Dramatic Regression of Parathyroid Gland Swelling After Conversion of Calcimimetic Medication From Cinacalcet to Etelcalcetide

Dear Editor,

Etelcalcetide, a new calcimimetic compound that can be administered intravenously, has been clinically available since February 2017 in Japan. Etelcalcetide reduces parathyroid hormone (PTH) secretion in Japanese patients with secondary hyperparathyroidism, as demonstrated in the recent article (1). However, whether etelcalcetide can reduce the size of an already-swollen parathyroid gland (PTG), especially in patients whose PTG swelling was not reduced by cinecalcet treatment, is unclear. Here, we report our observations on changes in PTG size in a single case of secondary hyperparathyroidism treated with cinacalcet. The PTG size was followed with a digital ultrasound machine (TUS-X200S, Toshiba Medical Systems, Tochigi, Japan).

The patient was a 59-year-old man who had been receiving hemodialysis since December 2003 for diabetic end-stage renal failure. In March 2013, elevated levels of serum intact PTH were found (783 pg/mL), irrespective of the intravenous administration of the vitamin D analogue maxacalcitol (Oxarol, Chugai Pharmaceutical Co., Ltd., Tokyo, Japan). Therefore, cinacalcet tablets (Regpara, Kirin Pharma Co., Ltd., Tokyo, Japan) were prescribed.

However, the serum intact PTH level was still not adequately controlled. An ultrasound examination revealed swelling of the right upper, right lower, and left upper lobes of the PTG; over time, the PTG (especially the left lower lobe) gradually enlarged (Table 1). The patient and his elder brother who was living with the patient denied poor adherence to oral cinacalcet treatment.

In April 2017, instead of oral cinacalcet, the intravenous administration of 10 mg/session etelcalcetide (Parsabiv, Ono Pharmaceutical Co., Ltd., Osaka, Japan) was prescribed. This resulted in a reduction in serum intact PTH levels and a decrease in the size of all PTG lobes (Table 1). Especially, the size of enlarged left lower lobe dramatically declined from 1142.3 to 629.7 to 33.6 mm³ (Fig. 1).

**TABLE 1. Clinical data including the size of parathyroid glands**

| Parathyroid glands, mm³ | 2015 | 2016 | 2017 |
|------------------------|------|------|------|
| Right upper            | 146.5| 117.2| 165.8| 18.1 | 24.3 |
| Right lower            | 553.6| 222.9| 171.8| 39.2 | nd   |
| Left upper             | 37.2 | 77.4 | 69.1 | 69.5 | 24.7 |
| Left lower             | 223.1| 519.2| 1142.3| 629.7| 33.6 |
| Total                  | 960.4| 936.7| 1549.0| 756.5| 82.6 |
| ALP, U/L               | 177  | 198  | 190  | 185  | 179  |
| Intact PTH, pg/mL      | 783  | 486  | 792  | 185  | 289  |
| cCa, mg/dL             | 10.2 | 9.9  | 10.5 | 9.5  | 9.5  |
| Pi, mg/dL              | 8.4  | 6.0  | 7.3  | 4.1  | 6.5  |
| Dose of calcimetics    |      |      |      |      |      |
| Cinacalcet, mg/week    | 25   | 50   | 75   | —    | —    |
| Etelcalcetide, mg/week | —    | —    | —    | 30   | 30   |

1. ALP, Alkaline phosphatase; cCa, corrected calcium; nd, not detected; Pi, inorganic phosphorus; PTH, parathyroid hormone.
To the best of our knowledge, this is the first report to show that etelcalcetide can reduce the size of the PTG in a clinical setting. In addition, these observations suggest that etelcalcetide can reduce the size of the PTG, even in patients who did not respond to cinacalcet. At present, it is unclear whether etelcalcetide induces apoptosis in hyperplastic parathyroid cells in the same manner as cinacalcet (2,3). However, owing to the equivalent or even superior suppressive effect of etelcalcetide on PTH secretion compared to that of cinacalcet (4), etelcalcetide may also induce PTG apoptosis. Although the patient claimed that he took cinacalcet every day without forgetting, the possibility of poor adherence to oral cinacalcet therapy could not be excluded, and thus intravenous administration of the therapeutic drug – etelcalcetide, in this case – might have led to more satisfactory PTG suppression. In conclusion, intravenous etelcalcetide might offer a curative treatment for secondary hyperparathyroidism, even in patients who do not fully respond to oral cinacalcet treatment.

Conflicts of Interest
None.

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FIG. 1. The shrinkage of swollen left-lower parathyroid gland after the administration of etelcalcetide. (A) March 18, 2017, (B) July 15, 2017, (C) December 28, 2017.