Indian J Med Res 142, December 2015, pp 644-645
DOI:10.4103/0971-5916.174540

Commentary

A new era of diagnostic modalities for type 1 leprosy reactions: Promise for the future

Type 1 reactions (T1R) are known to occur in upto 30 per cent of patients in the borderline spectrum of leprosy[1]. It indicates an unstable immunity in a patient. The reactions can be either upgrading, towards the tuberculoid pole or downgrading, towards the lepromatous pole. These may be purely cutaneous, neural or a combination of both[2].

In early stages the diagnosis may be missed and hence, initiation of treatment delayed. This may have detrimental effects including permanent neurological sequlae. Though a thorough clinico-histological evaluation still remains the gold standard for diagnosis, various diagnostic assays are being used in research. These include cytokine mRNA levels, *e.g*. interferon-γ (IFN-γ), interleukin (IL)-1β, IL-2, IL-12, tumour necrosis factor α (TNFα) and enzyme-inducible nitric oxide synthase (iNOS)[3]. Previous studies indicate that potential biomarkers of T1R include CXCL10 and IL6 whereas IL7, platelet derived growth factor-BB (PDGF-BB) and IL6, may be markers of type 2 reaction (TR2)[4].

Cytokine assays have been the focus of research in the recent past. The gene expression of CXCL10 and its receptor, CXCR3 has been the focus of several recent studies. CXCL10 is a chemokine induced primarily by IFN-γ, produced by macrophages, T cells, and keratinocytes. It causes recruitment of CXCR3+ cells into the tissue. CXCR3+ cells also release Th1 cytokines leading to further upregulation of CXCR3 ligands leading to T1R response and granuloma formation[5]. The expression of these cytokines is higher in type 1 reaction, in comparison to non-reactional skin biopsies throughout the whole spectrum of leprosy. However, serological assays at baseline and immediately before T1R have not been predictive[4].

It has been seen that patients with high cytokine levels have a poor recovery from nerve function impairment during an acute episode of TIR[6]. They also have a high risk of reactivation of symptoms during treatment, and a high risk of recurrence of T1R within two months of completing the steroid regimen. Manandhar *et al*[7] found that the levels of IFN-γ and TNF-α fell during treatment with steroids. However, the levels of TNFα increased as the steroid dose was reduced. The levels of IL-10 increased throughout the duration of treatment for T1R[7]. It would be worthwhile to study the utility of aforementioned markers to objectively document response to treatment.

Though the study by Sharma and colleagues in this issue[8] supports these observations, unfortunately, no assay has yet been described which can predict accurately the development of T1R. TNFα and CXCR3 have shown some promise and should be researched more extensively. It would also be worth studying the utility of newer markers to further subclassify the reaction into ‘ upgrading ‘ and ‘downgrading’ reactions and to predict neural involvement and severity. This might give us better insight into the pathomechanisms of reactions in leprosy.

The use of cytokine assays is currently restricted to research, and as of today, we are relying on a thorough clinical assessment and histology if available, is still the most cost-effective, rapid and reliable way to diagnose T1R.

Mary Thomas
Department of Dermatology
Poornima Hospital, Bangaluru 560 032
Karnataka, India
mary_thomas121@yahoo.com

References

1. Walker SL, Lockwood DN. Leprosy type 1 (reversal) reactions and their management. *Lepr Rev* 2008; *79* : 372-86.
2. Sehgal VN, Bhattacharya SN, Jain S. Relapse or late reversal reaction? *Int J Lepr Other Mycobact Dis* 1990; *58* : 118-21.
3. Madan NK, Agarwal K, Chander R. Serum cytokine profile in leprosy and its correlation with clinico-histopathological profile. *Lepr Rev* 2011; *l82* : 371-82.
4. Stefani MM, Gverra JG, Sousa AL, Costa MB, Oliveira ML, Martelli CT, *et al*. Potential plasma markers of type 1 and type 2 leprosy reactions: a preliminary report. *BMC Infect Dis* 2009; *9* : 75.
5. Pandhi D, Chhabra N. New insights in the pathogenesis of type 1 and type 2 lepra reaction. *Indian J Dermatol Venereol Leprol* 2013; *79* : 739-49.
6. Lockwood DN, Suneetha L, Sagilli KD, Chaduvula MV, Mohammed I, van Brakel W, *et al*. Cytokine and protein markers of leprosy reactions in skin and nerves: baseline results for the North Indian INFIR cohort. *PLoS Negl Trop Dis* 2011; *5* : e1327.
7. Manandhar R, Shreshta N, Butlin CR, Rosche PW. High levels of inflammatory cytokines are associated with poor clinical response to steroid treatment and recurrent episodes of type 1 reactions in leprosy. *Clin Exp Immunol* 2002; *128* : 333-8.
8. Sharma I, Singh A, Mishra AK, Singh LC, Ramesh V, Saxena S. Is CXCL10/CXCR3 axis overexpression a better indicator of leprosy type 1 reaction than inducible nitric oxide synthase? *Indian J Med Res* 2015; *142* : 681-9.