Acromegalic arthropathy: current perspectives

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Acromegaly is associated with manifestations in many organs including the heart, colon, skin, bone, and many joints. Both weight and non-weight bearing joints are affected including shoulders, wrists, knees, hips, and the spine [1–3].

Patients with long-term cure or long-term biochemical control of acromegaly still suffer from acromegalic arthropathy. The prevalence of clinical and radiological osteoarthritis of the hip, hand, and knee reaches even up to 80 % [1]. In comparison with primary osteoarthritis, secondary osteoarthritis in patients with long-term cured acromegaly is characterized predominantly by osteophytes, which were observed frequently without joint space narrowing indicating preservation of articular cartilage. Patients with acromegaly report less functional disability of the hips and knees than the patients with primary generalized osteoarthritis [1]. Radiological features of acromegalic arthropathy progress despite long-term biochemical remission of acromegaly. In contrast to the cross-sectional observations, which indicate widened joint spaces in patients cured or controlled from acromegaly, prolongation of follow-up is characterized by a decrease in joint space widening and progression of osteophytosis, despite long-term biochemical control. Thus, this arthropathy appears to be a progressive joint disease that is not merely halted or reversed by control of acromegaly [4]. Remarkably, medically well-controlled patients show more radiographic progression compared with surgically cured patients. In previous studies, GH secretion was still slightly

abnormal during treatment with SMS analogs, despite appropriate biochemical control according to current criteria [5]. However, persistent abnormal GH secretion despite somatostatin analogs is not a straight forward explanation, since active acromegaly is associated with joint space widening, rather than with joint space narrowing. Alternatively, it may be hypothesized that SMS analogs have a direct effect on the cartilage of joints. Therefore, it may be possible that SMS analogs contribute to the pathophysiology of the progression of acromegalic arthropathy.

In addition to arthropathy, patients with active and cured/controlled acromegaly suffer from an increased prevalence of vertebral fractures, although these patients are considered to have a low risk of osteoporosis since bone mineral density is not decreased [6]. More than 50 % of these patients suffered from vertebral fractures. There was no association with the duration of disease control, bone mineral density, markers of bone turnover, or acromegalic disease characteristics. There was a striking number of fractures per patient (mean 3.4 ± 0.3 , range 1–8) [7]. It should be realized that the most of these fractures were asymptomatic. Fractures were also evident in men, especially in the presence of hypogonadism. In view of the significant morbidity associated with vertebral fractures, the inclusion of lateral conventional radiographs of the thoracic and lumbar spine has been proposed in the screening of all patients with acromegaly both at diagnosis and during follow-up after establishment of disease control. Longitudinal studies are required to assess both the contribution of risk factors for these fractures including vitamin D, (replacement for) hypopituitarism, and of glucocorticoid replacement at a low dose and the optimal treatment modalities to prevent (additional) vertebral fractures.

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Patients with acromegaly suffer from an extremely rare disease, but this disease is associated with a very high prevalence of acromegalic arthropathy. In the assessments of the joint complaints of these patients, careful consideration should be given to the extent of the contribution of acromegaly to the arthropathy, because the pretest likelihood of the presence of acromegalic arthropathy in these patients is remarkably high. In addition, it is possible that some of these patients suffer from more prevalent rheumatological diseases that may interact at the level of the joints with the pathophysiological effects of acromegaly.

In the study by Örü̇k et al. [8], published in this issue of endocrine, the focus was on the manifestations of other rheumatological diseases in patients with acromegaly, who were all treated with SMS analogs. From the description of the methods, it is unclear to which extent standardized radiological assessment of the joints was performed. Nonetheless, non-specified radiological abnormalities were present in 62.5 % of the patients, in line with circumstantial evidence of a high prevalence of acromegalic arthropathy. This included radiological evidence of diffuse idiopathic skeletal hyperostosis (DISH) in six patients (15 %). This most likely represents a severe form of acromegalic arthropathy, rather than an idiopathic manifestation of another disease process, because DISH *per se* is a rather rare disease. Moreover, chronic GH and IGF-I excess result in radiological alterations of the axial skeleton with development of severe alterations of spine morphology and function and ultimately manifestations of DISH [3]. In this study by Scarpa et al. features of DISH were observed in 20 % of the patients with active acromegaly, in accordance with the study by Örü̇k et al.

In the study by Örü̇k et al. [8] in 3 of the 40 acromegalic patients evidence was found for inflammatory rheumatological diseases. This illustrates the notion that joint problems in patients with acromegaly are most frequently caused by acromegalic arthropathy. In incidental patients with acromegaly (concomitant) manifestations of more

prevalent rheumatological diseases may occur, which will require other treatment modalities.

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