Prevention and treatment of secondary hyperparathyroidism: still a challenge for the nephrologist?

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Abstract

Secondary hyperparathyroidism is a well-known complication of chronic renal insufficiency. It is not only a state of increased parathyroid hormone secretion but also a state of parathyroid gland hyperplasia. Prevention and treatment of secondary hyperparathyroidism is a huge challenge for the nephrologist, despite new agents for the treatment of hyperphosphataemia, new vitamin D analogues and calcimimetics. The importance of parathyroid gland hyperplasia and the possibility of its reduction frequently are neglected issues. Ultrasonography could be very useful in detection of parathyroid gland size and shape and in the management of secondary hyperparathyroidism.

Keywords: parathyroid gland hyperplasia; secondary hyperparathyroidism; ultrasonography

Introduction

Secondary hyperparathyroidism (SHPT) is a well-known complication of chronic renal insufficiency. Bone disease, i.e. high-turnover bone disease, is not the only consequence of SHPT. There are also many extrarenal effects of parathyroid hormone (PTH), e.g. on the heart and blood vessels. It is thus very important to prevent and properly treat parathyroid gland overactivity.

The factors involved in the pathogenesis of SHPT are phosphate retention, decreased serum levels of calcitrol, and hypocalcaemia [1]. More important is that SHPT is a disorder of growth, and these factors are also involved in parathyroid gland (PTG) hyperplasia [2].

Prevention and treatment of SHPT is a huge challenge for the nephrologist, despite the availability of new agents such as treatment of hyperphosphataemia (new phosphate binders, e.g. sevelamer hydrochloride), new vitamin D analogues (paricalcitol, doxercalciferol, 22-oxacalcitriol) and calcimimetics [3]. These agents are, however, still not available in many countries. On the other hand, in our opinion, the importance of PTG hyperplasia and the possibility of its reduction frequently are neglected issues.

Ultrasonography in the management of secondary hyperparathyroidism

More than 15 years ago, we started to use sonography to detect enlarged PTGs [4]. We believed then that the number and localization of enlarged PTGs are important [5]. With the advance of ultrasonography and progress in basic research of parathyroid cell function, we have changed our view. Today, we know that SHPT is not only a state of increased PTH synthesis and secretion, but also a state of PTG hyperplasia [2]. There are two forms of PTG hyperplasia, diffuse and nodular [1,2]. PTGs with nodular hyperplasia are larger (>0.5 cm³ or 1 cm in diameter), and the nodules are made up of cells with a significantly reduced number of vitamin D- and calcium-sensing receptors [1,6]. Patients with nodular PTG hyperplasia are often resistant to vitamin D therapy.

Ultrasonography (7.5 or 10 MHz linear probe with colour Doppler for small parts) is used regularly in the follow-up of our uraemic patients, together with measurement of the intact PTH and biochemical markers of bone turnover. By sonography, we are able to detect the size and shape of PTGs. Furthermore, different echo patterns of PTGs can be found. Uniform echoes are found in smaller glands (diffuse hyperplasia). A nodular echo pattern and, occasionally,
degenerative changes (calcificates, cystic and fibrotic changes), are found in larger PTGs (nodular hyperplasia) (Figure 1) [7]. By use of colour Doppler, a difference in vascularity could be detected. In larger glands, we have observed more frequently either paranodulary vascularity or the presence of a hypervascular capsule [8].

Our approach to treatment of uraemic patients is the following. The severity of hyperparathyroidism is diagnosed by the level of intact PTH and PTG sonography. If diffuse hyperplasia is suspected (one or more PTGs enlarged <0.5 cm³), the patient is treated by phosphate binders and calcitriol. In some patients with very high PTH levels, after normalization of the calcium or phosphate level, we try oral pulse calcitriol therapy (3–4 μg twice weekly). In the case of one or two more enlarged PTGs (>0.5 cm³), we perform ablation of the PTG by percutaneous ethanol injection (PEIT), which is performed on an out-patient basis. Usually, we inject up to 1 ml of ethanol. The effect of PEIT is monitored by ultrasound after 3–4 weeks (changes in echo pattern and blood supply) and by measuring serum PTH levels. If there are no significant changes, further PEIT is performed. In the case of two glands with nodular hyperplasia, ablation is done first in one and a few days after in the other gland. All patients are then followed-up with medical therapy, i.e. calcitriol oral pulse therapy. If more than two glands are suspected to have nodular hyperplasia, parathyroidectomy is unavoidable [9].

Conclusion

Despite new drugs, prevention and treatment of SHPT is still a challenge for the nephrologist. Based on our experience, and that of our Japanese colleagues, ultrasonography is very important in detection of the size and shape of PTGs and the severity of SHPT [10]. It is an inexpensive and non-invasive method. PEIT could be a useful and powerful method in the hands of an experienced operator.

References