

Vertebral Fractures in Acromegaly-Mini Review

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Abstract

The purpose of this review is to give a point of view about Vertebral Fractures (VFs); an underestimated complication of acromegaly which lead to increased morbidity and affect quality of life (QOL). They can occur, even in normal Bone Mineral Density (BMD) levels and after remission. Imaging studies to evaluate bone morphometry are suggested in all patients at diagnosis, regardless of the disease status. Further studies are needed to understand the role of bone targeting agents in prevention and treatment of VFs in acromegaly.

Keywords: Acromegaly; Vertebral fractures; Bone mineral density; Morphometry

Introduction

Excessive Growth Hormone (GH) levels, mostly due to a pituitary adenoma and consequent high levels of Insulin-Like Growth Factor 1 (IGF-1) are associated with a wide range of systemic symptoms which lead increased mortality [1]. Vertebral Fractures (VFs) are one of these complications associated with high morbidity and low Quality of Life (QOL) [1]. GH and IGF-1 are important for bone remodeling [2,3]. They stimulate both osteoblasts and osteoclasts, resulting increased bone turnover, most often in favor of bone formation [2,3]. The alterations in calcium and phosphate homeostasis due to high levels of GH and IGF-1 also contribute to the deterioration in bone microarchitecture, causing increased skeletal fragility [3]. The overall median prevalence of VFs in acromegaly is about 40%, a fracture risk which is three- to eight-fold greater compared to control subjects [2,3]. In a study that biochemically controlled acromegaly patients were enrolled, the prevalence of VFs was reported in up to 63% even in remission [4]. VF incidence was found to be 20% despite normal BMD values especially in men and in case of >2 VFs at baseline [4]. The incidence of VFs was estimated 42% in a prospective follow-up study, which was associated with hypogonadism, femoral neck BMD changes, previous vertebral fractures and duration of active acromegaly [5].

Discussion

It is difficult to diagnose VFs according to clinic or BMD; morphometric and radiological evaluations are emerging tools for the assessment of VFs in acromegaly [6-8]. Anteroposterior and lateral X-rays or Dual X-ray Absorptiometry (DXA) with a morphometric approach can be used for the evaluation of VFs [6,7]. demonstrated the association between acromegaly and VFs by using this approach [7]. The fact that VFs can be seen in patients with normal BMD; measured by DXA [7-9], prompts to further studies assessing alternative diagnostic methods instead of BMD such as quantitative ultrasound [10,11], quantitative computed tomography [12], or trabecular bone score [13]. The Fracture Risk Assessment Tool (FRAX) score which has been widely used in osteoporosis, was not useful in acromegaly population [14]. Hypogonadism, change in femoral neck bone mineral density during the follow-up, and present VFs at the study entry found to be associated with vertebral fracture incidence in cured/controlled acromegaly patients whereas the duration of active acromegaly was found to be associated with vertebral fracture incidence in patients with uncontrolled disease [5]. Controversially, another study showed no correlation with vertebral fracture and BMD

values or changes in BMD in biochemically controlled acromegaly patients [4]. This study also suggest that an abnormal bone quality persists in these patients after remission in the absence of osteopenia or osteoporosis [4]. In a cross-sectional study in which postmenopausal women with acromegaly were enrolled, vertebral fractures were found to be related with the activity of disease [7]. In patients with active acromegaly, vertebral fractures occur even in the presence of normal BMD, whereas in patients with controlled acromegaly, vertebral fractures are always accompanied by a pathological BMD [7]. In another study, evaluated males with acromegaly and control subjects revealed that despite similar BMD values, the prevalence of vertebral fractures was higher in acromegalic patients as compared with the control subjects [9]. The duration of active acromegaly was the only risk factor significantly correlated with the occurrence of fractures [9]. Diabetes has also been described as an absolute risk factor for vertebral fracture in acromegaly patients [6]. The fact that active acromegaly has been associated with high incidence of vertebral fractures compared to cured/controlled disease [3], prompts immediate treatment of the patients. In terms of medical treatment to achieve biochemical control in acromegaly patients, a study showed that VFs were more frequent in pegvisomant group than pasireotide group, regardless of IGF-1 levels [15]. The pathophysiology may include different impact of pegvisomant vs. pasireotide on GH signaling in bone and effect of somatostatin receptor ligands on bone turnover [15]. No controlled studies were available on the bone active agents, regarding prevention and treatment of vertebral fractures in acromegaly [16]. An observational study of 111 active acromegaly patients revealed that use of bone active drugs may be associated with a lower risk of incident VFs [17].

Conclusion

Imaging studies to evaluate bone morphometry are suggested in all patients at diagnosis, regardless of the disease status [2,18,19]. BMD is not effective in evaluation of bone quality in acromegaly [2,18,19]. Further studies are needed to understand the role of bone targeting agents in prevention and treatment of VFs in acromegaly [18].

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