Bone Formation in Psoriatic Arthritis: A Report from the GRAPPA 2013 Annual Meeting

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ABSTRACT. The simultaneous presence of bone erosions and bony spurs (osteophytes, enthesophytes) in the joints of patients with psoriatic arthritis (PsA) suggests that the disease leads to enhanced bone resorption as well as increased bone formation, the latter of which has not been observed in patients with rheumatoid arthritis. At the 2013 Annual Meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), members heard an update on the current research into the cytokine signature in PsA and its effects on new bone formation. (J Rheumatol 2014;41:1218–9; doi:10.3899/jrheum.140173)

Key Indexing Terms:
PSORIATIC ARTHRITIS | PSORIASIS | BONE DESTRUCTION
BONE FORMATION | ENTHESES | CYTOKINES

Bone and cartilage destruction are typical clinical findings in patients with psoriatic arthritis (PsA)[1]. Similar to rheumatoid arthritis (RA), the chronic inflammatory character of the disease alters bone architecture and changes the anatomical properties of the joint affected by PsA. Bone lesions also irreversibly impair the functional properties of the joint by destroying the physiological insertion sites of tendons and ligaments in the joint.

In PsA, bone is directly exposed to the inflammatory tissue and is therefore particularly prone to damage. Hence, 1 site of inflammation in PsA — the enthesial organ — represents the interphase between the inflamed periarticular tissue and the bone surface, which explains why PsA leads to extensive bone damage in some patients with PsA[2]. In contrast to RA, however, bone changes in PsA are characterized by the concomitant presence of catabolic and anabolic bone changes, features in the typical clinical picture of PsA that are fundamentally distinct from RA.

The simultaneous presence of bone erosions and bony spurs (osteophytes, enthesophytes) in the joints of patients with PsA suggests that the disease is characterized by both enhanced bone resorption and increased bone formation. These structural bone changes are initiated by the inflammatory tissue, in particular by cytokines produced by enthesitis and synovitis, which disturb bone homeostasis. Therapeutic responses to cytokine blocking agents suggest that inflammation in PsA, as in psoriasis, is dominated by tumor necrosis factor-α (TNF-α) and the interleukins (IL)-23 and IL-17, whereas other proinflammatory cytokines, such as IL-6 and IL-1, play only a minor role in disease pathogenesis[3].

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TNF-α is an important trigger for bone erosion because it induces osteoclast differentiation through the induction of expression of receptor activator of nuclear factor-κB ligand in the joints, which is the essential differentiation factor for the bone-resorbing osteoclasts[4]. In contrast, TNF-α represents a potent suppressor of osteoblast differentiation and new bone formation[5], which suggests that expression of TNF-α in patients with PsA is a good explanation for development of bone erosions but not for excessive bone formation. In accordance with this notion, the inhibition of TNF-α by neutralizing antibodies does not inhibit the progression of new bone formation and enthesophyte growth in patients with PsA[6]. In contrast, inhibition of TNF-α is effective in retarding the progression of bone erosions in PsA, which is in accordance with the observations made in RA[6,7,8].

These findings suggest that cytokines other than TNF-α may be responsible for the new bone formation in PsA. An attractive concept has recently linked IL-infiltration with IL-22-producing T cells. Local bone responses, triggered by these T cells, are part of an IL-17 cytokine signature, which is typically seen in psoriasis and also seems to play a role in triggering inflammation in PsA and in spondyloarthritis[9].

Induction of anabolic factors, which stimulate the formation of hypertrophic chondrocytes as well as osteoblasts, thereby promoting rapid formation of new bone, can be considered as an essential step for new bone formation in PsA. However, it is still unclear how cytokines drive new bone formation in PsA. Nonetheless, wingless signaling pathway, bone morphogenic, and hedgehog proteins have been identified as the essential mediators for bony proliferation in arthritis, and it is likely that these pathways are responsible for new bone formation in PsA as well[10,11,12]. Further work is necessary, however, to tease out the functional links between the cytokines that trigger enthesitis and the bone anabolic factors, to better understand why bone formation starts early in patients with PsA but is rarely

seen in patients with RA. In this context, mechanical factors may play an important modulatory role, because the dominant sites of bone formation are the entheses, which represent mechanosensitive tissues.

The concomitant presence of bone formation and bone erosion in PsA has also been observed in radiographic imaging. However, bone erosion has received far more attention than bone formation in patients with PsA. Moreover, standard radiographic scores used to assess skeletal damage in PsA focus on bone erosion rather than bone formation and thus miss an essential part of the progressive architectural changes observed in patients with PsA. Interestingly, even bone erosions in PsA are different from their counterparts in RA and show distinct signs of bone formation, which are missing in RA. Hence, despite a similar frequency of bone erosion in PsA and RA, the lesions in patients with PsA are smaller and are typically associated with periosteal bone proliferation[6]. This process gives them a bottleneck (or inverted omega)-shaped appearance when imaged by high-resolution computed tomography. Further, bony spurs usually do not emerge at the same sites where bone erosions are found. They usually emerge from the bone surface, where the entheses insert, and are localized proximal to the erosive sites. Such enthesophytes are usually localized at the lateral, and to a lesser extent, at the medial sites of the hand joints, which represent the typical anatomical sites where tendons insert. If severe, bone formation can affect the entire circumference of the joint and form a "bony corona," which grossly impairs joint function.

Enhanced bone formation is a typical but poorly understood feature of PsA. It leads to bony swelling of the joint, a well-described feature of PsA, known as bony ankylosis, a state characterized by irreversible structural damage impairing the functional state of the patient. Current treatments, which effectively downregulate inflammation in PsA and also retard the progression of bone erosion, do not halt new bone formation, suggesting that the factors that link inflammation with new bone formation are different from those linking inflammation with bone erosion. Current imaging data on new bone formation in PsA are limited, and no reliable soluble markers have been developed that allow measurement of the presence or the degree of new bone formation in patients with PsA. This surprising situation warrants further research in this important area of the disease.

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