Radiological vertebral fractures in patients with acromegaly and coexistent secondary hypopituitarism treated with L-thyroxine

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BACKGROUND

Acromegaly is associated with skeletal fragility and high risk of vertebral fractures (VFs), but the determinants of such a risk are still under investigation and it is not clear whether replacement therapies of coexistent hypopituitarism may influence prevalence and incidence of VFs.

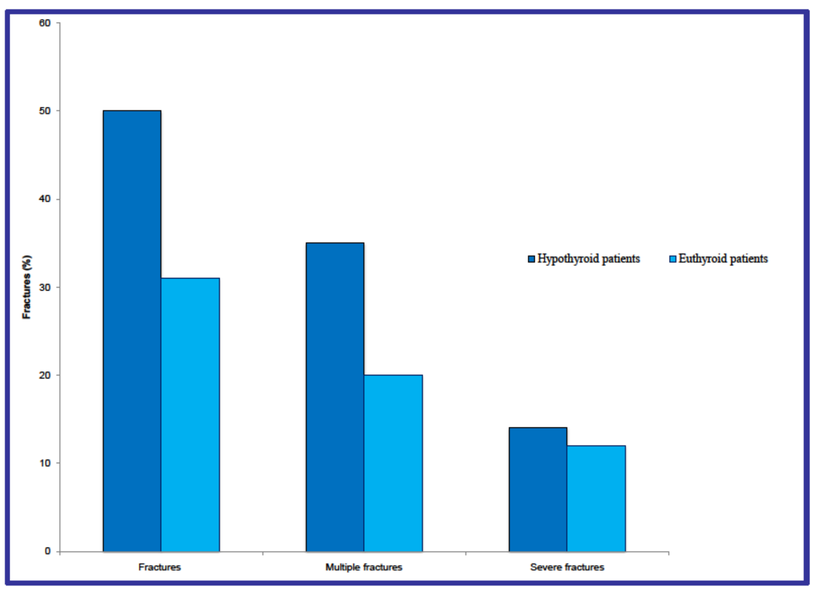
Table 1

Cases	40
Sex (F/M)	24/16
Age (yrs)	57 (25-72)
BMI (Kg/m2)	28 (21-34)
Serum IGF-I (ng/ml)	187 (115-1387)
Active acromegaly (cases)	20 (50%)
Duration of active acromegaly (months)	24 (6-112)
Neurosurgery (cases)	19 (47,5%)
Somatostatin analogs therapy	26 (65%)
Pegvisomant therapy	2 (5%)
Radiotherapy	0
Untreated hypogonadism	19 (47,5)
Post-menopausal females	16 (42,5%)
Pre-menopausal females	2
Males	1
Treated hypoadrenalism	7 (17,5%)
Treated hypothyroidism	14 (35%)

Table 2

	No VFs	VFs	P-values
Cases	25	15	
Sex (F/M)	15/10	9/6	1
Age (yrs)	49 (25-71)	63 (47-72)	<0.001
BMI (Kg/m2)	27 (19-42)	28 (21-42)	0.58
Controlled/cured acromegaly (cases)	11 (44%)	9 (60.0%)	0.33
Duration of active acromegaly (months)	4 (0.7-15)	5 (3-14)	0.01
Untreated hypogonadism	8 (32.0%)	11 (73.3%)	0.01
Treated hypoadrenalism	4 (16.0%)	3 (20.0%)	0.75
Treated hypothyroidism	7 (28.0%)	7 (46.7%)	0.23
Lumbar spine BMD (Z-score)	+0.35 (from -2.8 to +4.4)	+0.01 (from -3.2 to +4.9)	0.45
Femoral neck(Z-score)	+0.60 (from -1.1 to +4.5)	+0.1 (from -1.1 to +2.0)	0.16
Total hip BMD (T-score)	+0.45 (from -1.3 to +4.2)	-0.10 (from -1.4 to +2.0)	0.10

Figure 1



METHODS

- In this cross sectional study, forty acromegaly patients (24 M, 16 F; median age, 57 years; range, 25-72), 20 with active disease, were evaluated for the effects of replacement therapy of central hypothyroidism on radiological VFs. Seven patients had glucocorticoid deficiency, 14 had hypothyroidism and 25 were hypogonadal (5 men and one pre-menopausal woman were on replacement therapy)(Table 1).
- The assessment of VFs was performed using a morphometric X-ray absorptiometry method using images of the spine (T5-L4) acquired by DXA. According to quantitative morphometric approach, the fractures were defined mild, moderate and severe based on a height ratio decrease of 20-25%, 26-40% and more than 40%, respectively.
- Bone mineral density (BMD) of the lumbar spine, total hip, femoral neck and distal radius was measured in patients with acromegaly by DXA (Explorer Hologic Inc., Waltham, MA).

RESULTS

VFs were found in 15 patients (37.5%), witt a trend in prevalence greater for patients with hypothyroidism vs euthyroid subjects (50.0% vs. 30.8%; p=0.23)(Table 2) and without differences for the number of fractures and their severity (Figure 1). Among patients with hypothyroidism, those with VFs showed higher daily levo-thyroxine (L-T4) dose (1.43 µg/kg, range: 1.29-1.58 vs. 0.92 µg/kg, range: 0.7-1.1; p=0.009)(Figure 2a) and serum FT4 (13.0 pg/ml, range: 7-17 vs. 9.7 pg/ml, range: 9-16; p=0.02)(Figure 2b) while serum FT4 and daily dose of L-T4 were not significantly associated with BMD at lumbar spine, femoral neck and total hip. VFs were also significantly associated with age of patients (odds ratio: 1.16; C.I.95% 1.05-1.3), untreated hypogonadism (odds ratio: 5.8; C.I.95% 1.4-24.2) and duration of active acromegaly (odds ratio: 1.21; C.I.95% 1.01-1.4), whereas no significant associations were found with treated hypoadrenalism, sex, BMI and BMD at either skeletal sites (Table 2).

Figure 2a

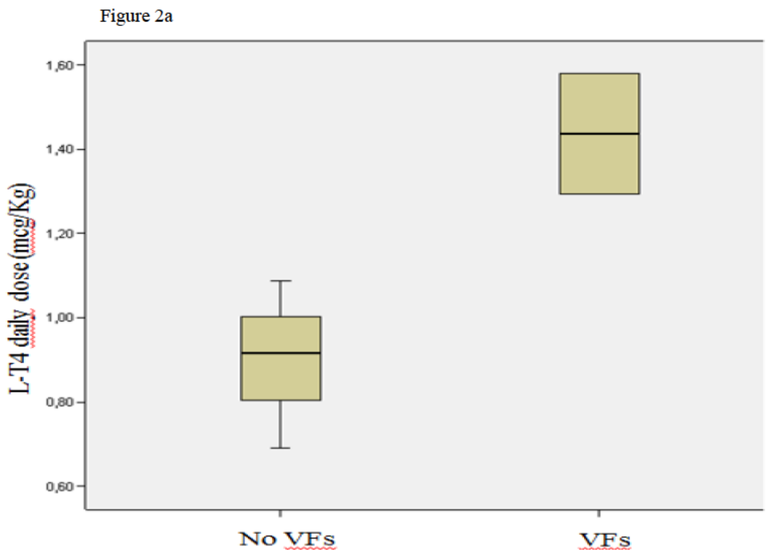
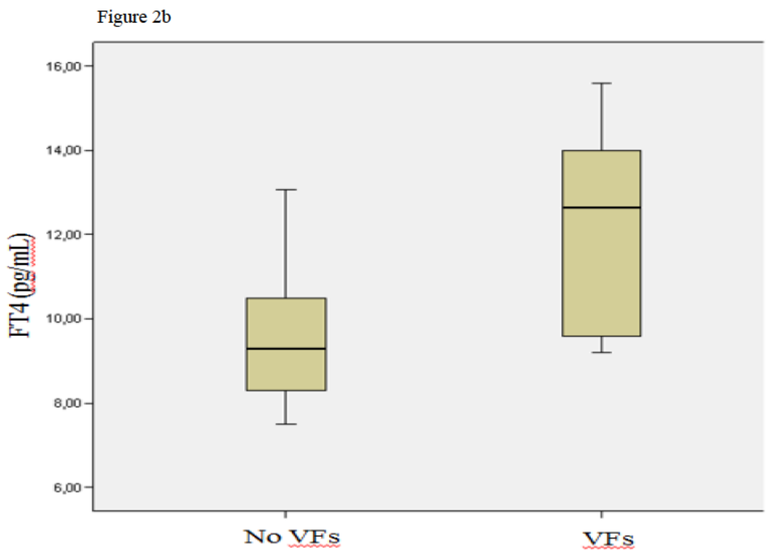


Figure 2b



CONCLUSIONS

In conclusion, this study provides a first evidence that a relative overtreatment of central hypothyroidism may influence the fracture risk in patients with acromegaly, consistently with the pathophysiological hypothesis that thyroid hormone excess and GH hypersecretion may have additive negative effects on bone remodeling and skeletal health.

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