Sirolimus protective effects on bone: the need to be demonstrated

Sir,

We read with great interest the article by Ralf Westenfeld et al. [1] regarding the reduced serum levels of bone resorption markers (TRAP-5b and sRANKL) in patients treated with sirolimus (SRL) after renal transplantation compared to a calcineurin inhibitor (CI)-based regimen, and in vitro, SRL reduced osteoclast differentiation and osteoclast precursor proliferation. So the authors concluded that SRL may have the potential to balance osteoclast promoting effects of glucocorticoids and CI.

Multiple risk factors have been suggested to play a role in the pathogenesis of post-transplant bone disease, such as immunosuppressive drugs, persistent secondary hyperparathyroidism, impaired renal function and several other factors [2]. In this study, the authors emphasize the role of non-glucocorticoid immunosuppressants, SRL versus CI (including cyclosporine and tacrolimus). However, present studies investigating the effects of tacrolimus or cyclosporine on bone metabolism yielded conflicting data: cyclosporine may counterbalance the depressive effect of prednisone [3], while bone resorption effects were seen in both tacrolimus and cyclosporine [4]. So we consider that it is not appropriate to group the patients who took tacrolimus or cyclosporine together. And in vitro, the authors did not study the cyclosporine effect on osteoclast and osteoclast precursors. As there were only 15 patients in the CI group, a large sample analysis is needed to
investigate if there was some different effect on bone metabolism between tacrolimus and cyclosporine.

In addition, no definitive examinations were performed to investigate whether SRL was beneficial to prevent bone loss in this study. We investigated 72 renal transplant recipients in our hospital, all of which received a triple immunosuppressive therapy consisting of steroids plus tacrolimus plus mycophenolate mofetil and time since transplantation >5 months. We examined the serum TRAP-5b levels and bone mineral density (BMD) at the lumbar vertebrae L1–L4 and neck of the femur simultaneously. The results showed that the mean level of TRAP-5b was 5.08 ± 2.26 U/L (normal range 1.3–4.82 U/L), and no correlation was observed between TRAP-5b levels and T-scores of BMD at any site (P > 0.05). So elevated TRAP-5b levels may not result in bone loss. If SRL treatment is useful to balance osteoclast promoting effects of glucocorticoids and CI as the authors concluded, BMD examinations or bone biopsy should be performed to demonstrate the better bone status in SRL treatment group other than CI group.

Editorial Note: Westenfeld et al. were invited to reply to this letter but we did not receive a response.

Conflict of interest statement. None declared.

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