9. Innate immunity

1 THE ROLE OF PROLACTIN, AS SEX HORMONE, AND ITS RECEPTOR INVOLVED IN RHEUMATOID ARTHRITIS

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Background and objective Rheumatoid arthritis (RA) is a rheumatic disease mainly affecting women. Prolactin (PRL) is a sex hormone, which apart from inducing lactation, has also immunomodulatory properties. High prolactin levels are associated with an increased disease activity postpartum and some studies have shown that bromocriptin, decreasing prolactin levels, improves clinical activity of patients with RA. Furthermore, hyperprolactinemia is observed in 6% of RA patients compared to 3% in the normal population.

Recently, the prolactin receptor (PRLR), belonging to the family of cytokine receptors, has been described in atherosclerotic plaques, mainly on macrophages.

The objective of the study is to determine (1) the level of PRL in RA patients related to treatment effect (2) PRLR expression in synovial tissue of RA, psoriatic arthritis (PsA) and osteoarthritis (OA) patients (3) the phenotype of the PRLR expressing cell.

Material and methods Serum prolactin levels were measured using immunofluorescent metric assay in patients with RA before and after tumour cecrosis factor α (TNFα) blockade (n=118). The expression of PRLR was determined in synovial tissue (ST), of RA (n=91), PsA (n=15) and OA (n=9) patients. Immunofluorescence (IF) was used to detect the PRLR expressing cell type.

Results Hyperprolactinemia was observed in 4,2% of the patients with RA (PRL level 16–36 µg/l). Prolactin level is respectively highest in premenopausal, postmenopausal females compared to male. The level of prolactin was decreased in the group of responders compared to the non-responders to TNF treatment, respectively 7.0 (2.0–36) and 8.5 (4.0–19) (median (range) µg/l; p=0.048). Higher tertiles of prolactin levels, still within physiological range, were associated with reumafactor positivity (p=0.031), anticyclic citrullinated peptide (p=0.075) and erosive disease (p=0.095).

The number of patients expressing PRLR in the synovium was comparable between RA and PsA (66% and 73%, respectively) versus 25% of the patients with OA (p=0.050). The levels of PRLR expressions were significantly higher in RA and PsA compared to OA, 0.055 (0.000–5.673), 0.182 (0.000–5.336) and 0.000 (0.000–0.908) (median (range) IOD/nuclei per mm^2; p=0.024), see figure 1. There was no significant difference in PRLR expression between males and (pre/postmenopausal) females. Using IF, colocalisation was observed with markers of macrophages and endothelial wall.

Conclusion Higher levels of prolactin were found in patients not responding to anti-TNF treatment. The expression of the prolactinreceptor in synovial tissue, mainly by macrophages, is higher in the inflammatory diseases (RA and PsA) compared to OA. Our data suggest a role of prolactin as sexhormone in rheumatoid arthritis.