Lipoadenoma of the parathyroid: characteristics of a rare cause of hyperparathyroidism

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Abstract. Parathyroid Lipoadenoma (PLA) contains abundant mature adipose tissue and is a rare cause of hyperparathyroidism. This study aimed to investigate the clinical features of PLA in nine patients with primary hyperparathyroidism, including two men and seven women, with ages ranging from 45–84 years (median 60 years). PLA accounted for 0.5% of all parathyroid tumors during the study period. One patient presented with anorexia due to hypercalcemia; however, the other eight patients were asymptomatic. The median preoperative serum intact-parathyroid hormone (iPTH) and calcium levels were 143 pg/mL (range, 102–378) and 10.8 mg/dL (range, 10.3–11.3), respectively. PLA was difficult to identify using ultrasonography (US) as it appears as a moderately hyperechoic nodule and is difficult to distinguish from the surrounding adipose tissues. Only 33% of the lesions (three out of nine lesions) were accurately identified. However, they could be distinctly differentiated from the surrounding tissue using computed tomography (CT). All PLAs were also detected using the sesta-methoxyisobutylisonitrile single-photon emission-computed tomography (SPECT). All the patients were treated by a single gland extirpation. The median size and weight of the PLA were 14 mm (range, 10–22) and 567 mg (range, 200–1,533), respectively. In conclusion, the clinical manifestations of PLA are similar to those of ordinal parathyroid adenomas, except for their unique US and CT images. PLA should be considered as a potential etiologic factor in cases of hyperparathyroidism when the lesions are demonstrated as hyperechoic nodules or unidentified by US but detected by CT or SPECT imaging.

Key words: Parathyroid lipoadenoma, Hyperparathyroidism, Diagnostic imaging

PARATHYROID LIPOADENOMA (PLA) is a rare parathyroid tumor that contains abundant mature adipose tissue and/or myxoid stroma with scattered nests, cords, and/or delicate anastomosing trabeculae of chief cells [1]. These lesions are also referred to as hamartomas [2]. The etiology of this disease has not been clearly described. Clinically, it is known to present as hyperparathyroidism, and its function is normalized by lesion excision. To date, fewer than 100 cases of the disease have been reported [3]. Prior to the development of recent diagnostic technology, cases of large lobular masses had been reported as typical lesions [1, 2, 4, 5]. However, in recent years, with improvements in diagnostic techniques, PLA has been identified as small oval nodules similar to ordinal parathyroid adenomas (PAs) [6, 7]. The characteristic features from imaging studies and differences in biochemical findings of these PLAs compared to those of ordinal PAs have not been adequately described. This study aimed to describe the clinical features of PLA by investigating the treatment results of nine patients recently treated at our hospital, and is one of the largest case series of patients with this disease.

Patients and Methods

An electrical search of the pathological database of our hospital identified 10 patients with PLAs from a total of 1876 patients that underwent surgery between 2007 to 2021 due to parathyroid tumors. The pathological diagnosis was confirmed by a pathologist (H.M.) who specialized in endocrine pathology, by reviewing the histology results of these 10 patients. There was no clear agreement among specialists regarding the minimum adipose tissue content required for a PLA diagnosis. A recent study by Juhlin et al. reported that the majority (74.5%) of 149 ordinal PAs had an adipose tissue content of less
than 5%, and none of the tumors had an adipose tissue content more than 20% [3]. Therefore, nine tumors from nine patients, with an adipose tissue content of 20% or more, were chosen for this study.

Patient background, preoperative symptoms, initial cause for the visit, biochemical findings, and bone mineral density quantification (described as the T-score) were extracted retrospectively from the medical records. Serum intact parathyroid hormone (iPTH) and calcium levels were measured by electro-chemiluminescence immunoassay method (Eclusys PTH, Roche Diagnostics, Tokyo) and enzymatic method (Acuras auto Ca, Shino-test cooperation, Tokyo), respectively, using a standard automatic analyzer (Cobas 8000, Roche Diagnostics). Bone mineral density was quantified by a measuring devise (Prodigy Fuga, GE health care Japan, Tokyo). Diagnostic imaging findings (cervical ultrasonography (US), cervical plane-and contrast-enhanced computed tomography (CT), and sesta-methoxyisobutylisonitrile (MIBI)-single-photon emission-computed tomography (SPECT)) were also collected. Surgical findings, post-operative course, and biochemical laboratory findings one month after surgery were also collected. US images and reports recorded at the time of the initial visit were evaluated to determine whether the lesion could be identified based on the surgical findings. A similar evaluation was performed on the CT and SPECT images taken during the localization analysis. CT attenuation values were expressed, according to a linear density scale, as Hounsfield units (HU). The HU of each lesion was calculated as the average value of the maximum cross-section of the tumor by plain CT. To compare the lesions was observed by SPECT in all nine patients (100%) (Fig. 1D).

Specific accumulation of radioisotopes in the tracheal location; however, in the other five cases, the responsible lesion demonstrated by CT or SPECT could not be identified by US. In contrast, CT examination identified the lesions in all nine patients. The CT attenuation value of PLA lesions (0–47.6 HU; mean, 35.6) was significantly lower than those of ordinal PA in 14 patients (24.9–73.2 HU; mean, 46.1) ($p = 0.03$). However, each PLA was distinctly contrasted with the surrounding adipose tissue (Fig. 1C). In some patients, there was a mottled internal density, suggestive of adipose tissue within the tumor (Patient 9), and the non-uniformity in contrast enhancement was conspicuous (Patient 7) (Fig. 2). Specific accumulation of radioisotopes in the lesions was observed by SPECT in all nine patients (100%) (Fig. 1D).

Single-gland excision was performed in all nine patients, and left thyroid lobectomy was performed owing to the accompanying thyroid nodule(s) in three patients. Five upper left, two lower left, one upper right, and a lower right gland were excised surgically. The median size of the tumor was 14 mm (range, 10–22 mm), and the median weight was 566.5 mg (range, 200–1,533

### Results

Table 1 shows the demographic characteristics of the nine patients with PLA. PLA was found in 0.53% of all parathyroid tumors. Two male patients and seven female patients were included in this study. Their ages ranged from 45–84 years (median, 60 years). The initial cause for the hospital visit was to investigate asymptomatic hypercalcemia in eight patients. An 84-year-old female patient (Patient 5) had progressive anorexia due to hypercalcemia (11.5 mg/dL; reference range, 8.8–10.2 mg/dL) and was treated with calcitonin and zoledronate by a local physician before the initial visit to our hospital. None of the patients had a family history of parathyroid disease. There were three instances of a former history of urolithiasis, two instances of constipation, and one instance of rib fracture in five patients. Their median body mass index was 22.7 kg/m$^2$ (range, 19.8–30.4 kg/m$^2$). Two patients (22.2%) were on medication for hypertension.

The median preoperative serum iPTH and calcium levels were elevated in all patients up to 143 pg/mL (range, 102–378 pg/mL; reference range, 15–70) and 10.8 mg/dL (range, 10.3–11.3 mg/dL; reference range, 8.2–10.2), respectively. The median T-score of the forearm was –3.0 (range, –4.7–0.2). T-scores did not decrease in a young female patient and two male patients (Table 1).

Typical diagnostic imaging findings are shown in Fig. 1. US imaging could identify the responsible lesions in only three of the nine patients (33.3%). In one patient, the lesion could not be detected by US owing to its retrotracheal location; however, in the other five cases, the responsible lesion demonstrated by CT or SPECT could not be identified by US. In contrast, CT examination identified the lesions in all nine patients. The CT attenuation value of PLA lesions (0–47.6 HU; mean, 35.6) was significantly lower than those of ordinal PA in 14 patients (24.9–73.2 HU; mean, 46.1) ($p = 0.03$). However, each PLA was distinctly contrasted with the surrounding adipose tissue (Fig. 1C). In some patients, there was a mottled internal density, suggestive of adipose tissue within the tumor (Patient 9), and the non-uniformity in contrast enhancement was conspicuous (Patient 7) (Fig. 2). Specific accumulation of radioisotopes in the lesions was observed by SPECT in all nine patients (100%) (Fig. 1D).
### Table 1  Demographic characteristics of patients

| #  | Age & Sex | Symptom                          | HT¹ | BMI³ (kg/m²) | PTH³ (pg/mL) | Ca⁴ (mg/dL) | T-score⁴ | US | CT | SPECT | Operation | Location | Size (mm) | Weight (mg) | Adipose tissue content⁴ |
|----|-----------|----------------------------------|-----|-------------|-------------|-------------|-----------|-----|----|-------|------------|----------|-----------|-------------|------------------------|
| 1  | 77 F      | none                             | no  | 22.9        | 143         | 11.0        | –4.1      | N ⁷ | D ⁸ | D     | Lt Lob ⁹ | Lt Upper | 19        | —           | 60%                    |
| 2  | 56 F      | neck tumor, rib fracture         | no  | 19.8        | 207         | 10.8        | –3.5      | N ⁷ | D ⁸ | D     | Lt Lob ⁹ | Lt Upper | 10       | 421         | 50%                    |
| 3  | 45 F      | none                             | no  | 22.8        | 136         | 10.3        | –0.3      | N ⁷ | D ⁸ | D     | IGE ¹¹  | Rt Lower | 11       | 583         | 40%                    |
| 4  | 55 F      | neck tumor                       | no  | 22.7        | 293         | 11.0        | –3.0      | N ⁷ | D ⁸ | D     | Lt Lob ⁹ | Lt Upper | 20       | 1,533       | 20%                    |
| 5  | 84 F      | Anorexia, Urolithiasis, Constipation | yes | 20.7        | 378         | 10.6 ¹²     | –4.7      | N ⁷ | D ⁸ | D     | IGE ¹¹  | Rt Upper | 13       | 550         | 70%                    |
| 6  | 66 M      | none                             | no  | 25.4        | 102         | 10.9        | –1.9      | N ⁷ | D ⁸ | D     | IGE ¹¹  | Lt Lower | 22       | 769         | 50%                    |
| 7  | 60 F      | Urolithiasis                      | yes | 30.4        | 349         | 11.0        | –3.0      | N ⁷ | D ⁸ | D     | IGE ¹¹  | Lt Upper | 14       | 200         | 30%                    |
| 8  | 59 M      | Urolithiasis                      | no  | 22.3        | 120         | 11.2        | 0.2       | D ⁸ | ⁴| D     | IGE ¹¹  | Lt Upper | 16       | 248         | 30%                    |
| 9  | 84 F      | Constipation                      | no  | 22.1        | 140         | 10.5        | –4.1      | D ⁸ | ⁴| D     | IGE ¹¹  | Lt Lower | 11       | 730         | 20%                    |
| 10 | 60 M      |                                |     |             |             |             |           |       |    |       |            |          |           |             |                        |

1) HT: Hypertension, 2) BMI: Body Mass Index, 3) PTH: Serum intact-PTH level at initial presentation, 4) Ca: Serum calcium level at initial presentation, 5) T-score of the forearm, 6) Histological adipose tissue content in adenoma, 7) N: Not depicted, 8) D: Depicted, 9) Lt Lob: Parathyroidectomy with thyroid left lobectomy, 10) Not measured due to intrathyroidal location, 11) IGE: one gland exploration, 12) Treated with calcitonin and zoledronate before the initial visit, 13) Depiction not possible due to retrotracheal location, 14) D*: Depicted doppler echo information, 15) Median value or prevalence are demonstrated as a footnote.

According to a recent report investigating hyperparathyroidism patients by Juhlin et al. [3], the occurrence of PLA was as low as 0.5%, showing the frequency of PLA is higher than that of current diagnostic imaging modalities. The report reviewed data from 66 case reports, including 35 reports published before 2000. The occurrence of PLC has been reported as 0.1% to 0.5% [3, 4, 5, 6, 9], suggesting that PLA is difficult to identify using diagnostic imaging. However, the definition of PLA might differ from those of current diagnostic imaging modalities. PLA in their study is consistent with our result of 0.5%.

### Discussion

PLA is typically depicted as a lesion is commonly observed as a well-defined, homodense nodule [5, 6, 9, 11] because of the reflection of ultrasonic waves due to a considerable number of boundaries within the tumor between adipose tissue and tumor nests. The increase in echogenicity that was used in the present study. In ordinal PA, the reflection of ultrasonic waves within the tumor is commonly used as a well-defined, homodense nodule [5, 6, 9, 11] because of the reflection of ultrasonic waves due to a considerable number of boundaries within the tumor between adipose tissue and tumor nests. The increase in echogenicity that was used in the present study. According to a recent report investigating hyperparathyroidism patients by Juhlin et al. [3], the occurrence of PLA was as low as 0.5%, showing the frequency of PLA is higher than that of current diagnostic imaging modalities. The report reviewed data from 66 case reports, including 35 reports published before 2000. The occurrence of PLC has been reported as 0.1% to 0.5% [3, 4, 5, 6, 9], suggesting that PLA is difficult to identify using diagnostic imaging. However, the definition of PLA might differ from those of current diagnostic imaging modalities. PLA in their study is consistent with our result of 0.5%.

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often made it difficult to distinguish PLA from the surrounding tissues by US, as shown in Fig. 1A and 1B. Without prior diagnostic imaging results, such as those obtained by CT or SPECT, PLA might easily be overlooked. Doppler echo is a useful method to distinguish PA from lymphadenopathy. Inflow vessels could be

Fig. 1  Results of imaging studies (Patient 6) were demonstrated. The cervical ultrasonography could not identify the responsible lesion. Only a vague area of similar echo density as the surrounding tissues (circle) was demonstrated (A, B). In contrast, the lesion was distinctly identified by plane computed tomography (C) and SPECT (D). Histological appearance of the tumor removed (E: HE ×100).

Fig. 2  Mottled internal density (Patient 9) (A) and the uneven enhancement (Patient 7) (B) suggestive of adipose tissue within the tumor were occasionally found by high-resolution computed tomography images.
identified in two of the three PLA demonstrated by US in this study. However, this technique is difficult to use in a situation where candidate lesions cannot be demonstrated, and we could not perform a search using Doppler echo in this study as well. In contrast, all PLA lesions were visualized as distinct masses on examination by CT and SPECT in the present study. There is a supposed bias in this study as it investigates a retrospective cohort of patients in which surgery was performed because lesions were identified; however, it can be judged that the identification of PLA by CT or SPECT is more effective than that by US. A recent study by Yang et al. reported similarly that isoechoic parathyroid tumor could be found in water-clear cell parathyroid adenoma. However, decreased sensitivity by MIBI scintigraphy was reported in this rare parathyroid adenoma, in contrast to PLA [12].

The limitations of this study were as follows: 1) the number of cases examined was small owing to its rarity; 2) it could not be denied that only patients with distinct abnormal values above a certain level were extracted from all PLA patients because this was a retrospective analysis of cases for which surgery was conducted in a single institution. Patients with mild hyperparathyroidism might be missed if localization studies fail to identify the responsible lesion.

**Conclusion**

Parathyroid lipoadenoma presents with primary hyperparathyroidism and demonstrates findings in line with ordinal parathyroid adenomas. Parathyroid lipoadenoma is a moderately echogenic nodule that is difficult to distinguish from the surrounding tissues by US. Parathyroid lipoadenoma should be considered when the lesions are obscured by US but can be identified clearly by CT or SPECT.

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**Disclosure**

The authors declare no potential conflicts of interest associated with this research.

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