Reviewer's report

Title: Association between synovial fluid proinflammatory cytokines and radiographic grading and pain-related scores in 47 consecutive patients with osteoarthritis of the knee

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Reviewer: Frank Pessler

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Using a cohort of consecutive OA patients seen in several practices, the authors investigated whether synovial fluid levels of TNFa, IL-6 or NGF correlated with parameters of radiographic disease progression and pain/disability. While NGF could not be detected in any of the samples, a negative correlation between IL-6 and the KL score, and a positive correlation between TNFa and the WOMAC score, and a negative correlation between IL-6 and the stiffness subscore are reported. These results are of some interest, although not entirely new.

Major compulsory revisions

• Brenner SS, et al. (Osteoarthritis Cartilage. 2004 Jun;12(6):469-75) published a similar study, but in addition involving synovial tissue, where no correlation between KL score or WOMAC score and IL-6 or TNFa was detected. This study and its discrepancies from the present study must be discussed.
• Hay CW et al, Am J Vet Res. 1997 Sep;58(9):1027-32 is a highly relevant study of IL-6 and TNF in OA in dogs and should also be discussed.
• The numbers of patients in Table 1 do not add up correctly (16 men, 24 women, but a total of 47)

The lack of NGF detection may be due to a variety of factors including technical failure, as the authors acknowledge. In the absence of the appropriate control experiments (e.g., spiking synovial fluid with recombinant NGF to test whether there are fluid factors that lead to precipitation or inhibit detection; or use of a different assay, etc. ) these negative results are not very meaningful. I would recommend to either provide convincing data demonstrating the reason for this lack of detection or to just remove the NGF aspect from the paper and focus on TNF and IL-6.

• The authors are correct that the lack of data from normal SF is a weakness. There are certainly ethical ways to obtain normal SF in an orthopedic environment (e.g., during otherwise indicated arthroscopy or surgery from non-OA knees). I would be more enthusiastic about this manuscript if the authors could provide data on normal SF for TNF and IL-6 for purposes of comparison.

• There are no data on disease duration. It is inferred that a higher KL score means longer standing disease. Can the authors provide temporal disease duration?
• The Discussion needs to be more concise
• Minor comments
• There are still some rough edges in terms of English language use and grammar.
• Caption to presumed Fig. 3 is labeled incorrectly as Fig. 2.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests