Eleven Cases of Nonfunctioning Parathyroid Cyst - Significance of Needle Aspiration in Diagnosis and Management

TAKAYA KODAMA, TAKAO OBARA, YOSHIHIDE FUJIMOTO, YUKIO ITO,
TOHRU YASHIRO AND AKIRA HIRAYAMA*

Departments of Endocrine Surgery and Surgical Pathology,
Tokyo Women's Medical College, Kawadacho 8-1, Shinjuku-ku, Tokyo 162, Japan*

Abstract

Eleven cases of nonfunctioning parathyroid cyst are reported. Ultrasonography revealed the cystic nature of the asymptomatic lump in the neck. Clear watery fluid obtained by needle aspiration and the increased parathyroid hormone concentration in the fluid established the diagnosis. Five patients, in four of whom the cysts reappeared after one (3 cases) or seven (1 case) needle aspirations, underwent surgical resection of the cysts. Six other patients were followed conservatively after the aspiration maneuver. In four patients with enough follow-up time for evaluation, the cyst fluid has not reaccumulated 5, 2 and 2 years after only one aspiration, and 1 year after two aspirations. In one patient, the cyst reappeared 9 months after the initial aspiration. Simple percutaneous aspiration may be curative in some cases of nonfunctioning parathyroid cysts.

About 200 cases of nonfunctioning parathyroid cyst have been reported in Japanese (Ishida *et al.*, 1983, 46 cases) and English (Rosenberg *et al.*, 1982, 143 cases) literature, while a correct preoperative diagnosis had been rarely made (Asfar *et al.*, 1982). In addition to the 6 cases previously reported (Fujimoto *et al.*, 1976; Fujimoto *et al.*, 1977), we present 11 new cases of nonfunctioning parathyroid cyst, ten of which were diagnosed preoperatively. This report offers some answers to the question: What is the long-term natural history of the nonfunctioning parathyroid cyst treated by aspiration

(Rosenberg *et al.*, 1982)?

Report of Cases

Operative cases

Case 1.—A 35-year-old woman was seen in September, 1980 with a lump, about 5×3 cm, in the right anterior neck. The lump was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded clear colorless fluid, suggesting a nonfunctional parathyroid cyst. However the serum calcium level was found to be elevated, i.e., 11.5 mg/dl (normal 8.8 to 10.6 mg/dl). The plasma carboxyterminal parathyroid hormone (c-PTH) level was 0.3 ng/ml (normal less than 0.6 ng/ml). Surgical exploration was performed on April 15, 1981.

Received April 21, 1987

The address for correspondence: Takaya Kodama, MD, Department of Endocrine Surgery, Tokyo Women's Medical College, Kawadacho 8-1, Shinjuku-ku, Tokyo 162, Japan

There was a thin-walled translucent cyst, 3 cm in diameter, behind the inferior pole of the right thyroid lobe. The cyst was easily excised, with some adjacent thyroid tissue. Other parathyroid glands were searched for, but could not be identified. The serum calcium level remained elevated after the operation. Two and a half years later, $^{201}\text{TlCl}-^{99\text{m}}\text{TcO}_4$ subtraction scintigraphy and ultrasonography revealed a small lesion in the left thyroid lobe. Left lobectomy of the thyroid was performed on October 21, 1983. A tumor, measuring $1.3 \times 1.1 \times 0.5$ cm, was embedded in the thyroid tissue. Histologically, carcinoma of the left upper parathyroid was suggested because of the thick calcified capsule, fibrous trabeculae and infiltrative growth into the surrounding thyroid tissue. Two years after the second operation, the serum calcium level was normal.

Case 2.—In June, 1981 we examined a 52-year-old woman with a lump, 3.5 cm in diameter, in the left anterior neck. Needle aspiration of the cyst yielded clear watery fluid. The c-PTH level in the cyst fluid was 2.3 ng/ml. The plasma c-PTH level was 0.4 ng/ml, and the serum calcium level was 8.8 mg/dl. Subsequently, needle aspiration was performed 7 times at intervals of several months. About 50 ml of clear fluid was obtained at each aspiration. The c-PTH level in the cyst fluid was 1.0 and 6.4 ng/ml at the 4th and 5th aspirations, respectively. Surgical exploration was performed on July 20, 1984. There was a left lower parathyroid cyst, measuring $6.5 \times 4.5 \times 1.5$ cm, which extended into the upper mediastinum. The c-PTH level in the resected cyst fluid was 66.6 ng/ml, and the intact PTH level (N-tact PTH, measured at the Mitsubishi Yuka Laboratory of Medical Science Co., Ltd., Tokyo) in the fluid was 3040 pg/ml (normal less than 120 pg/ml in plasma). The postoperative course was uneventful.

Case 3.—A 32-year-old man had a

lump, 2 cm in diameter in the left anterior neck, pointed out incidentally by a physician in April, 1982. The lump was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded 5 ml of clear watery fluid. The c-PTH level in the cyst fluid was 1.7 ng/ml. The plasma c-PTH level was 0.1 ng/ml, and the serum calcium level was 9.5 mg/dl. The cyst fluid reaccumulated, and surgical exploration was performed on May 26, 1982. There was a small (1.5 cm in diameter) left upper parathyroid cyst, which was easily excised. The postoperative course was uneventful.

Case 4.—A 51-year-old woman was seen in October, 1984 with a neck mass on the left side, which had been present for 2 years. The mass, about 4 cm in diameter, was shown to be cystic by ultrasonography, but it was interpreted as a cystic nodule of the thyroid. She was normocalcemic. Surgical exploration was performed on November 7, 1984. Behind the inferior pole of the left thyroid lobe, there was a thin-walled cyst, measuring $4 \times 3 \times 3$ cm, which extended into the upper mediastinum. Needle aspiration of the cyst at the operation yielded clear watery fluid. The c-PTH level in the cyst fluid was 11.4 ng/ml. The postoperative course was uneventful.

Case 5.—In October, 1985 we examined a 23-year-old woman with a lump, 5 cm in diameter, in the left anterior neck. The lump was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded 20 ml of clear colorless fluid. The c-PTH level in the cyst fluid was 384.2 ng/ml. She was normocalcemic. The lump reappeared 3 months later. Surgical exploration was performed on September 29, 1986. A left lower parathyroid cyst, measuring $6 \times 5.5 \times 2.3$ cm, was easily excised. The postoperative course was uneventful.

Nonoperative cases

Case 6.—In May, 1981 we examined a

42-year-old woman with a lump, 6 cm in diameter, in the right lower neck. The lump had been present for 4 years. It was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded 48 ml of clear colorless fluid, which contained 2.2 ng of c-PTH per ml. She was normocalcemic. Five and a half years later, the cyst fluid had not reaccumulated.

Case 7.—In December, 1984 we examined a 43-year-old woman with a lump, 4 cm in diameter, in the right lower anterior neck. The lump was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded 6 ml of clear colorless fluid, which contained 72.1 ng of c-PTH per ml. She was normocalcemic. Two years later, the cyst fluid had not reaccumulated.

Case 8.—In January, 1985 we examined a 30-year-old woman with a lump, 3 cm in diameter, in the left lower anterior neck. The lump was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded slightly brownish serous fluid. The c-PTH level in the cyst fluid was 78.5 ng/ml. She was normocalcemic. Two years later, the cyst fluid had not reaccumulated.

Case 9.—A 43-year-old woman was seen in August, 1985 with swelling of the anterior neck. She had a diffuse goiter. She was euthyroid and normocalcemic, but positive for thyroid autoantibodies. The trachea was shifted to the right side. Ultrasonography showed a cystic mass, $4.5 \times 3.2 \times 2.4$ cm, in the left lower neck. The mass extended deeply into the upper mediastinum. Needle aspiration of the cyst yielded 20 ml of clear colorless fluid. The c-PTH level of the cyst fluid was 379.3 ng/ml. The cyst fluid had reaccumulated two months later. The second aspiration yielded 13 ml of slightly brownish serous fluid, which contained 336.9 ng of c-PTH per ml. One year later, the cyst fluid had not reaccumulated.

Case 10.—A 38-year-old woman noticed

a lump on the left side of the neck in May, 1985. She visited a physician on May 30. The lump, 1.5 cm in diameter, increased in size, and she was referred to us on September 3. There was a smooth-surfaced firm mass, 3.5 cm in diameter, in the left lower anterior neck. Ultrasonography showed that the mass was cystic. Needle aspiration of the cystic mass yielded clear colorless fluid. The c-PTH and N-tact PTH levels in the cyst fluid were 50.2 ng/ml and 95 pg/ml, respectively. The plasma c-PTH level was 0.1 ng/ml, and she was normocalcemic. After the aspiration maneuver, the mass disappeared. However, in June, 1986 the cyst fluid reaccumulated, forming a mass 3.5 cm in diameter. We are still waiting for the results of the second aspiration of the cyst, performed on October 21, 1986.

Case 11.—A 43-year-old man with diabetes mellitus had a lump pointed out in the right lower anterior neck by a physician in November, 1986. The lump, 3 cm in diameter, was shown to be cystic by ultrasonography. Needle aspiration of the cyst yielded 19 ml of clear watery fluid. The c-PTH and N-tact PTH levels in the fluid were 0.5 ng/ml and 30 pg/ml, respectively. The plasma c-PTH level was less than 0.1 ng/ml, and she was normocalcemic. The lump disappeared after the aspiration, and he will be followed up.

Pathologic Findings

The walls of the cysts consisted of a large (Cases 1, 3 and 4) or small (Cases 2 and 5) amount of dense fibrous tissue. In Cases 2, 4 and 5, the cyst loculi were lined with a single layer of cuboidal cells (Fig. 1), but in Cases 1 and 3, no lining cells were observed in the specimens examined. Parathyroid tissues embedded in the cyst wall were found in Cases 1, 2 and 5. In Case 5, there were parathyroid tissues in almost

Fig. 1. Histologic section of the parathyroid cyst shows a single layer of cuboidal cells lining the cyst (Case 4, hematoxylin-eosin, $\times 130$).

the entire wall of the cyst (Fig. 2).

Analysis of the Cyst Fluid

The concentrations of calcium, sodium, potassium and chloride in the cyst fluid varied considerably from case to case, but they were roughly on the same levels as those in the serum, respectively (Table 1). The concentrations of total protein and phosphate were extremely low.

Discussion

It has been pointed out that there are two distinct groups of patients with parathyroid cyst, those with nonfunctioning and

those with functioning cysts (Fujimoto *et al.*, 1976; Fujimoto *et al.*, 1977; Rosenberg *et al.*, 1982). From an epidemiological standpoint, the former group is characterized by the predominance of female and younger patients, as compared with the latter, and by extreme predisposition for the inferior, preferably left, parathyroid gland (Clark, 1978; Rosenberg *et al.*, 1982; Asfar *et al.*, 1982; Ishida *et al.*, 1983). Of our own 11 patients, 9 were female, with an average age of 39 years. Except for Case 3, all of the parathyroid cysts were found in the inferior, usually left (7 cases), position.

From the standpoint of pathogenesis, three types of parathyroid cyst are proposed (Clark, 1978; Rosenberg *et al.*, 1982; Asfar *et al.*, 1982). The first is of vestigial origin, such as Kürsteiner's canalicular rudiment.

Fig. 2. Histologic section of the parathyroid cyst demonstrates diffuse parathyroid tissues in the wall (Case 5, hematoxylin-eosin, $\times 50$).

Table 1. Concentrations of PTH, total protein and electrolytes in the cyst fluid.

Case No.	c-PTH (ng/ml)	N-tact PTH (pg/ml)	TP** (g/dl)	Ca (mg/dl)	P (mg/dl)	Na (mEq/l)	K (mEq/l)	Cl (mEq/l)
1								
2	2.3, 1.0 6.4, (66.6)*	(3040)*	0.15	8.7	0			
3	1.7		0.79	12.6	<0.1	132	6.0	120
4	(11.4)*							
5	384.2							
6	2.2		0.33	7.3	0.1			
7	72.1							
8	78.5		0.8#					
9	379.3 336.9							
10	50.2	95	0.06	3.2	0	168	9.7	174
11	0.5	30	0.05##	4.9	0	112	3.5	97

*The cyst fluid was obtained at operation. **TP: Total protein.

& ## Albumin accounted for 72% and 78% of TP, respectively.

Fig. 3. A small parathyroid cyst incidentally found in a patient with secondary hyperparathyroidism. Note the presence of parathyroid tissue (arrow) and a solitary layer of cuboidal cells lining the cyst wall (hematoxylin-eosin, $\times 16$).

The second is due to cystic degeneration of a parathyroid adenoma and the third results from retention cysts. Recently, we incidentally found a small parathyroid cyst, 6 mm in diameter, in a 58-year-old woman with secondary hyperparathyroidism, who had undergone hemodialysis for 14 years (Fig. 3). In this patient, four parathyroid glands were enlarged, and the cyst was found as the fifth gland in the right thymic tongue. The morphological features of the cyst suggest its embryological origin. We believe that it represents an early stage of a nonfunctioning parathyroid cyst, even if

the endocrine activity of the lining cells of the cyst wall is enhanced under the condition of secondary hyperparathyroidism. Pathological findings in our operated cases are almost identical to those thus far reported (Fujimoto *et al.*, 1976; Rosenberg *et al.*, 1982; Ishida *et al.*, 1983). Diffuse parathyroid tissues in the cyst wall in Case 5 suggest probable anomalous proliferation, not neoplastic growth (Fig. 2). The concentrations of protein in the cyst fluid were uniformly low in our cases (Table 1) and those reported by Takai *et al.* (1987). The extremely low viscosity of the cyst fluid

Fig. 4. Cystic degeneration of a parathyroid adenoma. Note the extremely thick cyst wall and two deposits of cholesterol crystals. There are several nodules of oxyphilic parathyroid cells surrounded by fibrous tissues (hematoxylin-eosin, $\times 9$).

probably reflects this characteristic, and it may also be interpreted as suggesting the embryological origin of nonfunctioning parathyroid cysts rather than degeneration or retention origin. It is not clear, however, why nonfunctioning parathyroid cysts of vestigial origin are prevalent in middle-aged women but not in children. The preference of the cyst for the left side probably reflects embryological asymmetry in the lower neck region; such laterality is also observed in thyroid hemiagenesis (Melnick and Stemkowski, 1981), piriform sinus fistula (Miyachi *et al.*, 1981) and thyroid carcinoma in childhood (Kodama *et al.*, 1986).

Functioning parathyroid cysts are rarer than nonfunctioning ones; only about 30 cases have been reported (Rosenberg *et al.*, 1982). Most functioning parathyroid cysts seem to be the result of spontaneous necrosis of preexisting parathyroid adenomas (Fujimoto *et al.*, 1976; Calandra *et al.*, 1983). From 1981 to 1986, when our 11 patients with nonfunctioning parathyroid cyst were treated, 100 patients with primary hyperparathyroidism visited our clinic. Among these 100 cases, there were 6 with a macroscopic cystic change in the resected specimen. Four of the 6 cases showed the pathologic findings of degeneration and early

Fig. 5. Multiple cysts in a parathyroid adenoma (hematoxylin-eosin, $\times 8$).

or late organization such as an extremely thick, sometimes calcified, cyst wall, accompanied by turbid cyst fluid (Fig. 4). Multiple cysts suggesting retention cysts were observed in the adenomas in the other 2 cases (Fig. 5). Thus from our experience also it seems that three types of pathogenesis are really involved in parathyroid cysts.

Of a total of 9 cases (Case 4 without the aspiration maneuver and Case 11 with too short a follow-up time for evaluation were excluded), only one needle aspiration led to regression of the nonfunctioning parathyroid cyst for 5, 2 and 2 years in 3 cases. On the other hand, the cyst fluid reaccumulated after the initial aspiration in 6 patients, 4 of whom underwent surgical resection of the cyst. The other 2 patients are going to be followed up after 2 aspirations. Although there have been 17 reported cases in which there was complete resolution of the cyst after percutaneous aspiration (Clark, 1978; Ginsberg *et al.*, 1978; Rosenberg *et al.*, 1982; Katz and Dunkleman, 1984; Pacini *et al.*, 1985; Silverman *et al.*, 1986), the follow-up periods were generally too short to draw the conclusion that the needle aspiration was curative, because the intervals between aspiration and reaccumulation of the cyst fluid were as long as several months and up to 9 months in the cases reported here and in our previous article (Fujimoto *et al.*, 1977).

Nonfunctioning parathyroid cyst does not seem to be an extreme medical curiosity (Pacini *et al.*, 1985). The watery, usually colorless, fluid obtained from the cystic mass in the lower neck of a normocalcemic patient and the elevated c-PTH level in the cyst fluid are pathognomonic for a nonfunctioning parathyroid cyst. However, amino-terminal-specific PTH (n-PTH, including N-tact PTH) assay of the cyst fluid is misleading, because it gave normal or slightly elevated results in our 2 cases (Table 1) and 5 cases reported by Ishida *et al.* (1983) and Silverman *et al.* (1986). Ultrasono-

graphy is very useful for revealing the cystic nature of the mass before needle aspiration. Needle aspiration may lead to long regression of the cyst in some cases, but surgical intervention is warranted for patients in whom the cyst fluid reaccumulates, probably after 2 aspirations. Different amounts of lining cells and parathyroid tissue in the cyst wall may reflect the different responses in regard to the cyst fluid reaccumulation after aspiration, but it seemed that the c-PTH level in the cyst fluid did not necessarily predict the outcome of the aspiration maneuver.

References

- Asfar, S., G. Smith and Z. H. Krukowski (1982). Parathyroid cysts. *World J. Surg.* 6, 777-781.
- Calandra, D. B., K. H. Shah, R. A. Printz, H. Sullivan, C. Hofmann, R. Oslapas, K. Ernst, A. M. Lawrence and E. Ployan (1983). Parathyroid cysts: A report of eleven cases including two associated with hyperparathyroid crisis. *Surgery* 94, 887-892.
- Clark, O. H. (1978). Parathyroid cysts. *Am. J. Surg.* 135, 395-402.
- Fujimoto, Y., A. Oka, M. Fukumitsu, T. Obara, T. Kimura, Y. Aiyoshi and M. Namiki (1976). Parathyroid cyst: A cystoma and a cystic degeneration of functioning parathyroid adenoma. *Nippon Geka Gakkai Zasshi* 77, 900-908. (In Japanese).
- Fujimoto, Y., T. Obara and T. Miura (1977). Parathyroid cyst as a cervical or cervicomedial mass. *Jpn. J. Clin. Oncol.* 7, 119-122.
- Ginsberg, J., J. E. M. Young and P. G. Walfish (1978). Parathyroid cysts. Medical diagnosis and management. *JAMA* 240, 1506-1507.
- Ishida, N., O. Hosono, K. Inoue, N. Abe, Y. Iino, T. Kawai and M. Izuo (1983). Non-functioning parathyroid cysts: Report of four cases and review of the Japanese literature. *Horumon To Rinsho* 31, 861-867. (In Japanese).
- Katz, A. D. and D. Dunkleman (1984). Needle aspiration of nonfunctioning parathyroid cysts. *Arch. Surg.* 119, 307-308.
- Kodama, T., Y. Fujimoto, T. Obara and K. Hidai (1986). Justification of conservative surgical treatment of childhood thyroid cancer: report of eleven cases and analysis of Japanese literature. *Jpn. J. Cancer Res.* 77, 799-807.
- Melnick, J. C. and P. E. Stemkowski (1981). Thyroid hemiagenesis (hockey stick sign): A review of the world literature and a report of four cases. *J. Clin. Endocrinol. Metab.* 52, 247-251.
- Miyauchi, A., F. Matsuzuka, S. Takai, K. Kuma and G. Kosaki (1981). Piriform sinus fistula. A route of infection in acute suppurative thyroiditis. *Arch. Surg.* 116, 66-69.
- Pacini, F., A. Antonelli, R. Lari, L. Gasperini, L. Baschieri and A. Pinchera (1985). Unsuspected parathyroid cysts diagnosed by measurement of thyroglobulin and parathyroid hormone concentrations in fluid aspirates. *Ann. Intern. Med.* 102, 793-794.
- Rosenberg, J., R. Orlando, M. Ludwig and L. J. Pyrek (1982). Parathyroid cysts. *Am. J. Surg.* 143, 473-480.
- Silverman, J. F., P. G. Khazanie, T. Norris and W. W. Fore (1986). Parathyroid hormone (PTH) assay of parathyroid cysts examined by fine-needle aspiration biopsy. *Am. J. Clin. Pathol.* 86, 776-780.
- Takai, S., A. Miyauchi and T. Kobayashi (1987). Parathyroid cysts. *Geka Shinryo* 29, 187-192. (In Japanese).