients experienced relapse of PTLD. Complications post chemotherapy included sepsis (eg fungal infection), neutropenic sepsis, anaemia requiring blood transfusions and gastrointestinal bleeding.

Conclusion

- The cumulative incidence of PTLD in over 1000 patients receiving our Alemtuzmab induction and a steroid sparing regime was 0.90%.
- The majority of the cases were B cell and not virally driven. 3/9 patients received treatment for rejection prior to diagnosis of PTLD.
- Patient outcomes were comparable. Only one patient has died.
- 6 out of 9 patients are in remission. Relapse was associated with aggressive B cell lymphoma and anaplastic T cell lymphoma.

This study showed that Alemtuzumab is not associated with an increased rate of PTLD and outcome after appropriate treatment is favourable.

References

[1]Caillard et al AJT 2006;6(11):2735-42]
[2] Govantes et al Transplant Proc. 2013;45(10):3592-4
[3] Kirk et al. AJT 2007; 7(11):2619-2625

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