Name of Scholar   : Deepti Bhatt

Name of Supervisor : Dr. Kapil Dev

Name of Co-supervisor: Dr. Syed Mansoor Ali

Name of Department : Department of Biotechnology

Title: Analyzing the role of Interleukin -17 and innate cells in synovium of osteoarthritis and rheumatoid arthritis

ABSTRACT

The present study was undertaken to investigate and compare various histopathological, ultrastructure changes as well as the significance of Interleukin IL-17 and its source TH-17 cells, MMP and innate cells especially macrophages and mast cells to understand the etiology of osteoarthritis and rheumatoid arthritis by determining expression levels of different markers. Further, these findings were correlated with clinical parameters in osteoarthritis and Rheumatoid arthritis. A total of 62 cases were taken in the arthritis and divided into two groups of osteoarthritis & rheumatoid arthritis as per diagnostic criteria of the diseases. The rheumatoid arthritis and osteoarthritis synovial tissue was collected with due consent from the patients once the ethical clearance was obtained from the Institute ethical committee. To achieve the objectives of the study, various methodologies which includes histopathological assessment, immunohistochemistry, Transmission Electron Microscopy, Scanning Electron Microscopy, Immunoelectron microscopy and western blotting were done in both the groups. The results show a significant difference in mean histopathological score and average percentage area stained with H&E between rheumatoid arthritis and osteoarthritis therefore, showing higher inflammation in rheumatoid arthritis than osteoarthritis. Further at the ultrastructure analysis suggesting the role of different mediators in pathology of rheumatoid arthritis. The T.E.M. micrographs showed the phenomenon of phagocytosis where

own type A synoviocytes start engulfing own collagen fibers illustrating autoimmunity in rheumatoid arthritis. In addition, Collagen fibers and several other cells are involved in processes of inflammation and interaction of active inflammatory cells with synovial cells was also observed through T.E.M. and S.E.M. We have also performed I.H.C. and western blotting for the studying the presence of IL-17, MMP-13, macrophage markers (CD68 & CD163), mast cell markers (MCT & c-kit) and Th-17cells through its markers (CD161&CCR6), (IL-6 & IL-23: required for initiation of differentiation of naive T cell to Th-17 cells & stabilization of Th-17 cells). The $IOD/\mu m^2$ of IL-6, IL-23, CD161, CCR6, IL-17, CD68, CD163 was significantly higher in rheumatoid arthritis than in osteoarthritis. Whereas, no significant differences were found in $IOD/\mu m^2$ of MMP-13 and mast cell markers (MCT & c-kit) between rheumatoid arthritis and osteoarthritis. The similar results were observed validating through western blotting. Further, the results of immunolabeling for IL-23, CD161, CCR6, IL-17, MMP-13 further validate our findings. Various clinical parameters were noted from the patient's history and their correlation was done by pearson's correlation coefficient. Its finding shows a significant difference in the mean values of lymphocytes count, neutrophils count, age, duration of disease and ESR. The results of the study concludes that the histological findings will be beneficial in the diagnosis and prognosis of osteoarthritis and rheumatoid arthritis as well as useful for differentiating rheumatoid arthritis from osteoarthritis at histological and molecular level. Further, IL-17, Th-17 cells, macrophage markers in rheumatoid arthritis synovium suggesting their critical involvement / role in pathophysiology of the rheumatoid arthritis. Therefore, these molecules may be used for the identification of new therapeutic targets for predicting disease course and therapy response and the development of novel drugs for the improved efficacy and safety that may lead to different therapeutic regime for treatment of various arthritis.