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 who 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 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). 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. These cases had an initial good response with clinical and haemotological improvement but the final patient outcome was unfavourable: one patient died due to haemophagocitic syndrome; two had graft loss and two have resulted in renal impairment.

Table 1. Treatment and outcome of visceral leishmaniasis relapses.

	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

CONCLUSION:

SOT-r with relapsing VL showed an immediate improvement but not a sustained response when treated with miltefosine. Future studies might explore the utility of combined treatments including miltefosine and L-AB. A resistance test was performed in one of the parasite isolates which did not show resistance to miltefosine.