Parathyroid and bone imaging in primary hyperparathyroidism

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Abstract Skeletal derangements occur quite often in patient with primary hyperparathyroidism (PHPT). We investigated parathyroid and bone imagings in 59 cases of pathologically proven PHPT. Forty-nine cases were pathologically proven parathyroid adenomas; 8 presented hyperplasia and the other 2 were adenocarcinomas. Parathyroid imaging (early phase imaging, EPI) was conducted at 30 min after injecting 740~925MBq ^{99m}Tc-MIBI and 2~3h later (delayed phase imaging, DPI) separately. The following thyroid imagings were performed at the same posture 10 min after intravenous injection of 74~111MBq $^{99m}TcO_4^-$. The $^{99m}Tc^-$ MIBI subtraction imaging data were obtained by subtracting thyroid imaging from that of DPI. Among 49 cases of proven hyperparathyroid adenoma 45 yielded positive imagings. Eight cases with hyperplasia gave negative results. The results were positive in 2 cases of parathyroid adenocarcinoma. Results of ^{99m}Tc-MDP/bone imaging: 35 cases of hyperparathyroid adenocarcinoma (disease duration 1-6 months) showed normal bone images, while 14 cases showed superscan images, course being 4~12 months. Bone imaging for 2 cases of adenocarcinoma showed multiple, radioactive aggregated foci (brown tumor imaging); course lasting 10~24 months. The results of bone imaging in 8 cases of hyperplasia/ hyperparathyroidism were normal. It was concluded that diagnostic accuracy for parathyroid was 79.6% and for parathyroid adenoma was 91.8%, and the technique has no diagnostic value for hyperplasia. The ^{99m}Tc-MDP / bone imaging results for PHPT can be classified into three categories, i.e. normal, superscan and brown tumor. The imaging results correlated well with the different categories and degrees of bone damage, the duration of clinical course and the pathological types. Therefore, it's important to use bone imaging data in association with therapy to reflect the stage and progress of PHPT.

Keywords Parathyroid imaging, Bone imaging, Primary hyperparathyroidism

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Skeletal changes occur quite often in patients with primary hyperparathyroidism (PHPT). Fifty-nine cases of PHPT proven pathologically were investigated by means of parathyroid imaging (PTI) and bone imaging (BI). The techniques and image formation were studied and compared, and the appearance of BI was highlighted.

1 Materials and methods

59 PHPT inpatients, 23 male and 36 female were enrolled. Age ranged from 17 to 74 (average 45.1). All patients were proven pathologically. Among them 49 were parathyroid adenoma, 8 were hyperplasia and 2 were adenocarcinoma.

Methods: Imaging machine – Toshiba SPECT, GCA 409A/SA, pinhole collimation. Delayed phase imaging (DPI) and subtraction imaging (SI) were applied at the same time individually. Each patient received 740~925MBq of ^{99m}Tc-MIBI. The first imaging (early phase imaging, EPI) was carried out 15 min after intravenous injection, and the second imaging (DPI) was carried out 2~3 h after the first injection. After the second imaging, 74~925MBq of $^{99m}TcO_4^-$ was injected immediately intravenously and the figure data mentioned above in the same posture (thyroid phase) were collected 5 min later. Thus the data were computerized to get SI figure (DPI minus TP). The diagnosis was made by reading the corresponding films of DPI vs SI in combination.

Bone imaging: Within two weeks after the completion of PTI, ^{99m}Tc-MDP were carried out with an injection dose of 925~1110MBq. Three hours later, emission computed tomography (ECT) was carried out on Toshiba GCA 409A/SA machine (low energy

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level, parallel pinhole collimator, ichnographic pictures were taken partly or from head to foot).

Imaging data were treated statistically using SPSS software package, the "*p*" value was calculated.

2 Results

2.1 Types of PTI figures

The imagings of the 59 patients with PHPT can be categorized into two groups except the 8 patients with hyperplasia (PTI -- negative).

a) Type 1 – Aggregated foci seen beyond the lower extreme of unilateral thyroid, i.e. thyroid lower border type. See Fig.1(a).

b) Type 2 – Radioactive aggregated foci seen in the unilateral gland body, i.e. thyroid body type. See Fig.1(b).

The former one accounts for 64.7% (30/47), and the latter – 35.2% (17/47).

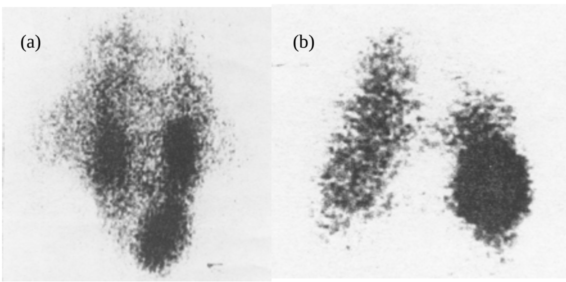

Fig.1 (a) PHPT, PTI (delayed phase image, thyroid lower border type) (b) PHPT, PTI (delayed phase image, thyroid body type)

2.2 Comparison of DPI (delayed phase image) and SI (subtraction image) on the diagnosis of PHPT

The results are shown in Table 1.

With parathyroid adenoma the data of DPI and SI showed significant difference (p=0.002). As regards the other two types, it is difficult to draw any conclusion as the number of cases was too few.

The results also indicated that for hyperplasia PHPT was nil uptake, therefore, it had no diagnostic value. DPI technique for the diagnosis of parathyroid adenoma is superior to SI.

2.3 Comparison of PTI, ultrasonography, and X-CT

The results are shown in Tables 2 and 3. The results indicated that there were differences between PTI, ultrasonography, and X-CT. However, the differences (PTI vs ultrasonography and PTI vs X-CT) were not highly significant (p=0.05; p=0.05). With regard to hyperplasia and adenocarcinoma it is difficult to draw any conclusion due to the small case number.

The results also indicated that for the diagnosis of parathyroid adenoma PTI was superior to X-CT and ultrasonography. However, for the diagnosis of hyperplasia, PTI was less superior to X-CT and ultrasonography. In general, as far as diagnostic accuracy was concerned the three techniques are comparable for PHPT.

Table 1 Comparison of DPI and SI on the diagnosis of PHPT

Type of PHPT	DPI		SI	
	Number of positive cases	Diagnostic rate (%)	Number of positive cases	Diagnostic rate (%)
Parathyroid adenoma (49 cases)	45	91.8	39	80.0
Hyperplasia (8 cases)	0	0	0	0
Adenocarcinoma (2 cases)	2	100	2	100

Table 2 Comparison of diagnostic value with PTI and ultrasonography (46 patients with PHPT)

Type of PHPT	Parathyroid image (PTI)		Ultrasonography	
	Case number of positive	Diagnostic rate (%)	Case number of positive	Diagnostic rate (%)
Parathyroid adenoma (36 cases)	34	94.4	29	80.5
Hyperplasia (8 cases)	0	0	3	37.5
Adenocarcinoma (2 cases)	2	100	2	100
Total case number (46)	36	78.2	34	73.9

Table 3 Comparison of diagnostic value with PTI and X-CT (33 patients with PHPT)

Type of PHPT	Parathyroid Image (PTI)		X-CT	
	Case number of positive	Diagnostic rate (%)	Case number of positive	Diagnostic rate (%)
Parathyroid adenoma (25 cases)	23	92.0	19	76
Hyperplasia (6 cases)	0	0	4	66.6
Adenocarcinoma (2 cases)	2	100	2	100
Total case number (33)	25	75.7	25	75.7

2.4 Bone imaging for PHPT

(1) Among 49 cases of parathyroid adenoma/PHPT thirty-five bone imaging results were negative, with the duration of disease from 1 to 6 months. The other 14 bone imaging figures were abnormal: ten of them appeared superscan (See Fig.2); and 4 cases presented restricted foci with radioactive, aggregated appearance in the bone. Among the 10 cases showing superscan (See Fig.2) 4 cases showed restricted foci with radioactive, aggregated appearance in the bone, 3 were fibrous osteitis, and the other one was fibrosteocy (See Fig.3).

(2) Bone imaging for 8 cases of hyperplasia PHPT showed normal, duration lasting 1~6 months.

(3) Bone imaging for 2 cases of parathyroid adenocarcinoma manifested brown tumor, which looked like metastasis bone cancer. Care must be taken clinically that it is easy to confuse this situation with bone cancer (See Fig.4).

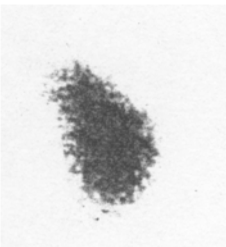

Fig.2-1 PHPT (Case 1) PTI showing parathyroid adenoma.

Fig.2-2 PHPT (Case 2) Non-typical osteopetrosis diagnosed by X-ray bone imaging –superscan.

Fig.2-3 PHPT (Case 1) Osteopetrosis, compact in bone-density by X-ray, cortex thickened, bone trabecula thickened.

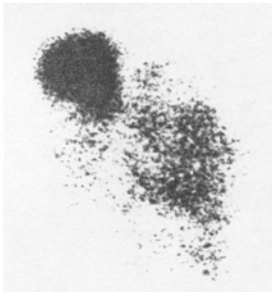

Fig.3-1 PHPT (Case 2) Bone imaging showing parathyroid adenoma.

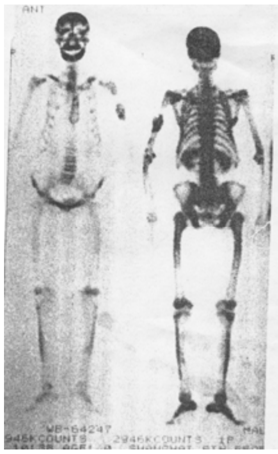

Fig.3-2 PHPT (Case 2) Bone imaging showing abnormal radioactivety aggregated in skull and mandible, increment in radioactivity at long bone, radioactivity aggregated in left humerus indicated fibrosteocyst.

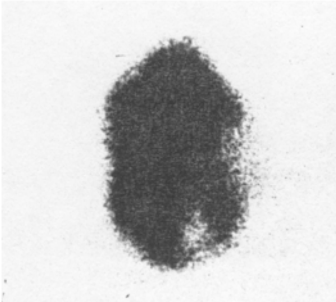

Fig.4-1 (Case 3) PHPT adenocarcinoma image, showing radioactive condensed aggregates in the tumor area. There were sparse radioactive region in the foci.

Fig.4-2 (Case 3) PHPT adenocarcinoma, bone image showing multiple radioactive condensed foci with brown tumor appearance.

3 Discussion

3.1 Regarding technical problems

Double phases imaging (i.e. delayed imaging) and subtraction imaging techniques are used frequently in parathyroid imaging. The reasons of false negative results for the double phase imaging technique are as follows: 1) Foci uptake is too low; 2) If the amount of injecting chemicals is too huge, the delayed time will not be enough and the background will be too dense; 3) Using parallel pinhole collimator, the thyroid image is getting smaller.

Subtraction imaging technique also makes false negative results. The reasons are as follows: 1) In case of thyroid body type of parathyroid adenoma (Fig.1(b)), after injecting $^{99m}TcO_4^-$ and taking thyroid phase, the thyroid image included the image of adenoma. Therefore, when this image minus delayed phase image of PTI image, it is easy to get false negative result; 2) During the process of subtraction imaging, if the posture of the patient moved, false negative result could appear.

In order to raise the accuracy rate in the PTI diagnosis, we recommend to adopt double phase imaging and subtraction imaging simultaneously; they are complementary.

According to Ref.[1], when positive scanning was conducted on thyroid using ^{99m}Tc-MIBI or ^{201}T1, 10% benign nodules in thyroid and 95% malignant thyroid cancer will manifest radioactive aggregation. Therefore, it is better to understand whether the patient had nodules in the thyroid before PTI to avoid making false positive result.

3.2 Comparison between ultrasonography and X-CT

The value of PTI, ultrasonography and X-CT on the diagnosis of PHPT seems controversial[1]: ultrasonography varies from 21% to 92%; X-CT — 58% to 100%; MRI — 57% to 78%; Nuclear medicine — 42% to 92%. Many factors influence the rate of accuracy, such as the percentage of hyperplasia in the patients, the size and position of adenoma and so on.

We suggest that PTI has no diagnostic value in the diagnosis of hyperplasia PHPT. The reasons are as follows: 1) The affected glands in patients with hyperplasia were enlarging bilaterally at the same time. Since ^{99m}Tc-MIBI is a tumor-philic developing chemical, uptake in the affected non-tumor tissue will be much limited; 2) ^{99m}Tc-MIBI is washed away quite fast in the proliferating gland; therefore, it is hard to distinguish the stained foci from the surrounding background.

However, the diagnostic accuracy rate of PTI for adenoma and adenocarcinoma are relatively high (>90%), and superior to X-CT and ultrasonography. The resonance waves from ultrasonographic instrument against thyroid adenoma and thyroid are similar; and they are difficult to discriminate. The density of parathyroid and its surrounding fatty tissue are almost alike; their response to X-CT is also the same. This might be the cause for false negative diagnosis; particularly small adenoma is difficult to be distinguished from the surrounding tissue. However, the technique is obviously superior to nuclear medicine with regard to diagnosis of hyperplasia PHPT.

The accuracy rates of these three techniques in the diagnosis of PHPT are comparable.

3.3 Bone imaging in the diagnosis of PHPT

PHPT affects mainly two organs, i.e. bone and kidney[2,3]. In 1974 Sy MW[4] reported that PHPT had specific bone imaging with enforced radioactivity in the mandible. Zhu[5] also reported that the bone imagine appearance in PHPT patients correlated with the stage and progress of the disease. Pathological changes in bone marrow of the patients reflected on osteocytes, osteoclasts, and osteogenic cells which became highly active; obvious osteolysis and osteopenia could be seen; under superscan condition osteoplastica may often be accompanied. Since secretion of PTH was overactive, original bone material was absorbed. Meanwhile, osteogenic process accelerated to form new bones and mal-calcification emerged. These pathological effects formed vast cystoid foci. See Fig.3. In the lesion area manifested radioactive foci, where individual foci showed a non-uniform and sparse radioactive distribution. These circumstances occurred mostly in osteopiphysis or mandible. When the previous bled blood in the cyst cavity turned into brown-yellow with time, it is called brown tumor. Brown tumor in bone is benign in character. Brown tumor will disappear after curing of PHPT. Therefore, it is important to discriminate brown tumor from metastatic bone tumor.

Osteopetrosis (Albert-Schonberg sickness or marble bones) is seldom seen in PHPT. See Fig.2. The appearance of osteopetrosis in bone imaging is superscan. The results of this paper indicated that there were 3 categories obtained from the bone images for PHPT, i.e. normal, superscan and brown tumor. The classification is of utmost importance on the severity of bone involvement as well as the progress of PHPT. Particularly, the latter two categories are quite easy to confuse with metastatic bone tumor. The clinical significance of bone imaging for PHPT is as follows: 1) With or without skeletal involvement; 2) The severity and position of skeleton involvement; 3) The results of bone imaging are referential to estimate the degree of disease severity and possible duration of the course.

Therefore, it provides important clinical information.

3.4 Parathyroid adenocarcinoma

In this paper two cases of parathyroid adenocarcinoma were included, only 2% of PHPT. The imaging showed an extreme radioactive condensed region. In bone imaging multiple radioactive condensed foci (brown tumor) can be seen. See Fig.4.

4 Summary

1) PTI is superior to X-CT and ultrasonography in the diagnosis of adenocarcinoma, but it has no diagnostic value for hyperplasia.

2) In order to increase diagnostic sensitivity of PTI, it is better to conduct delayed phase imaging and subtraction imaging simultaneously.

3) Bone imaging for PHPT is helpful to estimate the severity of bone affection and the duration of courses.

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