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CASE REPORT

IMMUNOLOGICAL OBSERVATION OF TH17 CELLS IN LUCIO'S PHENOMENON

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ABSTRACT

Lucio's phenomenon is a type of leprosy reaction found in Mexico and Caribbean countries. But uncommonly seen in India and seems to be an emergency for patients. Leprosy reactions are commonly classified as T1R (Type 1 Reaction) and T2R (Type 2 Reaction). T1R is characterized by the alternation in the T cells function and T2R is considered an acute event mediated by immune complex deposition. Th1 andTh17 cells shown protective role in localized leprosy and associated with immunopatology in reactions patients. Other hand FOXP3+ Treg cells associated with gernaliezed lepromatous leprosy and showed progression of leprosy. [1]. The aim of our study was to analyze their role in a patient who had suffered lucio phenomenon. Flowcytometry were used to cell phenotypes and the percentage of cytokines in 48 hours MLSA *(M. leprae sonicated antigen)* stimulated PBMC cultures in patients with lepromatous disease and lucio' phenomenon. Th17 cells showed increase Th17 in lucio's phenomenon. Although Th1 and Treg cells have not show any difference.

INTRODUCTION

Lucio's phenomenon is an emergency seen in Lucio's Leprosy patients. It mainly occurs in Mexico and Caribbean countries[2]. The condition has been classified by Rafael Lucio Najera and Alvarado as necrotizing skin reaction associated with non-nodular diffuse leprosy[2, 3]. Although its histopathological features are well known, the immunological aspects, in particular the T-cell pathology in the peripheral circulatory system, are not clearly defined[4]. T cell functions have been shown to be disturbed in lepromatous leprosy (LL) patients and measurable T cell anergy was noted during active form of their disease. Since leprosy lesions reflect inflammation in the skin, Th17 cells may be implicated specially in reactions.

MATERIALS AND METHODOLOGY

5 ml of blood was collected from four patients (one Lucio and 3 LL patients) and peripheral blood mononuclear cells (PBMCs) were isolated. The cells were cultured and stimulated with *M. leprae* (ML) antigens. After 48 hours, the cells were harvested and stained with anti-human CD4 (FITC), IFN-γ (PE-cy7), IL-17(Percp-cy5.5) and FOXP3 (APC). In brief, after surfer staining, cells were permeabilized with perm/fix buffer. Finally stained cells were acquired. Analysis was done using FACS aria (BD, biosciences) DIVA software.

RESULTS

The clinical features and histopathlology of the patient, a man in his thirties, have already been described in a recent communication to this journal[5]. He presented with purpuric and necrotic lesions over extremities and face. Histopathological findings confirmed the diagnosis as Lucio's phenomenon.

Of interest, we examined the immunopathology of these patients, as it has been previously reported that Th1 and Th17 cells play a protective role in leprosy[6], while $FOXP3^+$ cells are associated with the pathogenesis in leprosy patients [7]. We have explored Th1, Th17 and FOXP3+ cells in 48h ML stimulated PBMCs by multicolour flowcytometry (Figure 1). We found that there was statistically no significant difference in the numbers of Th1 (Lucio's; 10.3%, LL; 10.1%) and FOXP3+ (Lucio; 11.4 %, LL; 10.6 %) cells in our patient as compared to the 3 LL patients (Table 1). Therefore Th1 and FOXP3+ T cells did not show any difference in Lucio's phenomenon as compared to lepromatous leprosy. But unstimulated IL-17 producing Th17 cells showed a 6-fold increase and ML stimulated Th17 cells showed a 6.5 fold increase in Lucio patient as compared to LL patients (Figure 1 and Table 1).

Figure1 showed immuno-phenotyping of Th1, Th17 and FOXP3+ T cells. Cells were cultured and stimulated with *M. leprae* antigens. After 48 hours cells were harvested and stained with anti-human CD4 (FITC), IFN-γ (PE-cy7), IL-17(Percp-cy5.5) and FOXP3 (APC). In brief after surfer staining cells were permeabilized with perm/fix buffer. Finally stained cells were acquired and analysis with FACS aria (BD, biosciences).

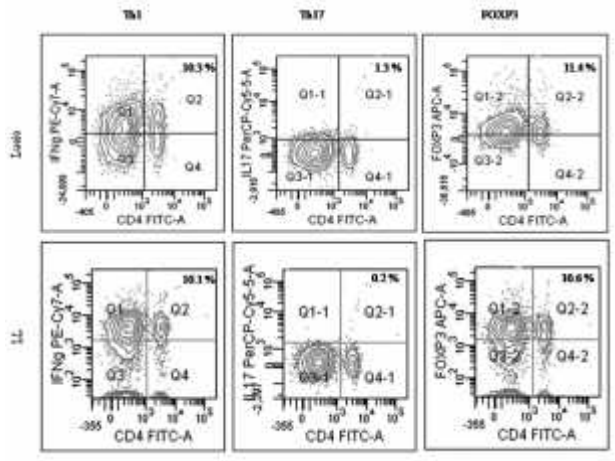

Figure 1

Table 1 Showed % of deferent T helper cells of patients.

	Un stimulated %		***M. Leprae antigen* (ML) %**	
	Lucio	LL	Lucio	LL
T helper 1	8.7	7.9	10.3	10.1
T helper 17	1.2	0.2	1.3	0.2
FOXP3+ cells	9.6	8.0	11.4	10.6

DISCUSSION

Immunopathology of leprosy is a well-known spectrum in which progression of the disease ranges from tuberculoid to lepromatous pole. Tuberculoid (paucibacillary; PB) patients show a leading Th1 response which clears *M. leprae*. Whereas, lepromatous patients demonstrate higher antibody titer resulting chronic gernaliezed clinical multibacillary (MB) leprosy. Lucio's leprosy which shows this phenomenon is a diffuse form of MB leprosy with high bacterial load. FOXP3+ Treg cells showed a high percentage in Lucio's phenomenon like the 3 LL patients (Table 1). However, FOXP3+ T cells also help to survival of the *mycobacterium* in infectious diseases like leprosy and TB. Despite high humoral responses against *M. leprae*, LL patients have the distinguishing inability to produced T helper 1 (Th1) cells against the *M. leprae*. Our earlier report on Th17 cells showed that non polarized T helper subsets produced IL-17A and were protective[6].

Lucio's patient showed high fold increase as compared LL patients. Since leprosy lesions reflect inflammation in the skin, Th17 cells may be implicated specially in reactions.

CONCLUSION

It is evident that T cell biology involves a balance of Th1, Th17 and Treg cells and is a double edged sword which may lead to protection against the *M. leprae* and/or result in tissue damage caused by Th17. In conclusion Th17 cells may play a key role in the immunopathology of Lucio's phenomenon.

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