THE ADVANTAGE OF DOUBLE PHASE ^{99M} TC-MIBI SCINTIGRAPHY OVER DUAL-TRACER SUBTRACTION METHOD IN TERTIARY HYPERPARATHYROIDISM WITH SICK EUTHYROID SYNDROME

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ABSTRACT

Pre-operative parathyroid scintigraphy can be performed by 2 major means, dual-tracer subtraction method and double-phase ^{99m}Tc-MIBI method. Although, the sensitivities of both techniques are similar, many types of patient cannot be studied using the former one. Here is a case of tertiary hyperparathyroidism in chronic renal failure who has co-existing sick euthyroid syndrome causing no uptake of ^{99m}Tc-pertechnetate. The double-phase ^{99m}Tc-MIBI technique in this type of patient is proven to be more useful.

Key words: Sick euthyroid syndrome, parathyroid scintigraphy, tertiary hyperparathyroidism; chronic renal failure

INTRODUCTION

Tertiary hyperparathyroidism develops from secondary hyperparathyroidism in which the parathyroid glands turn to be autonomous function. Some studies have proven that preoperative localization of parathyroid glands decreased the time required for surgery and lowered the incidence of complications.[1] Parathyroid scintigraphy using dual-tracer ^{99m}Tc-pertechnetate/^{99m}Tc-MIBI (methoxyisobutyl isonitrile) subtraction method has proven to be a bit more sensitive than double-phase ^{99m}Tc-MIBI imaging.[2] However, in patient with chronic disease, parathyroid scintigraphy using dual-tracer subtraction method will be less useful.

This paper presents a case of patient with tertiary hyperparathyrodism in chronic renal failure and the superiority of using double phase ^{99m}Tc-MIBI scintigraphy over subtraction method in this type of patient.

CASE REPORT

A 22 year old female patient underlying chronic renal failure for 7 years was treated by chronic ambulatory peritoneal dialysis (CAPD) for 5 years. Four months ago she had pelvic pain and was treated by oral vitamin D. . She was referred

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for parathyroidectomy. On physical examination, the patient looked chronically ill without other abnormal findings. Laboratory evaluation for PTH level is 1400 pg/ml (normal= 10-60), alkaline phosphatase = 3224 u/L (normal=98-279), serum calcium = 11.3 mg/dl (normal=9-10.5), serum phosphate = 7.7 mg/dl (normal=3-4.5). Ultrasonography of neck showed enlargement of bilateral superior parathyroid glands, size 0.95x1.44x0.48 cm on the right and 0.80x1.26x0.52 cm on the left, suggestive of adenomas. Parathyroid scintigraphy was then performed to confirm ultrasound diagnosis and to seek for other abnormal parathyroid glands. Two techniques were employed sequentially, the dual-tracer ^{99m}Tc pertechnetate/ ^{99m}Tc MIBI subtraction technique and double phase ^{99m}Tc MIBI technique . In the first technique (Fig. 1), the thyroid failed to take up ^{99m}Tc-pertechnetate. ^{99m}Tc MIBI was then injected to do the double phase technique (Fig. 2). The first phase obtainted immediately after injection of ^{99m}Tc-MIBI showed thyroid gland uptake with 2 foci of increased uptake in upper pole of both lobes and 2 other foci in lower neck area outside the thyroid gland. The late phase at 2 hr showed washout of radioactivity from the thyroid gland but remaining radioactivity in all 4 abnormal foci seen in early phase. This finding is suggestive of four parathyroid glands enlargement. There was neither positive history of high iodide intake or drugs that may cause poor ^{99m}Tc-pertechnetate uptake nor positive physical examination of thyroid hypofunction or thyroiditis. The blood test for T3 was 77 ng/dl (normal= 80-180 ng/dl), T4=4 mg/dl (normal=6-12 mg/dl), TSH = 0.2 IU/ml (normal=0.5-4 IU/ml).

At surgery, enlargement of 4 parathyroid glands were found and 3 ½ glands were resected. The histopathologic examination reveals nodular hyperplasia of all parathyroid glands.

Four months later, repeat thyroid scan with ^{99m}Tc-pertechnetate (Fig. 3) showed improvement of uptake in both thyroidal lobes compared to the first study. The blood test for T3=74 ng/dl, T4=8 mg/dl, TSH=9 IU/ml, FT4=0.7 ng/dl (normal=0.65-2)

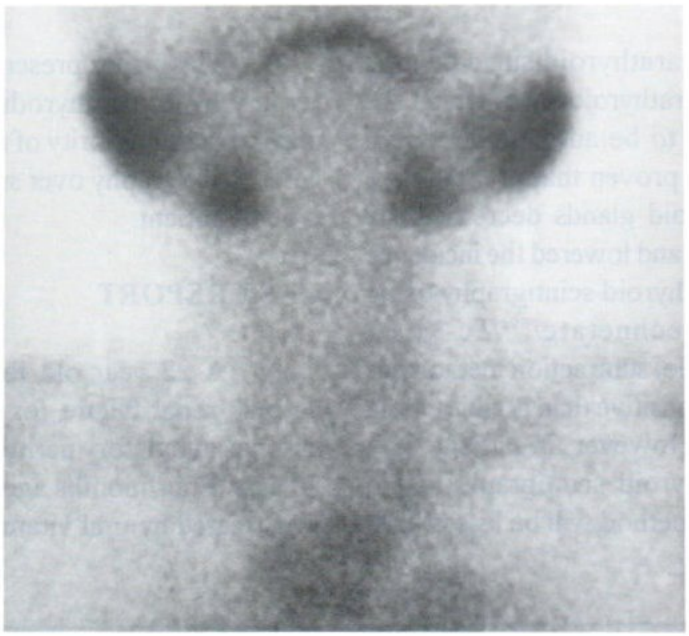

Fig.1 In the dual-tracer ^{99m}Tc-pertechnetate/ ^{99m}Tc-MIBI subtraction technique, ^{99m}Tc-pertechnetate scintigraphy which was performed first showed no uptake in the thyroid gland. This caused failure of the subtraction technique.

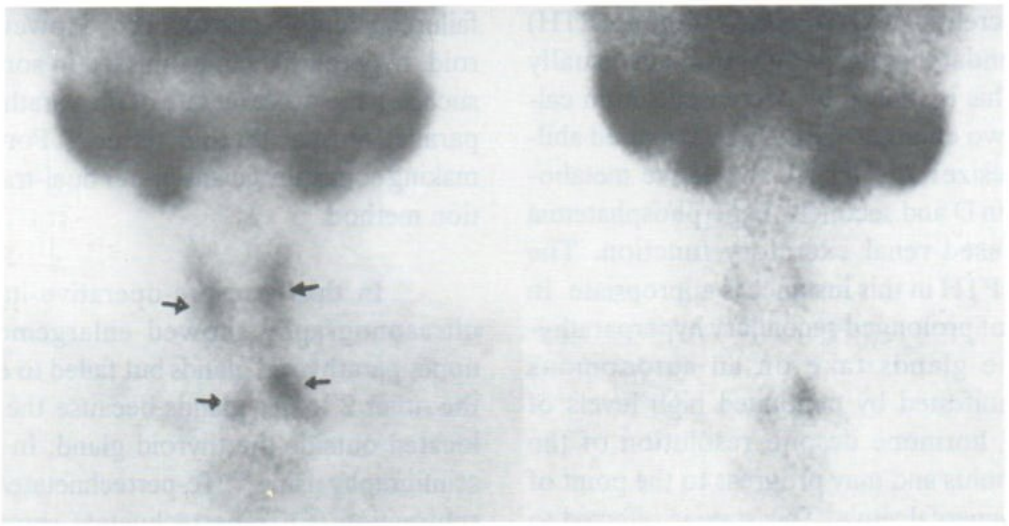

Fig.2 Double-phase ^{99m}Tc-MIBI scintigraphy: The immediate post injection scintigraphy (left) showed uptake in both the thyroid gland and parathyroid glands (arrows). The delayed 2-hour after injection scintigraphy (right) showed washout of radioactivity from the thyroid with remaining activity in 4 parathyroid glands.

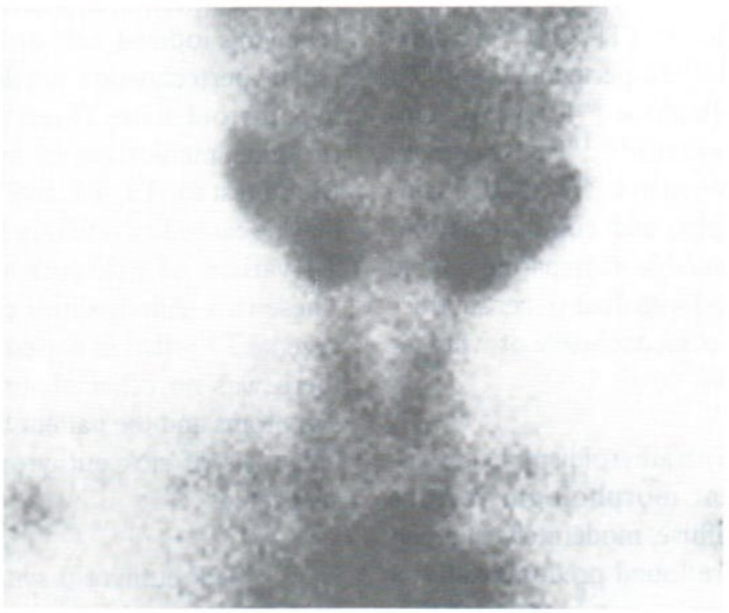

Fig.3 ^{99m}Tc-pertechnetate thyroid scintigraphy 4 months later showed faint but improved uptake in both lobes of thyroid gland.

DISCUSSION

In patients with chronic renal failure, increased secretion of parathyroid hormone (PTH) called secondary hyperparathyroidism usually develops. This is caused by decreased serum calcium from two etiologies. Firstly by impaired ability to synthesize1,25(OH_2)D, the active metabolite of vitamin D and secondly, hyperphosphatemia from decreased renal excretory function. The response of PTH in this instance is appropriate. In some cases of prolonged secondary hyperparathyroidism, the glands take on an autonomous function manifested by continued high levels of parathyroid hormone despite resolution of the original stimulus and may progress to the point of producing hypercalcemia. This state is referred to as tertiary hyperparathyroidism.[3,4]

Before surgery, localization of parathyroid glands can be done by many means. Comparison have been made among ultrasonography, computed tomography, dual-tracer (Tl-201/^{99m}Tc-pertechnetate, ^{99m}Tc-MIBI/^{99m}Tc-pertechnetate, ^{123}I / ^{99m}Tc MIBI), and double-phase ^{99m}Tc-MIBI scintigraphy with varying results.[3,5,6,7] The sensitivity and specificity of double phase ^{99m}Tc-MIBI scintigraphy, ultrasonography, and computed tomo graphy seem to be comparable. Comparing double phase ^{99m}Tc-MIBI method with dual-tracer subtraction method, the result is inconclusive of whether which modality is better.

In tertiary hyperparathyroidism, hyperplasia is the predominant morphologic feature accounting for 95%.[8] Diffuse, moderately enlarged hyperplastic glands were found predominantly in patients with renal transplants, whereas nodular, markedly enlarged hyperplastic parathyroids were observed more frequently in patients treated by dialysis as seen in this case. Four gland parathyroid enlargement is a frequent finding.[9] ^{99m}Tc-MIBI, which use different washout rate of thyroid and parathyroid, is able to identify more than 80% of hyperplastic parathyroid glands in renal failure patients in one report[10]. However, parathyroid hyperplasia can be missed in some instances such as if the washout rate of the parathyroid glands parallel normal thyroid tissue.[11] For this reason making some physicians prefer dual-tracer subtraction method.

In this case pre-operative imaging with ultrasonography showed enlargement of both upper parathyroid glands but failed to demonstrate the other 2 lower glands because the lower ones located outside the thyroid gland. In parathyroid scintigraphy using ^{99m}Tc-pertechnetate/^{99m}Tc-MIBI subtraction (^{99m}Tc-pertechnetate should be taken up by thyroid and ^{99m}Tc-MIBI should be taken up by both thyroid and parathyroid), thyroid did not take up ^{99m}Tc-pertechnetate but took up ^{99m}Tc-MIBI making it unable to perform subtraction. This raises the question of whether the patient had been receiving iodized salt or other medication that inhibit pertechnetate uptake, or the patient is in hypothyroid state. There was no positive history of either medication or hypothyroid symptoms. Blood test for T3, T4, and TSH were all low. This may be caused by pituitary hypothyroidism or low-T4 variant of sick euthyroid syndrome (SES). These two abnormalities can be differentiated by reverse T3[12] that is not currently available. Since there was no other abnormal pituitary signs or symptoms and the patient has chronic disease, the diagnosis of sick euthyroid syndrome was then suspected.

Sick euthyroid syndrome is an abnormality that is caused by severe illness which induce changes in thyroid hormone economy. Abnormalities in SES include alterations in the peripheral transport and metabolism of thyroid hormones; the regulation of TSH secretion; and in some cases changes in thyroid function itself. These lead to changes in the concentrations of the circulating

thyroid hormones[12]. SES in this patient was proven later by repeating thyroid scan with ^{99m}Tc-pertechnetate and thyroid hormone test when the patient condition improved. The repeat scan reveals improvement of uptake of ^{99m}Tc-pertechnetate and the blood test also improved.

The other question is why thyroid in sick euthyroid patient doesn't take up ^{99m}Tc-pertechnetate but does take up ^{99m}Tc-MIBI. This may be explained by the mechanism of uptake. Pertechnetate is trapped by the thyroid in the same manner as iodide but is not organified[13]. Since trapping is stimulated by TSH, lack of TSH can cause impair in ^{99m}Tc-pertechnetate uptake. Whereas for ^{99m}Tc-MIBI the uptake is neither mediated by iodide trapping mechanism[14] nor related to TSH control[15]. In cultured mouse fibroblasts, ^{99m}Tc-MIBI uptake and retention were determined by both mitochondrial content and plasma membrane potentials.[16] This can be concluded that the hyperparathyroid patients in whom chronic disease is the problem such as in chronic renal failure, the technique using double-phase ^{99m}Tc-MIBI scintigraphy might be better than dual-tracer subtraction methods.

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