B cell synovitis and clinical phenotypes in rheumatoid arthritis: relationship to disease stages and drug exposure.

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Arthritis Rheumatol. 2019 Nov 29. **https://doi.org/10.1002/art.41184**

Lay title

The cell types in the joints of people with rheumatoid arthritis at different stages of the disease

Lay summary

A medication used in rheumatoid arthritis (RA), Rituximab (RTX), works by wiping out B cells, a type of immune cell that produces antibodies - small bullets normally used by the immune system to fight infections, but in RA these are wrongly directed against the joints. RTX can be very effective in eliminating the source of this unwanted "friendly" fire but unfortunately only works in about 60% of people with RA. We know that approximately half of people with RA have very few B cells in their joints, so we thought that in people with few/absent B cells in the joints, a medication targeting B cells, such as RTX, would not work.

This theory is being explored in clinical trials in which we are studying small pieces of the joint tissue (synovium) obtained by a minimally invasive procedure called synovial (joint) biopsy. We counted B cells under the microscope in which a score from 0 to 4 is given to each joint sample, where 0 stands for absence of B cells, and 4 for abundant B cells.

We checked this scoring method by comparing it with digital image analysis (scores obtained with the help of a computer); and molecular analyses (studying genes known to be present only in B cells). The different methods were performed on samples obtained from the joints of people with RA at two different stages of the disease: before starting any treatment – "early RA" and after the first line treatment was ineffective – "established RA".

Our results show that in both populations, counting B cells is a reliable way of measuring B cells in the joints. Additionally, by looking at the differences between the two groups, we found that people with established RA (those who had already tried more than one medication) are more likely to have many B cells in the joints.

Because of the role played by B cells in RA, one would expect people with more B cells in the joints to have aggressive disease, which was true in the early RA group (those who had not yet started treatment).

Conversely, in the established RA group, we found no clinical differences related to the numbers of B cells. This means that doctors currently have no way of knowing which people have more B cells (and thus more inflammation in the joints) unless they perform a synovial biopsy. Also, these results suggest that that the clinical scores we currently use are not fully representative of what is happening in the joints.

While the final results of the ongoing clinical trials will confirm whether the analysis of B cells can help to predict response to treatment, the results presented in this manuscript show that the direct analysis of biopsies from joints in people with RA can provide valuable information, which is not currently available using standard routine blood tests, or clinical assessment.