B lymphocyte involvement in ankylosing spondylitis: the heavy chain variable segment gene repertoire of B lymphocytes from germinal center-like foci in the synovial membrane indicates antigen selection

ABSTRACT

Comparable with RA and reactive arthritis, there is a biased repertoire of selected VH genes, whereas the panel of represented genes is different and less clonal expansion was observed.

INTRODUCTION

Introduction AS is an inflammatory rheumatic disease mainly involving the axial skeleton. Forty percent of AS patients develop periphery mono-/oligoarthritis. The SM of inflamed peripheral joints in AS (Fig. 1) in certain cases resembles RA with intense mononuclear cell infiltration forming foci similar to germinal centers (GC) that contain B and T lymphocytes as well as plasma cells. Recent immunohistologic analysis of five AS SMs demonstrated B cell rich infiltrates in two cases, whereas no B cells were detected in the three others. The VH germline repertoire consists of 123 (44 functional) VH segments subdivided into seven VH families (see supplementary material). Antibodies are encoded by one VH segment rearranged to one or several of 25 heavy chain diversity segments (DHs) and one of six JHs. The locus of rearrangement, individual for each B lymphocyte clone, is the CDR3. Only rearrangements with translatable nucleotide triplets lead to antibody formation, others are nonfunctional. There is a biased use of particular germline VH genes in the VH repertoire. An over-representation of VH4 genes in the autoimmune repertoire has been described. A negative selection of VH4 takes place in the peripheral blood lymphocytes from healthy individuals as a means of avoiding autoimmunity. An antigen-driven immune response, characterized by a ratio of mutations leading to amino acid replacement to silent mutations (R:S ratio) >3 within the complementarity determining region (CDR), takes place within the GC of lymphatic organs. Similar clonal development of antibody VH genes has been demonstrated in the SM in RA patients and in reactive arthritis (ReA) patients. The B cell subset in AS joints has not yet been characterized. We analyzed the repertoire and distribution of rearranged VH genes to elucidate B lymphocyte involvement in AS, and to investigate similarities to and differences from RA.

CONCLUSION

An active immune reaction with GC formation occurs in the inflamed SM in AS. B cell affinity maturation with generation of somatically mutated antibody-coding genes characteristic for memory cells occurs in these GC formations, indicating an antigen-driven response. Comparable with RA and ReA, there is a biased repertoire of selected VH genes, whereas the panel of represented genes is different and clonal expansion was observed less frequently.