P1321
Poster Session V
Infections in transplant recipients

IS MILTEFOSINE AN OPTION AS SECOND-LINE TREATMENT FOR RELAPSING VISCERAL LEISHMANIASIS IN SOLID ORGAN TRANSPLANT RECIPIENTS? A CASE SERIES REPORT

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OBJECTIVES:
Since 2009 there is an ongoing outbreak of Leishmaniasis in Madrid with an overwhelming impact in the solid organ transplant recipient (SOT-r) population. Liposomal amphotericin B is the present first-line treatment for visceral leishmaniasis (VL), however the high relapse rate among immunocompromised patients remains a problem. Miltefosine has shown good efficacy in treating VL in India, but there is no data in SOT-r. Our aim is to describe the outcome of SOT-r with relapsing VL treated with miltefosine. To our knowledge, this is the largest series of VL in SOT-r treated with miltefosine.

METHODS:
We carried out a retrospective review of all SOT-r with relapsing VL treated with miltefosine. We describe the main characteristics of the patients, the clinical presentation, the diagnostic tests done and the outcome after the different treatments.

RESULTS:
Six SOT-r (5 kidney and 1 lung) developed VL a median of 14 months (Q1-Q3 range: 8-28.5) after transplantation. They all received standard immunosuppression.VL was diagnosed after visualization of *Leishmania* amastigotes in bone marrow biopsy. Liposomal amphotericin B (L-AB) was used as first-line treatment together with a reduction of immunosuppression.
Two out of six patients did not respond at all to L-AB, and the remaining four relapsed after L-AB treatment. The median time for the first recurrence after treatment was 51.5 days (Q1-Q3 range: 9-525). A second cycle of L-AB was administered in three cases and all of them had a second relapse. Miltefosin was used as a second-line drug in 3 cases, and as a third-line treatment in the remaining 3 that did not respond to L-AB. Four of the six cases treated with miltefosine relapsed, with a median time to recurrence of 53 days (Q1-3 range: 23-122). A resistance test was performed in one of the isolates and did not show resistance to miltefosine. In one of the patients with no recurrence, immunosuppression was stopped due to graft loss, the other one relapsed after L-AB treatment with mucosal involvement and after miltefosine treatment a healing of the lesions is currently observed. All cases had an initial good response with clinical and hematological improvement but the final patient outcome was unfavourable: one patient died due to hemophagocytic syndrome; two had graft loss and two had renal function impairment.

CONCLUSION:
SOT-r with relapsing VL showed an immediate improvement but not a sustained response when treated with miltefosine. Miltefosine resistance does not seem to be the cause of clinical failure in these patients. Future studies might explore the utility of combined treatments including miltefosine and L-AB.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Transplanted Organ	Kidney	Kidney	Kidney	Kidney	Lung	Kidney
Treatment 1 (T1)*1	L-AB*2	L-AB	L-AB	L-AB	L-AB	L-AB
Time to recurrence (TR) after T1 (days)	47	466	698	64	0	0
Treatment 2 (T2)	MILT*3	L-AB	L-AB	MILT	L-AB	MILT
TR after T2 (days)	77	13	130	46	0	
Treatment 3 (T3)	L-AB+PROF*4 L-AB	MILT	MILT+PROF L-AB	L-AB+PROF L-AB	MILT	
TR after T3 (days)				0	168	
Treatment 4 (T4)				GLUCAN*5+PROF L-AB	MILT	
TR after T4 (days)					20	
Treatment 5 (T5)					MILT+L-AB	
TR after T5 (days)					0	
Impaired renal function	*			*		
Graft loss		*				*
Outcome (O)	Disease free	Hemodyalisis	Mucosal disease improving	Disease free	Death	Hemodyalisis
Time from O to last visit (days)	56	5	11	22		15

*1 Treatment after first episode of Visceral Leishmaniasis

*2 Liposomal Amphotericin B

*3 Miltefosine

*4 Glucantime

*5 Prophylaxis