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## A Case of Primary Hyperparathyroidism Found by Parathyroid Crisis

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**Abstract** A 75-year-old woman, who had been well until 2 weeks ago, consulted a psychiatrist because of stupor and appetite loss. A high serum calcium level (16.4 mg/dl) was found and she was referred to our department. Calcium level rapidly increased to 25.2 mg/dl within a week regardless of a large amount of saline infusion with simultaneous administration of diuretics, calcitonin and prednisolone. Serum calcium level decreased gradually after six times of hemodialyses and infusion of bisphosphonate, pamidronate disodium. The level of intact PTH turned out to be extremely high (520 pg/ml) and PTH-related protein was in the normal range. Parathyroid crisis due to primary hyperparathyroidism was diagnosed. Procedures aim to localize the affected parathyroid glands including ultrasonography, computed tomography, magnetic resonance imaging and subtraction scintigraphy failed. Technetium 99m sestamibi scan after sedation with diazepam showed an abnormal image just below the right lobe of the thyroid. During the neck operation, an adenoma (3 x 1 cm) was detected and resected completely. No other affected glands were found. The levels of serum calcium and intact-PTH decreased gradually into their normal ranges but renal dysfunction due to persistent hypercalcemia remained six months later after the operation.

*Key words:* hyperparathyroidism, parathyroid crisis, intact-PTH, hypercalcemia

### Introduction

Primary hyperparathyroidism is characterized by hypercalcemia and elevated parathyroid hormone (PTH) level. In the past, the disease was considered to be uncommon and be associated with characteristic clinical features, such as osteitis fibrosa cystica and renal calculus disease. With the appearance of the automated serum chemistry autoanalyzer in the 1970s in the United States, the diagnosis of primary hyperparathyroidism became much more common, with four- to five-fold increase in incidence.<sup>1-3)</sup> Classic symptoms, con-

comitantly, became much less common. The diagnosis in its asymptomatic stage is difficult unless serum calcium is measured, and then a substantial number of the patients may be undiagnosed. In rare occasion, some stress may trigger a rapid aggravation and causes a life threatening condition called as parathyroid crisis. In such case, early diagnosis, with aggressive medical management followed by surgical cure, is essential for a successful outcome. We here report such a case with some discussion.

## Case Presentation

A 75-year-old house wife of living alone consulted a psychiatrist accompanied by her daughter because she abruptly became stuporous and lost appetite. She had been well until 2 weeks ago when she saw a general doctor because of common cold. Family or past history was noncontributory. A routine blood examination showed an extremely high level of serum calcium, 16.4 mg/dl. She was referred to our department and admitted on the day. The consciousness level was 2 - 3 in Japan Coma Scale. She appeared restless and hyperkinetic. Height was 148 cm and weight was 50.0 kg. Blood pressure was 111/77 mmHg and pulse rate was 90/min with regular rhythm. Physical examination revealed no abnormal findings. Blood examination on admission showed some abnormalities as follows: calci-

um concentration was 16.4 mg/dl, whereas phosphorus concentration was close to the lower limit of the normal range (2.9 mg/dl). C-reactive protein (CRP) was 11.1 mg/dl, total cholesterol level was 274 mg/dl. White blood cell count was 10,400/ $\mu$ l. Serum creatinine concentration was 1.0 mg/dl but creatinine clearance measured on Day 10 was decreased to 11.1 l/day. Urinary excretion of calcium was 481 mg/day. We initiated fluid transfusion on the day of admission with 3 liters of saline with furosemide (20 - 40 mg/day), prednisolone (40 mg/day) and elcatonin (80 units/day). Serum calcium decreased to 14.8 mg/dl on Day 2 but gradually increased thereafter and reached to the peak of 24.5 mg/dl on Day 6. Application of every day hemodialysis from Day 6 and injection of 30 mg pamidronate on Day 9 successfully decreased calcium level around 13 mg/dl (Fig. 1).

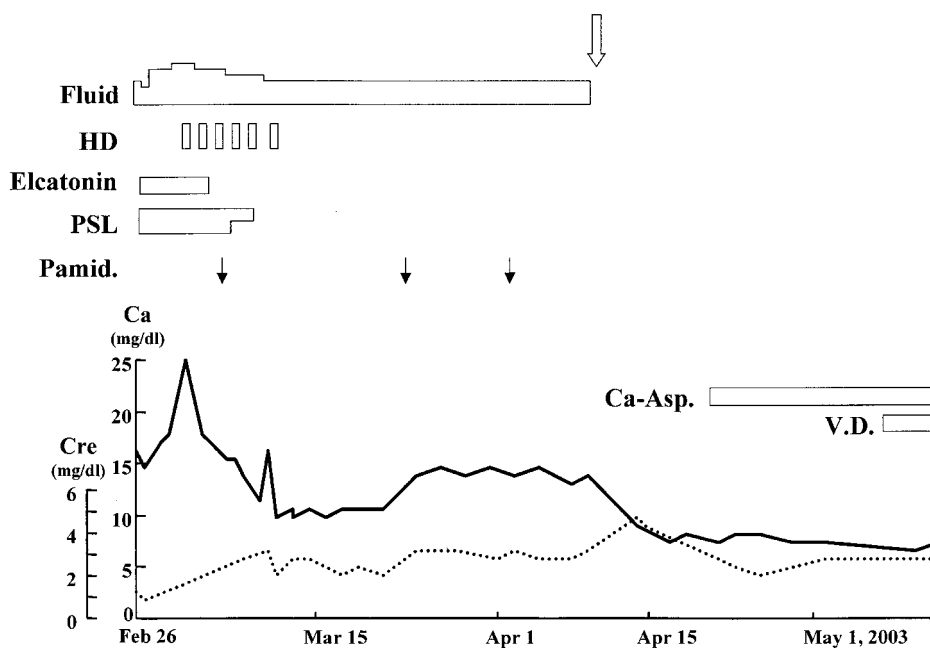


Fig. 1 Clinical course and changes in serum calcium and creatinine levels. The solid and dotted lines represent fluctuations in serum calcium and creatinine levels, respectively. White arrow shows the date of the operation for a parathyroid adenoma. Fluid: Two to 4 liters/day saline was transfused every day during the period indicated by open column. HD: Hemodialysis was repeated 6 times, Elcatonin: Eighty units elcatonin were injected daily for a week, PSL: Forty mg/day prednisolone were given intravenously, Pamid.: Thirty mg pamidronate disodium was administered three times as indicated by black arrows, Ca-Asp.: Calcium L-aspartate (1,200 mg/day) was given orally, V.D.: alphacalcidol (1  $\mu$ g/day) was administered orally.

We initially searched for a malignant tumor causing malignant hypercalcemia. Whole body CT scan with contrast medium, however, did not reveal any obvious malignancy. On day 6, we got an information that intact PTH was extremely high 520 pg/dl (normal range: 10 - 65 pg/dl) and PTH-related peptide was in normal range, 39 pmol/l.

We interpreted that her condition was hyperparathyroid crisis caused by primary hyperparathyroidism. We planned a series of examinations trying to localize the affected parathyroid gland(s). Ultrasonic scan on the neck detected no affected gland in the scope. Neither magnetic resonance imaging (MRI)

nor a subtraction scintigraphy using technetium and thallium produced diagnostic images. The pictures were blurred because she was restless and hyperkinetic. Transfusion with 2 liters of saline daily was continued and 2 more injections of 30 mg pamidronate were done on Day 27 and Day 36. Serum calcium levels fluctuated between 9.8 and 14.7 mg/dl. Serum creatinine level also elevated and maintained around 2.5 - 3 mg/dl.

Technetium 99m sestamibi scan after sedation with diazepam showed an abnormal image in the late phase just below the right lobe of the thyroid (Fig. 2). Surgical neck exploration was operated on Day 44 and a parathyroid

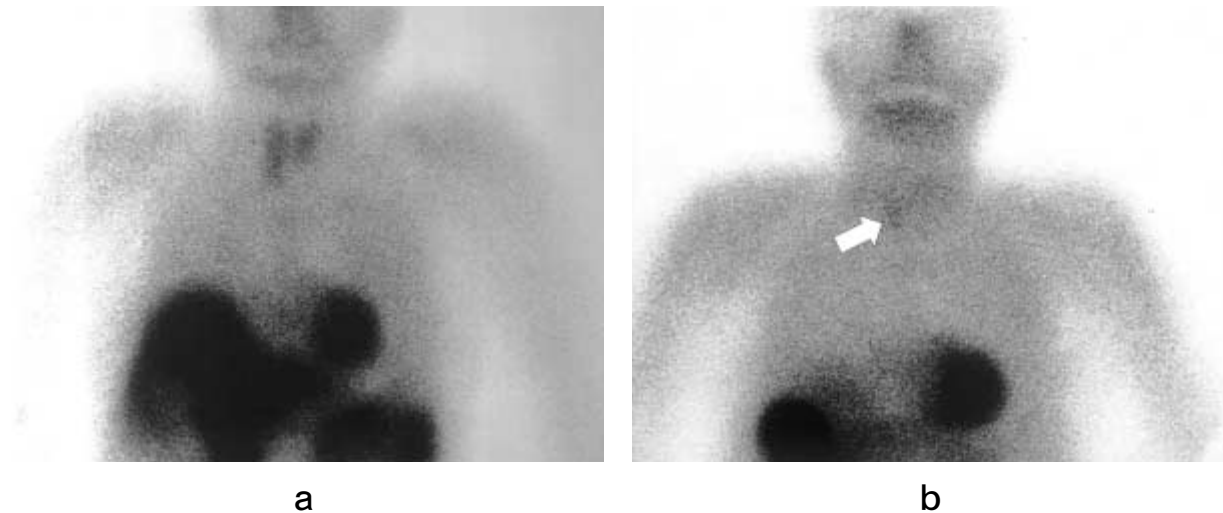


Fig. 2 Technetium 99m-labeled sestamibi was injected intravenously. The first scan was done 20 minutes later (the early phase: Figure 2a) and the second scan was performed 3 hours later (the late phase: Figure 2b). A positive scan demonstrating a parathyroid adenoma just below the right lobe of the thyroid (Figure 2b; white arrow). Both the thyroid and parathyroid take up sestamibi, but its uptake is stronger and the signal persists longer in parathyroid adenomas or hyperplasia.

adenoma 1 x 3 cm in size located behind the trachea in the upper mediastinum was resected completely. No other affected glands were found. Serum intact PTH level returned to the normal range (31 pg/ml) on Day 48. She was discharged on Day 78.

Serum calcium level decreased gradually to the subnormal range and calcium L-aspartate and alfacalcidol were administered for 2 months thereafter. Serum calcium level returned to the normal range without medication but serum creatinine level remained around 2.5 mg/dl

thereafter.

## Discussion

Acute, severe hypercalcemia, usually defined as a serum calcium concentration greater than 14 mg/dl, is unusual because most patients with hypercalcemia have primary hyperparathyroidism, in which hypercalcemia is typically chronic and mild. Most often, acute severe hypercalcemia occurs in patients with underlying malignancy, in whom bone resorp-

tion is accelerated. Episodes of acute, severe hypercalcemia may occur occasionally in primary hyperparathyroidism, however. These patients typically have large parathyroid adenomas and very high PTH levels. The severe hypercalcemia develops in the setting of dehydration due to diarrheal illness, protracted vomiting, or diuretics, recovery from major surgery, immobilization, ingestion of large amounts of oral calcium salts, or parathyroid carcinoma.<sup>4)</sup> Infection is also a potential trigger and it may be involved in the development of the crisis in this case since CRP value and WBC count on admission were high.

In the present case, a malignant disease was firstly suspected because symptoms due to hypercalcemia developed acutely. Initial search for malignant lesions with whole body CT scan failed. It takes a week to obtain the result of PTH assay, which is necessary for diagnosis of primary hyperparathyroidism. During this period, serum calcium concentration increased in spite of treatments. We have some regret for use of loop diuretics in the early stage of treatment because furosemide may have exacerbated extracellular volume depletion through concomitant sodium diuresis.<sup>4)</sup> And we should have used pamidronate earlier though the national health insurance system does not support the use of bisphosphonates in non-malignant cases.

In the textbooks published in the United States,<sup>4)5)</sup> authors emphasize that a surgical neck exploration should be tried at first when primary hyperparathyroidism is diagnosed. Preoperative localization studies are not necessary because the initial surgical cure rate is as high as 95%, which is superior to the sensitivity of any of the available localization techniques. This idea may be derived partly from economical reasons<sup>6)7)</sup> and is not familiar to our customs. The positive result in Tc 99m sestamibi scan finally determined to undergo a surgical operation. Sestamibi scan has been reported to offer excellent sensitivity of 70% to 90% in detecting morbid parathyroid glands.<sup>7-10)</sup> The highest sensitivity is demonstrated in the case of solitary adenoma, but this method is also useful for visualization of multiple hyperplastic lesions. According to Johnston et al., Tc 99m sestamibi scan is a powerful tool for detecting parathyroid tumors

in the patients who had had previous parathyroid surgery.<sup>9)</sup> Although this procedure is very useful, the present health insurance system restricts the application of the method only for evaluation of myocardial perfusion.

Her renal function already deteriorated when admitted. The creatinine clearance value measured in the early hospital course was extremely low whereas the serum creatinine level was not so high. Hedbäck and Odént reported that renal impairment brought by primary parathyroidism of substantial degree or of long duration is not necessarily disclosed by the creatinine value alone.<sup>11)</sup> They also described that the greater the amount of diseased parathyroid tissue had the lesser the renal function. The adenoma in this case was large in size.

We got some valuable instructions from this case. Firstly, bisphosphate should be administered earlier in the course in spite of health-insurance regulations. Secondly, surgical treatment should be chosen without hesitation when the crisis is not restored by all kinds of non-surgical approaches. And Tc 99m sestamibi scan was useful for detecting parathyroid adenomas locating in the mediastinum and we hope that this method will be adopted as a first-line technique for detecting ectopic parathyroid adenomas.

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