

Denosumab, cortical bone and bone erosions in rheumatoid arthritis

Takeuchi *et al*¹ demonstrate an additional inhibitory effect on the progression of bone erosions in rheumatoid arthritis (RA) with the addition to methotrexate of an anti-receptor activator of nuclear factor kappa-B ligand (RANKL) antibody, denosumab, confirming results already reported 8 years ago by Cohen and colleagues.² Insufficient inhibition of structural joint damage by disease-modifying antirheumatic drugs (DMARDs) was reported despite clinical improvement,^{3–5} and recently two meta-analysis^{6,7} showed that methotrexate combined with biologics is statistically superior to methotrexate in inhibiting radiographic progression, but the estimated mean change with all treatments was less than the minimal clinically important difference.

On the other side, from the bone point of view, we previously observed that low bone mineral density (BMD) at the cortical site was significantly associated with the presence of bone erosions,⁸ and recently Zhu and colleagues reported alterations in the density and microstructure of the cortical bone of patients with RA, providing new insight into the microstructural basis of bone involvement in RA.⁹ In particular, in patients with anticitrullinated protein antibodies, cortical thinning might be present even before the clinical onset of RA and it seems strictly related with the risk of bone erosions.¹⁰

Denosumab is a well-known, effective agent for increasing BMD, both at trabecular and cortical sites,^{11,12} and has been showed to prevent metacarpal bone loss in patients with RA,¹³ and improve cortical porosity.¹⁴ An intriguing hypothesis is that the effects of denosumab in terms of prevention of bone erosions are mainly due to its positive effects on cortical BMD and porosity.

We think that, in the future, treatment with agents not only targeting inflammation but improving cortical bone should deserve more consideration in order to achieve better prevention of bone erosions in RA. Non-responders to the DMARDs in terms of progression of bone erosions could be indeed the consequences of a concomitant osteoporosis. The lack of data about BMD might represent an important bias for meta-analysis on effects of DMARDs on radiographic progression of RA.

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