Osteoporosis: A Disappearing Manifestation of Cushing's Syndrome

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Citation

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Abstract

It was our clinical impression that skeletal health in untreated non-iatrogenic Cushing's syndrome was less adversely affected than previously described. Therefore an observational study was carried out to determine if this is the case. Cross-sectional analysis of BMD (Bone Mineral Density) measurement in 23 patients with untreated Cushing's syndrome was undertaken; Osteoporosis was uncommon, with only 5% osteoporotic (38% normal) at the lumbar spine and 10% osteoporotic (43% normal) at the LFN (Left Femoral Neck). In the modern era, earlier diagnosis as well as detection of disease of milder intensity has changed the skeletal contribution to the clinical presentation of Cushing's syndrome.

INTRODUCTION

Osteoporosis is considered to be a cardinal feature of Cushing's syndrome with a reported incidence as high as 90% [1]. It was our clinical impression that skeletal health was less adversely affected than previously reported. With the approval of the local ethics committee, all patients with non-iatrogenic Cushing's syndrome treated in this Unit since 1975 were identified. The notes of 81 patients were reviewed. Patients with Cushing's syndrome due to ectopic ACTH secretion were excluded as well as those who did not undergo baseline BMD measurements at this Unit. A baseline BMD measurement was considered to be one taken before any treatment had commenced, or within 6 months of treatment starting, as previous studies have shown there to be little improvement in BMD within this time period [2]. A cross-sectional analysis of baseline BMD was conducted in the 23 identified patients (4 males) aged 18-66 (median, 37) years. The diagnosis of Cushing's syndrome had been confirmed conventionally in all; 20 patients had pituitary dependent disease and 3 patients had adrenal adenomas.

METHODS

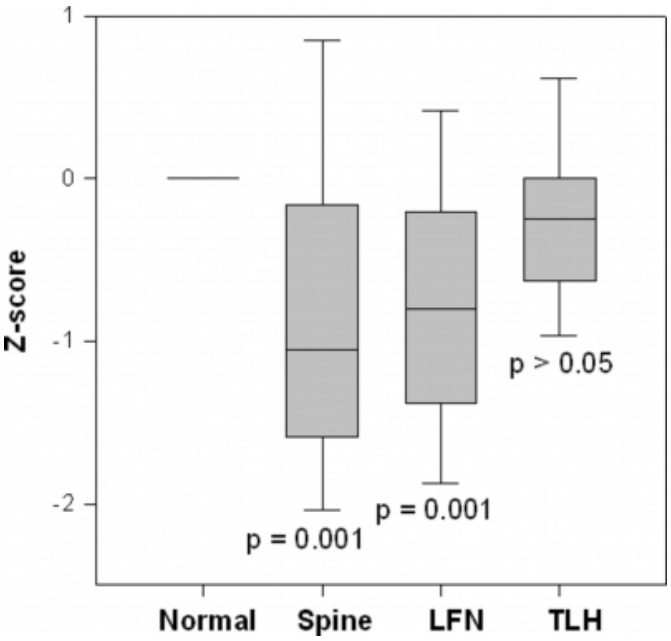
All BMD measurements were performed at the Department of Clinical Radiology – University of Manchester, using DEXA (Dual Energy X-ray Absorptiometry) for the spine (L1-L4), LFN and TLH (Total Left Hip). DEXA measures bone density using X-ray beams of two peak energies. The simultaneous measurement of radiation of two different energies allows for correction of soft tissue and fat. The energies used are selected to optimise separation of the mineralised and soft tissue components of the area analysed. DEXA measures integral bone density with cortical/trabecular ratios of 50/50 in the lumbar spine (PA), 10/90 in the lateral projection lumbar spine and 60/40 in the proximal femur [3]. Results are expressed as BMD (in g/cm^2), and the accuracy of DEXA is 3-8% [4]. These results were compared with an age and sex matched reference group, and a group of healthy young normals to provide Z- and T-scores respectively. Z-score analysis allowed comparison with the BMD results of the normal population, taking in to account age and gender. T scores were used to assess whether patients were osteoporotic as defined by WHO criteria [5].

RESULTS

The Z-scores of the 23 patients were significantly reduced (compared with normal population; mean Z-score = 0) at the lumbar spine (mean SD; -0.765 1.13; $p = 0.001$) and the LFN (mean SD; -0.791 0.878; $p = 0.001$) (Figure 1). The Z-scores at TLH (mean SD: -0.263 0.557) were not significantly different from normal ($p > 0.05$) (Figure 1).

Figure 1

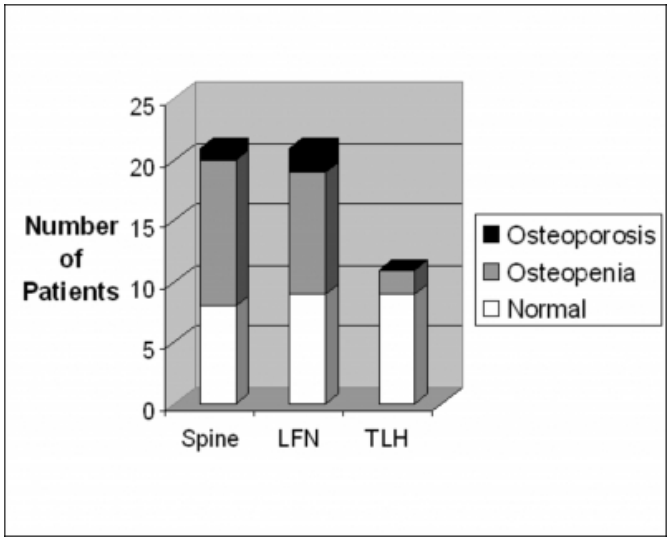
Figure 1: Baseline Z-scores in Cushing's Syndrome Patients (n = 23)



T-scores (bone mass compared to a reference group of young healthy individuals) were available in 21 patients, one of whom had osteoporosis (T-score < -2.5; WHO criteria) at the lumbar spine; eleven being osteopenic (T-score between –1.5 and –2.5) and nine normal (T-score > -1.5) (Figure 2). Similarly at the LFN only two patients were osteoporotic, nine osteopenic and ten normal (Figure 2). No patient gave a history of low trauma fractures.

Figure 2

Figure 2: Prevalence of Osteopenia and Osteoporosis at Different sites (n = 21)



The only significant relationship between the severity of the Cushing's syndrome and skeletal health, was a moderate negative correlation between the lumbar spine Z-score and the mean 24hr urinary free cortisol ($r = -0.44$; $p < 0.05$). There was no correlation between any BMD measure and the estimated duration of disease, based on a careful examination of the presenting history as recorded in the patient notes.

DISCUSSION

Our results show that although bone mineral BMD is still significantly adversely affected in the majority of patients, the prevalence of osteoporosis is far lower than previously reported. Indeed at presentation very small numbers exhibited osteoporosis, defined by the WHO criteria [5]. Consistent with the latter observation, the BMD was within the normal range in 38% of patients at the lumbar spine and 43% of patients at the femoral neck.

In conclusion, reduced BMD in Cushing's syndrome is mostly encountered in weight bearing skeletal sites rich in trabecular bone such as the lumbar spine. The textbooks, however, are in need of revision as osteoporosis is no longer a common feature of Cushing's syndrome.

In the modern era, earlier diagnosis as well as the detection of disease of milder intensity has changed the skeletal contribution to the clinical presentation of Cushing's syndrome.

CONTRIBUTORS

E. Searle did data collection and analysis and prepared the manuscript. K. Darzy and S. Shalet initiated the project, contributed to the writing of the manuscript and advised on statistical analysis and methodology. J. Adams provided all BMD measurements and contributed technical advice.

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