Pediatric Rheumatology

Poster presentation

Different pattern of synthesis and secretion of IL-1beta in patients with CIAS-1 and TNFRSF1A mutations responding to IL-1 blockade

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from 15th Paediatric Rheumatology European Society (PreS) Congress
London, UK. 14–17 September 2008

Published: 15 September 2008

Pediatric Rheumatology 2008, **6**(Suppl 1):P212 doi:10.1186/1546-0096-6-S1-P212

This abstract is available from: http://www.ped-rheum.com/content/6/S1/P212

Aim

To compare the *in vitro* secretion of IL-1β in patients carrying *CIAS-1* mutations and TRAPS patients, in an effort to understand the mechanism modulating IL-1β secretion in the different pathologies responding to anti IL-1 treatment.

Methods

Monocytes from 6 CINCA and 4 TRAPS patients selected for treatment with Anakinra were activated with 1 μg/ml of LPS for 3 hours, at baseline and after 7 days from the beginning of the treatment. For comparison, monocytes from 24 healthy donors were also studied. Intracellular pro-IL-1β and secreted IL-1β were analysed by Western blotting and ELISA before and after a short exposure (15 min) to exogenous ATP that accelerates IL-1β secretion.

Results

In healthy subjects LPS-induced IL-1β secretion was variable but consistently ≤5 ng/ml and it was markedly increased by exposure to exogenous ATP (up to 20 ng/ml). Monocytes from CINCA patients secreted abnormally elevated amounts of IL-1β after LPS stimulation (up to 40 ng/ml) that were not increased by ATP. Conversely, monocytes from TRAPS patients did not secrete more IL-1β than healthy controls in response to LPS, but similarly to CINCA patients presented a low response to ATP.

Conclusion

Despite a similar clinical response to anti-IL1 treatment, the pattern of IL-1β secretion of monocytes from Anakinra-responder TRAPS patients significantly differ from that observed in patients CIAS-1 mutations. This study suggests a different hierarchy in the pathogenic mechanisms leading to the inflammatory response in different diseases responsive to anti-IL-1 treatment.