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Parenchymal Weight of the Parathyroid Gland and the Kidney in Chronic Glomerulonephritis

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MORI, S. Parenchymal Weight of the Parathyroid Gland and the Kidney in Chronic Glomerulonephritis. Tohoku J. exp. Med., 1978, 125 (1), 85-91 — This histomorphometrical study was performed on the kidney and the parathyroid glands of autopsy cases of chronic glomerulonephritis. The kidneys showed atrophy in varying degrees. Weight of the parathyroid glands increased because of proliferation of parenchyma. Weight of parathyroid parenchyma correlated negatively with weight of the kidney and volume density of tubules in renal cortex. —— morphometry; parenchymal weight; hyperplasia; atrophy

Secondary hyperparathyroidism is frequently observed in the course of chronic renal failure, and parathyroid hyperplasia of varying degrees is usually found but its pathogenesis is still unknown (Albright et al. 1937; Berson and Yalow 1966; Reiss et al. 1969; Roth and Marshall 1969; Brickman et al. 1974; Bordier et al. 1975). To solve this problem, the pathomorphological evidence of the relationship between reduction of the kidney volume and hyperplasia of the parathyroid gland is required. This paper concerns with the relationships disclosed between the two parameters mentioned above.

MATERIALS

Materials were 13 autopsy cases of chronic glomerulonephritis without clinical evidence of hyperparathyroidism. They were composed of 5 males and 8 females, their ages ranging from 25 to 71 years. Parathyroid glands were studied in all cases. Weights of the kidneys were measured in 11 cases and histological sections of the kidneys were obtained from 13 cases. Control 163 parathyroid glands were taken at necropsy from 49 subjects of ages ranging 21 to 69 years.

METHODS

Morphometry of the parathyroid gland

Weighing and sectioning of the parathyroid gland. The parathyroid glands fixed in 10% formalin were washed in tap water. After careful removal of the periglandular connective tissue, the glands were weighed by a torsion balance of Shimazu Manufactory Co., Ltd. Then the glands were processed into paraffin blocks by the routine method. Paraffin sections of 3 μm thick were stained with hematoxylin and eosin, and Weigert’s elastica with Masson-Goldner.

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Measurement of parenchymal weight. The notion of parenchymal weight of the parathyroid gland can be defined as weight of the parathyroid tissue other than the stromal adipose tissue. Parenchymal weight is approximated by the following equation.

\[ m' = \frac{P \cdot sp}{P \cdot sp + F \cdot sf} \times m \]  

- **m**: whole weight of the parathyroid gland (mg)
- **m'**: weight of the parathyroid parenchyma (mg)
- **P**: volume density of the parathyroid parenchyma (%)
- **F**: volume density of the stromal adipose tissue in the parathyroid gland (%)
- **sp**: specific gravity of the parathyroid parenchyma
- **sf**: specific gravity of the parathyroid stroma

Among these parameters, the values of (P), (F) and (m) were observed to fluctuate very widely from case to case in preliminary observations. On the other hand, the values of (sp) and (sf) were constant irrespective of cases. Therefore, in the following study, the values of (sp) and (sf) were determined at first, then the values of (P), (F) and (m) were measured in each parathyroid gland, and finally the parenchymal weight (m') was calculated by the equation (a).

i) Determination of the specific gravity of the parathyroid stroma (sf).

The value of (sf) was determined measuring the specific gravity of mediastinal adipose tissues taken from 9 autopsy subjects. Each adipose tissue was put into water solution of ethylalcohol at various concentrations. The solution of the same specific gravity as the adipose tissue was determined, and the specific gravity of the solution was measured by a Baume’s standard hydrometer. Possible fluctuation of the specific gravity of the solution due to dissolution of the adipose tissue in the alcohol medium during the measuring maneuver was minimal enough to be disregarded. The average value of the specific gravity of these adipose tissues was 0.94±0.11. It was reasonable to regard the value of (sf) as 0.94.

ii) Determination of the specific gravity of the parathyroid parenchyma (sp).

The whole weight of the parathyroid gland (m) and its specific gravity (s) are calculated as follows:

\[ m = v \cdot (F \cdot sf + P \cdot sp) \]  
\[ s = m/v \]

- **v**: volume of the parathyroid gland
- **s**: specific gravity of the parathyroid gland

Specific gravity of the parathyroid parenchyma (sp) is expressed as:

\[ sp = \frac{s - F \cdot sf}{P} \]

The values of (P) and (F) were represented by percentage of the parenchymal and stromal areas respectively in the largest cut surface of the gland. A point counting method was employed to evaluate the values of (P) and (F). The measurement of (s) was performed by the same method as that of (sf). Here, water solution of AlCl₃ of various concentrations was employed instead of ethylalcohol. As a value of (sf), 0.94 was used.

In order to determine the value of (sp), 10 parathyroid glands were collected from 5 autopsy cases. Values of (P), (F) and (s) were measured in each gland and (sp) was calculated by the equation (d). The average value of (sp) of these 10 glands was 1.049±0.011, and (sp) was determined to be 1.05.

iii) Calculation of parenchymal weight.

Values of (m), (P) and (F) were measured in each parathyroid gland of control subjects and cases of chronic glomerulonephritis. On the assumption that (sp) and (sf) were constant irrespective of cases, parenchymal weight of the parathyroid gland was calculated according to the equation (a).
Observation of the kidney

After weighing, 3 mm thick slices including cortex and medulla were obtained from both kidneys and fixed in 10% formalin and made into paraffin blocks. Sections of 3 μm thick were stained with Weigert’s elastica with Masson-Goldner and prepared for the light microscopy. Volume density of tubules was measured in renal cortex out of glomeruli and large blood vessels.

RESULTS

In our 13 cases of chronic glomerulonephritis, the stromal adipose tissue of the parathyroid glands was displaced in varying degrees by increased parenchyma as morphological signs of secondary hyperplasia (Fig. 1). In order to study in detail the degree of hyperplasia, parenchymal weight of the parathyroid gland was examined by the histometrical method mentioned previously.

In the 49 controls, effect of aging was not observed in whole weight of the parathyroid gland. On the other hand, parenchymal weight decreased slightly with advancing age but any statistical significance was not detected between age groups (Fig. 2). In these control cases, the average value of whole weight per one gland was 23.3±8.6 mg, and the average value of parenchymal weight per one gland was 18.6±6.0 mg. In cases of chronic glomerulonephritis, the parathyroid glands were higher in weight of the whole gland and of the parenchyma than the controls. In these cases, the single whole gland weighed 35.5±16.9 mg, and parenchymal weight was 28.5±13.6 mg. The differences were statistically significant according to the Student’s t test (Fig. 3, Table 1). On the other hand, cases
Fig. 2. Weight of the parathyroid gland of control cases. The weight is represented by mean±1 S.D. per one gland in cases of respective age groups. Whole weight of the parathyroid gland (open circle and dotted line) was constant with advancing age. A slight decrease in parenchymal weight (closed circle) was observed with aging, but any statistical significance was not detected between age groups.

Fig. 3. Weight of the parathyroid gland of cases of chronic glomerulonephritis. Shaded areas represent mean±1 s.D. of control cases. Closed circles represent the cases of chronic glomerulonephritis. The values represent mean weight per one gland in respective cases. In the cases of chronic glomerulonephritis, the parathyroid glands were higher in weight of the whole gland and of the parenchyma than the controls. These differences were statistically significant according to the Student’s t test.

of chronic glomerulonephritis showed no significant difference of stromal weight from the controls. These data indicated that parenchymal hyperplasia resulted in increase in weight of the parathyroid gland.

Then the relationship between weight of the parathyroid gland and that of the kidney was examined. The kidneys were contracted in varying degrees. The sum of the weight of the bilateral kidneys ranged from 95 g to 400 g (Table 1). As the degree of contraction of the kidney progressed, parenchymal weight of the parathyroid glands increased (Fig. 4). This relationship was statistically significant (r=-0.63, p<0.05). The volume density of tubules in the renal cortex also correlated negatively with parenchymal weight of the parathyroid glands (r=-0.68, p<0.01) (Fig. 5).

Discussion

Investigation of the parathyroid glands in chronic glomerulonephritis without clinical signs and symptoms of hyperparathyroidism has not yet been done
TABLE 1. Weight of the parathyroid gland, weight of the kidney, and volume density of tubules in the renal cortex in cases of chronic glomerulonephritis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Autopsy No. or Name</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Number of the gland</th>
<th>Weight of the gland (mg)</th>
<th>Weight of the kidney (g)</th>
<th>Volume density of tubules in the renal cortex (%)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Whole weight</td>
<td>Parenchymal weight</td>
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<td>Right</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(mg)</td>
<td>(mg)</td>
<td>(g)</td>
<td>(g)</td>
</tr>
<tr>
<td>1</td>
<td>351-75</td>
<td>29</td>
<td>M</td>
<td>2</td>
<td>63.0</td>
<td>36.2</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>275-73</td>
<td>30</td>
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<td>24.8</td>
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<td>32.7</td>
<td>70</td>
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<tr>
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<td>F</td>
<td>4</td>
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<td>25.3</td>
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<tr>
<td>13</td>
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<td>67</td>
<td>F</td>
<td>4</td>
<td>42.6</td>
<td>29.7</td>
<td>60</td>
</tr>
</tbody>
</table>

Mean±S.D. 35.5±16.9 28.5±13.6

Control: 49 cases, Mean±S.D. 23.3±8.6 18.6±6.0

The value of weight of the parathyroid gland was represented by the mean weight per one gland in respective cases.

Fig. 4. Relationship in weight of the parathyroid parenchyma to the kidney.
The values of parenchymal weight was represented by mean weight per one gland in respective cases. Weight of the parathyroid parenchyma correlated negatively with weight of the kidney. This correlation was statistically significant.

Fig. 5. Relationship in weight of the parathyroid parenchyma to the kidney.
The values of parenchymal weight was represented by mean weight per one gland in respective cases. Weight of the parathyroid parenchyma correlated inversely with the volume density of the tubules in the renal cortex. This correlation was statistically significant.
extensively. At first, we demonstrated that parenchymal weight of the parathyroid gland increased due to hyperplasia in autopsy cases of chronic glomerulonephritis. In general, the serum parathyroid hormone level is known to be elevated in this disease (Berson and Yalow 1966; Reiss et al. 1969; Brickman et al. 1974; Bordier et al. 1975). It is reasonable to consider that this elevation is attributed to hyperplasia of the parathyroid gland.

Concerning the relationships between hyperplasia of the parathyroid gland and atrophy of the kidney, no paper has been published. In this study, we pointed out that the degree of hyperplasia of the parathyroid gland was directly related to the degree of atrophy of the kidney. In chronic glomerulonephritis, the glomeruli are affected primarily, and atrophy of the tubules follows. Therefore, our data indicated that hyperplasia of the parathyroid gland was secondary to the lesions of the kidney. Reiss et al. (1969) stated that serum parathyroid hormone concentration increased in varying degrees in chronic renal failure and was directly related to the concentration of blood urea nitrogen, serum creatinin and inorganic phosphate. As the degree of damage of renal function correlates with the degree of atrophy of the kidney, the significance of these findings of Reiss et al. is thought to correspond well with our results reported here.

At present, it is generally believed that the relationship between the kidney and the parathyroid gland is linked with the active metabolite of vitamin D and calcium ion (Gray et al. 1971; Holick et al. 1971; Lawson et al. 1971). Namely, it is generally thought that hypocalcemia due to activation disturbance of vitamin D in the kidney stimulates the parathyroid gland, resulting in an increase in serum concentration of parathyroid hormone in chronic renal failure (Brickman et al. 1974, 1975). In our cases, it is clear that the functioning renal mass activating vitamin D reduced as a whole due to reduction in volume of the kidney. Therefore, it is possible to suspect that hyperplasia of the parathyroid gland was caused by the long-standing hypocalcemic stimuli caused by the formation of insufficient amount of active form of vitamin D. There was no information available, however, to confirm this speculation.

Furthermore, we demonstrated that the volume density of tubules in the renal cortex correlated inversely with parenchymal weight of the parathyroid gland. From these data, it was suspected that the location of activation of vitamin D existed in tubular epithelium of the renal cortex. But, to our regret, absolute volume of the renal cortex, volume density of the renal cortex in the whole kidney and quantitative relationships between different parts of renal tubules could not be examined. To realize the above speculation, further investigations are required.

Acknowledgment

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References


