Assessment of efficacy of pamidronate in undifferentiated spondyloarthropathy (uSpA): a molecular mechanism

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To the Editor,

I read with great interest the article by Sarkar and colleagues [1]. I would like to complete the discussion of Sarkar and colleagues by introducing a major route by which pamidronate could promote outcome of the management of undifferentiated spondyloarthropathy.

Undifferentiated spondyloarthropathy, which does not conform to the criteria for ankylosing spondylitis, is characterized by arthritis and inflammatory back pain [2]. Spondyloarthropathies-associated pain is directly related to the increased rates of bone resorption associated with osteoclast activity [3].

Studies have shown the essential role of the ligand for receptor activator of nuclear factor kappaB (RANKL) in recruitment of the osteoclasts. Osteoprotegerin, a decoy receptor of RANKL, is a potent inhibitor of recruitment effect of RANKL. Also, fusion of preosteoclasts is an essential initial step in osteoclast maturation. Cholesterol, which is produced from de novo synthesis via hydroxymethylglutaryl coenzyme A reductase (HMG-CoA reductase) in the membranes of monocytes, has an important role in the osteoclast-like cell formation via cellular membrane fusion events [4, 5].

Pamidronate effectively inhibit the enzyme, farnesyl diphosphate synthase, in the HMG-CoA reductase pathway. Also, pamidronate stimulate the osteoprotegerin production by osteoblasts that can lead to significant reduction in RANKL [6, 7]. Therefore, these important

mechanisms should be borne in mind as the major mechanisms by which pamidronate can improve outcome of the management of undifferentiated spondyloarthropathy.

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