



## Bone Health in Patients with Pituitary and Hypothalamic Tumors, Importance of Prevention of Bone Fracture

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### Abstract

Pituitary or hypothalamic disorders including hypopituitarism, Cushing disease, and hyperprolactinemia are major causes of osteoporosis. Patients with pituitary or hypothalamic lesions have tendency of association of hypopituitarism in both preoperative and postoperative endocrinological assessment. Growth hormone deficiency is also one of the considerable risks of osteopenia. Thus, in surgery for pituitary or hypothalamic lesions, preservation of pituitary function and postoperative appropriate hormone replacement therapy are required.

**Keywords:** Bone Health; Patients; Pituitary; Hypothalamic Tumors Bone Fracture

### Manuscript

Osteoporosis is a condition that is characterized by a decrease in bone mass and density, making bones fragile and fracturous. This condition is induced in aging process; primary osteoporosis, or evoked by pathology affecting bone mineral cycle; secondary osteoporosis. Secondary osteoporosis is associated with multiple myeloma, chronic renal disease, malabsorption syndrome, endocrine disorders including diabetes mellitus, hyperthyroidism, hyperparathyroidism, hypercortisolism, hypogonadism, etc. Also noted is osteoporosis induced by drugs: glucocorticoid, anticonvulsant, medroxyprogesterone, aromatase inhibitor, heparin, warfarin, proton pump inhibitor etc.

Other skeletal fragility with high risk of fractures includes osteoporosis associated with hypopituitarism, Cushing disease, and

hyperprolactinemia [1]. Hyperprolactinemia is among the most common causes of hypogonadotropic hypogonadism in both sexes [2]. Another important clinical entity is hypopituitarism. Patients with pituitary or hypothalamic lesions have tendency of association of hypopituitarism in both preoperative and postoperative endocrinological assessment.

Formerly, we published a paper of the measurement of bone mineral density (BMD) and urinary type I collagen N-telopeptide (uNTX) in 35 postoperative patients including 25 with pituitary tumor (PT), 6 with craniopharyngioma (CP), and 4 others who had not been on sex hormone replacement, raloxifene, or bisphosphonate therapy [3]. Compared with patients with PT, patients with CP had lower BMD and higher uNTX. Five out of 6 patients with CP had

BMD lower than 80% of young adult mean (YAM), whereas 11 out of 22 patients with PT had BMD less than 80% of YAM. Patients with CP had significantly lower serum levels of gonadotropins, and they also tended to have lower serum levels of sex steroids, although statistically not significantly. Two postoperative patients with CP on sex steroid replacement, who were not included in the current analysis, had normal BMD. Of all the subjects, the prominent difference between patients with normal BMD and normal value of uNTX and patients with low BMD and elevated uNTX value was that the latter received higher dose of hydrocortisone replacement. Postsurgical patients with pituitary or parasellar lesions, especially those with CP, are at high risk for osteopenia. In designing replacement therapy for those patients, it is important to consider bone by minimizing the dose of glucocorticoid, including sex steroids, and using other drugs that protect bone.

Glucocorticoid therapy is the most common cause of iatrogenic osteoporosis. Less is known regarding the effect of glucocorticoids when used as replacement therapy on bone remodelling in patients with adrenal insufficiency. Dineen R., *et al.* measured 24-h serum cortisol/cortisone sampling, measurement of bone turnover markers, and a 24-h urine collection for measurement of urinary steroid metabolites [4]. They found that serum cortisol and cortisone and total urinary corticosteroid metabolites are negatively associated with bone turnover markers in patients receiving replacement doses of hydrocortisone, with nocturnal glucocorticoid exposure having a potentially greater influence on bone turnover.

Another importance affecting bone turnover is growth hormone [5]. Growth hormone is protective for preservation of BMD. Adult patients with growth hormone deficiency have tendency of decreased BMD [6]. To investigate the influence of preoperatively elevated GH to bone mass in acromegalic patients, we analyzed bone mineral density (BMD) and urinary type I collagen N-telopeptide (uNTX) in postoperative patients with somatotroph adenomas (SA), in comparison with patients with clinically non-functioning adenomas (NF). The mean T- and Z-score of BMD in radius of postoperative patients with SA were significantly higher than whereas those of postoperative patients with NF. Meanwhile, there was no significant difference in the mean T- and Z-score of BMD in lumbar spine between postoperative patients with SA and those with NF. Thus, BMD in radius is preferentially maintained in postoperative patients with SA. Thus, the preoperative elevated GH and IGF-1 are beneficial in the maintenance of bone mass in acromegalic patients.

## Conclusion

In conclusion, hypopituitarism including adult GH deficiency is one of the considerable risks of osteopenia, and therefore in surgery for pituitary or hypothalamic lesions, preservation of pituitary function and postoperative appropriate hormone replacement therapy are required.

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