Serum thyroid-stimulating hormone is elevated in men with Gleason 8 prostate cancer

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OBJECTIVE

To measure the levels of serum thyroid-stimulating hormone (TSH) in men with prostate cancer, as those with a Gleason score of ≥8 are at high risk of skeletal metastases (and should be considered for bone scintigraphy at diagnosis), and because the structural integrity of the skeleton depends on constant remodelling controlled by many local and systemic factors, including TSH, an important regulator of this process.

PATIENTS AND METHODS

We evaluated 51 men referred for treatment of localized prostate cancer and 10 with biopsy-confirmed benign prostatic hypertrophy. Serum TSH was determined with a chemoluminescent immunoassay and a commercially available instrument (Immulite, Diagnostic Products Corporation, Los Angeles).

RESULTS

There was significant variation in TSH levels with Gleason score ($P = 0.004$); men with Gleason 8 tumours had the highest serum TSH levels. Because serum TSH levels increase with age, we used a multivariate analysis of variance with both age and Gleason score as covariates. The effect of Gleason score on TSH level was significant ($P = 0.036$) and independent of the effect of age ($P = 0.392$).

CONCLUSION

We propose that the high serum TSH levels in men with Gleason 8 prostate cancer is a result of the elaboration of TSH by cancer cells. Bone mineral density in the face of normal levels of thyroid hormone depends on an intact response to TSH, which ordinarily suppresses both osteoblast and osteoclast differentiation, thereby exerting control over bone remodelling. However, with abnormally high TSH levels this process may become deranged, promoting the development of bone metastases. If TSH production by prostate cancer cells could be suppressed, the incidence of bone metastases might be reduced.

KEYWORDS

prostate, cancer, thyroid-stimulating hormone, bone metastasis

INTRODUCTION

Men with prostate cancer of Gleason score ≥8 have a high risk of skeletal metastases and should be considered for bone scintigraphy at diagnosis [1]. However, the mechanism for these metastases is uncertain and various causes have been suggested [2]. The skeleton is a dynamic organ whose structural integrity depends on constant remodelling, controlled by many local and systemic factors. Thyroid-stimulating hormone (TSH) is an important regulator of this process [3]. The established function of TSH is to promote thyroid follicle development and hormone secretion. However, there is evidence for direct effects of TSH on both components of skeletal remodelling, i.e. osteoblastic bone formation and osteoclastic bone resorption [4]. Because of the relationship of Gleason 8 prostate cancer to bone metastases, and the relationship of TSH to bone remodelling, we measured serum TSH levels in men with prostate cancer or BPH.

PATIENTS AND METHODS

The participants of the study were identified through radiation oncology and other clinics, and were accrued between 2001 and 2004; all eligible patients were asked to participate. All patients with prostate cancer had been initially diagnosed on the basis of a rising PSA level or abnormal physical examination, with a histological diagnosis confirmed in all. All participants gave informed consent and the study had Institutional Review Board approval. In all, we evaluated 51 men (mean age 68 years, SD 9, range 50–84) referred for treatment of localized prostate cancer and 10 with biopsy-confirmed BPH. Serum TSH levels were measured using a chemoluminescent immunoassay and a commercially available instrument (Immulite, Diagnostic Products Corporation, Los Angeles, CA).

RESULTS

The serum TSH levels of the patients stratified by Gleason score is shown in Fig. 1; there was a significant variation in TSH level in the groups ($P = 0.004$) and men with Gleason 8 tumours had the highest serum TSH levels. Because serum TSH levels increase with age [5] (Fig. 2) we used a multivariate ANOVA with both age and Gleason score as covariates. The effect of Gleason score on serum TSH levels was significant ($P = 0.036$) and independent of the effect of age ($P = 0.392$).

DISCUSSION

Bone metastases in prostate cancer are predominantly osteoblastic, with more irregular bone trabeculae; markers of bone resorption also increase, although there are similar numbers of osteoclasts [2]. Prostate cancer cells release PSA, a kallikrein serine

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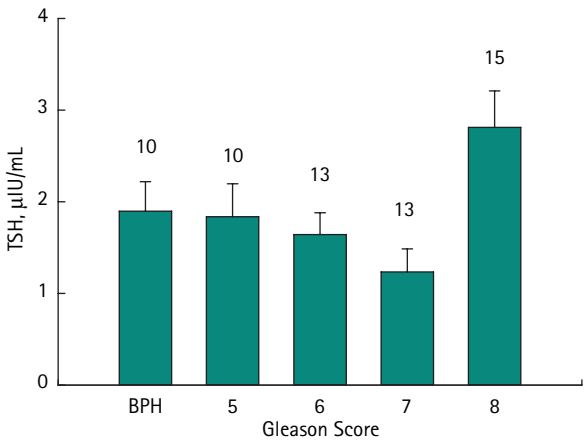

FIG. 1.
The mean (SEM) serum TSH level in 51 men with prostate cancer and 10 with biopsy-confirmed BPH, stratified by Gleason score. The variability is significant (P = 0.004, one-way ANOVA). The number of men in each group is indicated above the corresponding error bar.

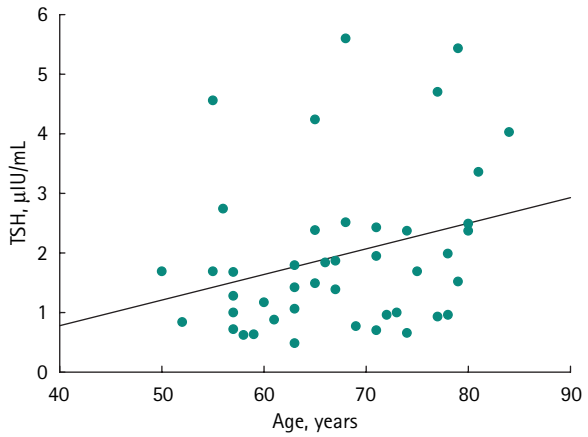

FIG. 2.
Serum TSH level plotted against age in 51 men with prostate cancer (r = 0.291, P = 0.056). The TSH values for normal men, assayed at our laboratory, is 0.4–4 μIU/mL.

protease that can cleave parathyroid hormone-related peptide, released by tumour cells [6], at the N-terminal. This cleavage may block tumour-induced bone resorption. In patients with prostate cancer high PSA levels are associated with bone metastases, but levels of bone resorption markers are also high in patients with bone metastases and reflect the extent of metastases more accurately than PSA level [2].

We suggest that the elevated serum TSH levels in men with Gleason 8 prostate cancer result from the elaboration of TSH by the cancer cells within the bone itself. The very high local level of TSH in the bone is reflected in the elevated serum TSH levels of patients with Gleason 8 tumours.

Bone mineral density in the face of normal levels of thyroid hormone depends on an intact response to TSH [4]. TSH ordinarily suppresses both osteoblast and osteoclast differentiation, thereby exerting control over bone remodelling. However, in the presence of abnormally high TSH concentrations, this process may become deranged, promoting the development of bone metastases. If TSH production by prostate cancer cells could be suppressed, the incidence of bone metastases might be reduced.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **TSH**, thyroid-stimulating hormone.