Hyperparathyroid Crisis: *

Survey of the Literature and a Report of Two Additional Cases

ROBERT L. PAYNE, JR., M.D., CLAIBORNE W. FITCHETT, M.D.

From the Department of Surgery, Norfolk General Hospital, Norfolk, Virginia

IN 1932, Dawson and Struthers [16] reported a case of hyperparathyroidism which pursued an acute and rapidly fatal course. Since that time a number of similar cases have been reported. The condition has been called acute parathyroid intoxication,[53] parathyroid crisis,[11] acute hyperparathyroidism,[4] parathormone intoxication [26] and calcium intoxication.[38]

In 1926, Collip [14] investigated parathyroid function by repeated injections of parathyroid hormone into dogs. This produced a lethal poisoning characterized by vomiting, diarrhea and atony. At the same time, distinctive blood changes appeared. Serum calcium level rose above 20 mg./100 ml. to fall somewhat just before death, whereas serum phosphorus and non-protein nitrogen levels rose terminally to high values. A terminal marked increase of other blood elements was further characteristic: rising values for hemoglobin, red blood cells, osmotic pressure and viscosity. Postmortem examination of the animals revealed an increased calcium content in certain tissues, especially the myocardium and kidneys. Microscopically, calcium deposits were observed in the majority of internal organs, especially myocardium, kidneys, gastric mucosa and lungs. Multiple venous thromboses in various parts of the vascular system, especially the liver, were observed.

Evidence that similar events occurred in man was first obtained in 1932 when Lowenberg and Ginsberg [39] reported a case of acute hypercalcemia due to excessive amounts of parathyroid extract given in the treatment of purpura in a 5-year-old boy. The child was given daily injections of calcium gluconate and parathyroid extract and by mistake got 100 units of parathyroid extract daily instead of 20 units. On this treatment he developed vomiting, depression and lethargy. On the sixth day it was noted that serum calcium level was 19.6 mg./100 ml. and phosphorus was 4.4 mg./100 ml. All drugs were stopped on this day and the child was given intravenous saline with prompt and rapid recovery. The report of this case did much to stimulate interest in this problem. Since that time further reports have become frequent.

Selection of cases from the literature has been difficult due to the lack of specific diagnostic criteria. Albright [1] limited the diagnosis to "those cases showing a rapid exit-chemical death, as it were, with calcium deposits in multiple tissues at postmortem and the absence of chronic changes in the kidney." Waife [64] in 1949 described the acute and chronic stages of hyperparathyroidism and emphasized differences between the two. In selecting cases for review we have accepted the author's opinion and clinical descriptions in earlier reports. Otherwise, we have accepted those cases

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TABLE 1. *Reported Cases of Hyperparathyroid Crisis*

Case	Author	Date	Age Sex	High CA	Low P	Operation	Pathology	Outcome
1.	Dawson & Struthers	1923	49-M	—	—	No	Adenoma	Fatal
2.	Wanke, R.	1930	38-F	20.0	—	No	Adenoma, chief, cell	Fatal
3.	Wanke, R.	1930	40-F	30.0	—	Yes	Adenomas 2, chief cell	Fatal
4.	Snapper, I.	1930	56-M	23.6	2.1	Yes	Adenoma	Survived
5.	Bergstrand, H.	1931	55-F	—	—	No	Hyperplasia	Fatal
6.	Lowenberg & Ginsberg	1932	5-M	19.6	4.4	—	Iatrogenic	Survived
7.	Herzenberg, H.	1933	45-M	—	—	—	Adenoma, chief cell	Fatal
8.	Morelle, J.	1934	51-F	18.0	1.4	Yes	Adenoma	Survived
9.	Mellgren, J.	1936	41-F	—	—	No	Adenoma, chief cell	Fatal
10.	Schrumpf & Harbitz	1938	58-M	21.5	1.2	Yes	Adenomas 2, chief cell	Survived
11.	Hanes, F. M.	1939	45-F	20.0	4.7	No	Adenoma	Fatal
12.	Oliver, W. A.	1939	57-F	17.4	—	No	Adenoma, chief cell	Fatal
13.	Oliver, W. A.	1939	56-F	19.6	—	No	Adenoma, chief cell	Fatal
14.	Arnold, W.	1940	40-M	—	—	No	Adenomas 2, chief cell	Fatal
15.	Smith & Cooke	1940	44-F	23.0	4.8	No	Adenoma, chief cell	Fatal
16.	Mellgren, J.	1943	51-F	—	—	No	Adenoma, chief cell	Fatal
17.	Alexander, *et al.*	1944	29-F	—	—	No	Adenoma, chief cell	Fatal
18.	McClure & Lam	1945	44-F	19.4	2.5	No	Hyperplasia	Fatal
19.	Rogers, H. M.	1946	36-M	—	—	No	Adenoma, chief cell	Fatal
20.	Rogers, H. M.	1946	53-M	—	—	No	Hyperplasia	Fatal
21.	Young & Halpert	1947	49-M	—	—	No	Adenoma, chief cell	Fatal
22.	Young & Emerson*	1949	54-F	22.4	3.4	Yes	Carcinoma	Survived
23.	Waife, S. O.	1949	30-M	17.5	1.8	Yes	Adenoma	Survived
24.	Waife, S. O.	1949	44-M	19.3	4.3	Yes	Adenoma, chief cell	Survived
25.	Waife, S. O.	1949	34-M	16.5	9.9	No	Hyperplasia	Fatal
26.	Kretschmer, H. L.	1950	35-F	16.3	2.6	No	Adenoma, chief cell	Fatal
27.	Staub, *et al.*	1950	50-M	14.1	2.1	No	Adenoma, chief cell	Fatal
28.	Anderson & McWhorter	1951	35-M	18.0	4.8	No	Carcinoma	Fatal
29.	Fitz & Hallman	1952	52-M	19.0	1.8	Yes	Adenoma	Survived
30.	Howard, *et al.*	1953	57-F	20.2	2.7	Yes	Adenoma, necrosis	Survived
31.	Schneider, H. O.	1953	58-M	29.0	2.1	Yes	Adenoma	Survived
32.	Lee, *et al.*	1955	60-M	—	—	No	Adenoma, chief cell	Fatal
33.	Goldman, L.	1955	71-M	14.8	1.9	Yes	Adenoma	Survived
34.	James & Richards	1956	22-F	17.0	1.8	Yes	Adenoma, chief cell	Survived
35.	Bradlow & Segel	1956	57-M	21.0	2.7	Yes	Adenoma, chief cell	Survived
36.	Harmon, M.	1956	7-M	19.0	1.8	Yes	Adenoma	Survived
37.	Kimberley, R. C.	1957	40-M	14.5	4.0	No	Adenoma	Fatal
38.	Hewson, J. S.	1958	38-M	18.9	5.2	No	Adenoma, chief cell	Fatal
39.	Horowitz & Berenbaum	1958	25-F	17.7	2.9	No	Adenoma	Fatal
40.	Thomas *et al.***	1958	69-F	18.3	2.2	Yes	Adenoma, chief cell	Survived
41.	Thomas *et al.***	1958	55-M	20.8	1.4	Yes	Adenoma, chief cell	Survived
42.	Thomas *et al.*	1958	65-F	17.3	4.3	No	Adenoma, chief cell	Fatal
43.	Atsmon *et al.*	1960	49-F	18.6	2.5	Yes	Adenoma, chief cell	Survived
44.	Carlson *et al.****	1960	53-F	16.9	6.0	No	Hyperplasia	Fatal
45.	Derbyshire & Angle	1960	61-M	26.0	3.6	Yes	Adenoma, chief cell	Fatal
46.	Gassman & Hass	1960	50-F	17.8	2.7	No	Adenoma, chief cell	Fatal
47.	Murphy *et al.*	1960	51-M	17.0	2.1	Yes	Adenoma, chief cell	Survived
48.	Silvestrini *et al.*	1960	31-F	18.4	2.5	No	Adenoma	Fatal
49.	Silvestrini *et al.*	1960	52-F	16.7	2.7	No	Adenoma	Fatal
50.	Spinner, S.	1960	62-M	18.4	3.1	Yes	Adenoma	Survived
51.	Bottino, C.	1961	48-M	20.0	5.6	No	Adenoma	Fatal
52.	Fink & Finfrock	1961	60-M	20.0	4.9	Yes	Adenoma	Fatal
53.	Nelson & Cantrell	1961	49-M	17.8	2.6	Yes	Adenoma, chief cell	Survived
54.	Reinfrank & Edwards	1961	13-F	22.4	3.4	Yes	Adenoma	Survived
55.	Veenema, R. J.	1961	56-F	19.4	—	No	Adenoma	Fatal
56.	Veenema, R. J.	1961	70-M	18.0	—	Yes	Adenomas 2	Fatal
57.	Gershberg *et al.*	1962	77-M	19.8	3.5	No	Adenoma, chief cell	Fatal

TABLE 1.—(*Continued*)

Case	Author	Date	Age Sex	High CA	Low P	Operation	Pathology	Outcome
58.	Klein *et al.*	1962	67-F	17.4	3.8	No	Adenoma, chief cell	Fatal
59.	Templeton, T. B.***	1962	61-M	19.8	3.6	Yes	Hyperplasia	Survived
60.	Smith *et al.*	1963	37-F	20.0	3.5	Yes	Ademona	Survived
61.	Mansberger *et al.*	1964	61-F	20.0	2.8	Yes	Adenoma	Survived
62.	Wilson *et al.*	1964	61-M	19.6	2.0	Yes	Adenomas 2	Survived
63.	Wilson *et al.*	1964	61-F	22.8	1.2	Yes	Adenoma	Fatal
64.	Wilson, *et al.*	1964	49-F	14.0	1.4	Yes	Hyperplasia	Fatal
65.	Lemann & Donatelli	1964	50-F	18.4	6.1	No	Adenoma, chief cell	Fatal
66.	Lemann & Donatelli	1964	60-F	24.0	4.6	Yes	Adenoma, hemorrhage	Survived
67.	Lemann & Donatelli	1964	62-F	16.4	2.7	Yes	Adenoma	Survived
68.	Lemann & Donatelli	1964	59-F	19.0	6.5	Yes	Adenoma	Fatal
69.	Payne & Fitchett	1965	62-F	22.8	2.9	Yes	Adenoma, chief cell	Survived
70.	Payne & Fitchett	1965	32-F	19.1	2.1	Yes	Adenoma, chief cell	Survived

* Case 22 also referred to by Wilson *et al.*[67].
** Cases 40 and 41 also referred to by Nelson and Cantrell[47].
*** Cases 44 and 59 also referred to by Smith *et al.*[56].

showing 1) rapid changes in the general condition of the patients, especially when acute symptoms involve gastro-intestinal, cardiovascular or central nervous systems, 2) rising serum calcium concentration above 15 mg./100 ml. and 3) rising blood urea nitrogen concentration or the onset of oliguria. Some cases reported did not fit these criteria and have been omitted.[7, 8, 18, 23, 28, 66] On this basis, we accepted 68 cases from the literature and have added two of our own (Table 1).

Case Reports

Case 1. A 62-year-old Negro woman was admitted to the Norfolk General Hospital on March 21, 1962 with a complaint of pain in her left flank and lower back of 7 months duration. About 1 month after the onset of pain she had been admitted to the hospital for several days with angina pectoris and was sent home with a sedative and nitroglycerin. During the ensuing months, the pain became worse and for 2 months prior to admission she was unable to get out of bed without help. She also noticed anorexia, weight loss and chronic constipation. She complained of arthritis in her lower extremities. There were frequent episodes of nausea but no vomiting. There was some recent mental confusion and loss of memory.

Past history revealed several episodes of urinary tract infection which had responded to treatment. There had been ten pregnancies. There was also a history of thyroid enlargement since childhood. She also had polyuria and polydipsia with nocturia.

Significant physical findings were a somewhat somnolent woman complaining bitterly of pain involving the lower back and lower extremities on motion or manipulation. There was a firm nodular mass in the region of the isthmus of the thyroid which extended somewhat to the right. There was tenderness in the left flank and in the lower lumbar area of the spine. Deep tendon reflexes were symmetrically depressed.

The clinical impression on admission was metastatic bone disease involving the spine and pelvis or possibly Paget's disease of the bone. X-ray films showed marked osteoporosis involving the lumbar spine and pelvic bones and cystic changes in the body of the innominate bone. There was also osteoporosis of the metacarpals and the skull and absence of the lamina dura of the maxillae. All these changes were interpreted as consistent with the diagnosis of hyperparathyroidism.

Initial laboratory studies revealed calcium of 17 mg./100 ml., phosphorus 3 mg./100 ml. and an alkaline phosphatase of 36 Bodansky units. Blood urea nitrogen was 15 mg./100 ml. Four days following admission her serum calcium was 17.8 mg./100 ml., phosphorus 2.9 mg./100 ml. and blood urea nitrogen 25 mg./100 ml. Twenty-four-hour urinary calcium level was 237 mg. and urinary phosphorus 630 mg. On April 2, serum calcium had risen to 22.8 mg./100 ml. and phosphorus to 4.6 mg./100 ml.; blood urea was 55 mg./100 ml. The patient's general condition appeared to be deteriorating rapidly. A diagnosis of hyper-

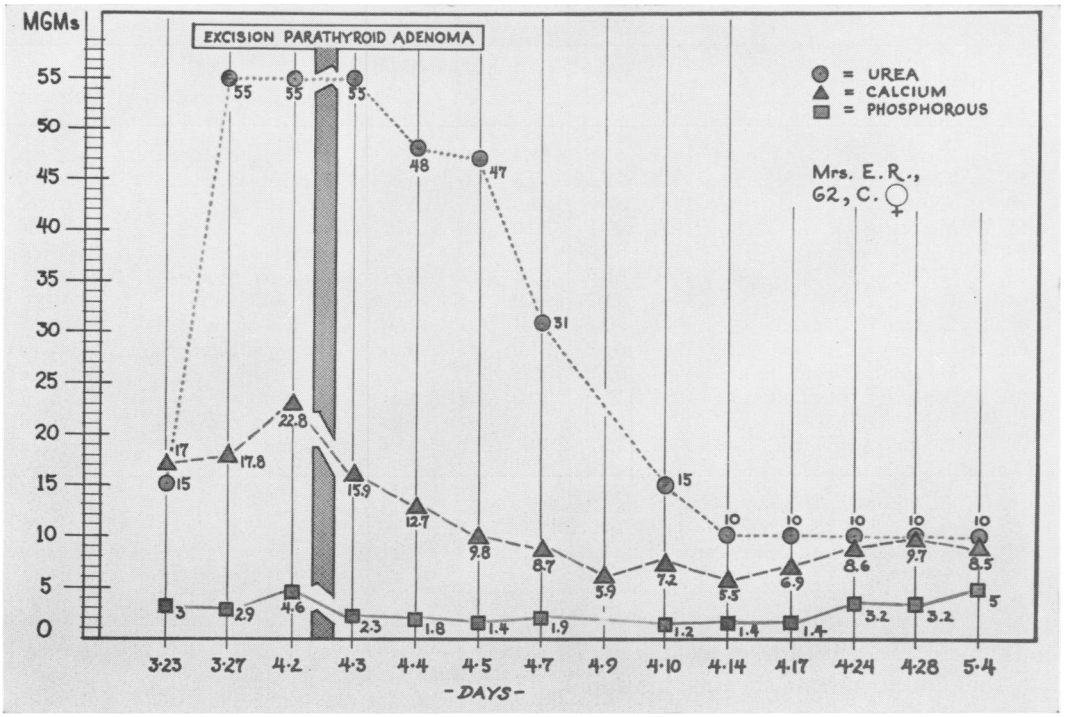

FIG. 1. Urea, phosphorus and calcium levels as a function of time following excision of parathyroid adenoma (Case 1).

parathyroid crisis was made and immediate surgical intervention was recommended.

Exploration of the neck revealed a single parathyroid adenoma in the region of the right superior pole of the thyroid gland. The mass which had been felt was a colloid adenoma of the thyroid and the parathyroid tumor had not been palpable. The remaining three parathyroids were exposed and appeared to be normal in size and shape. Following operation serum calcium levels dropped. She was given calcium and dihydrotachysterol by mouth. Tetany never developed. On a few occasions when the serum calcium level dropped below 8 mg./100 ml., she was given parathyroid hormone intramuscularly. After a few days when she was able to take calcium by mouth, all signs of impending tetany disappeared and her remaining postoperative course was uneventful. She was discharged from the hospital 32 days following operation and at that time was remarkably improved. She still complained of back and joint pains but this was less severe. Gastro-intestinal symptoms had disappeared, and her mental confusion completely cleared.

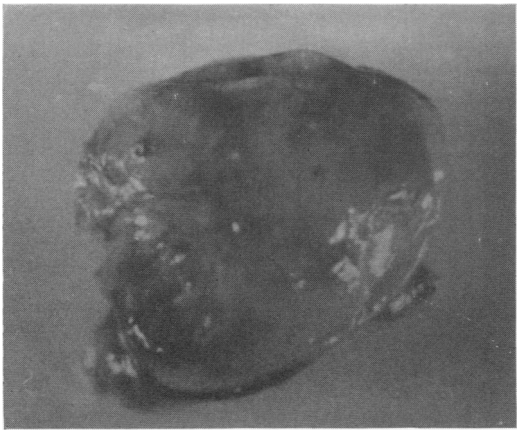

FIG. 2. Parathyroid adenoma measuring 3.4 × 2.3 × 1.4 cm. and weighing 4.0 Gm. (Case 1).

Since discharge, she has continued to improve. There was one episode of urinary infection which responded to treatment. At no time either before or after operation has there been any indication by x-ray of nephrolithiasis. X-rays of her lumbosacral spine made on Nov. 9, 1962 showed marked recalcification of the bony framework. There was considerable improvement of the cyst-like changes seen prior to the removal of the parathyroid adenoma.

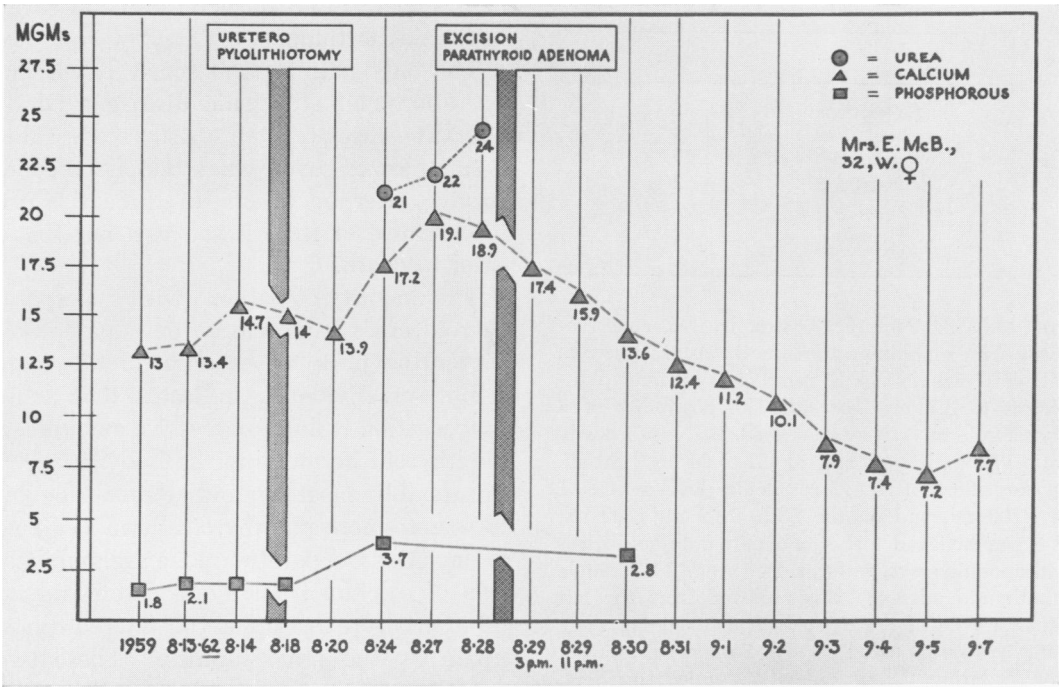

FIG. 3. Urea, phosphorus and calcium levels as a function of time following excision of parathyroid adenoma (Case 2).

The tumor measured 3.4 × 2.3 × 1.4 cm. and weighed 4.0 Gm. Pathologic examination showed a parathyroid adenoma of predominantly chief cell type.

Case 2. A 32-year-old woman was admitted to the Norfolk General Hospital on August 11, 1962, because of right ureteral colic. Initially there was evidence of multiple calculi in the left kidney and a solitary calculus in the right ureter. Admission laboratory tests were normal except for serum calcium and phosphorus levels of 13.4 mg./100 ml. and 2.1 mg./100 ml., respectively.

In the past she had first experienced an episode of right renal colic in 1950. In 1954 and in 1957 she had two normal deliveries and had no renal complications during either pregnancy. In 1959 a stone was surgically removed from the right ureter. At that time, serum calcium level was 13.0 mg./100 ml. and phosphorus 1.8 mg./100 ml. The possibility of hyperparathyroidism was considered.

Two days after admission serum calcium level was 14.7 mg./100 ml. and phosphorus 2.6 mg./100 ml. Dental x-ray films showed the presence of lamina dura. X-rays of the hands showed no evidence of bone resorption. Because of persistent pain, an extensive urologic procedure was carried out on Aug. 17. Attempts to remove the stone through the cystoscope were unsuccessful. The ureter was then surgically exposed and, because of extensive scar tissue from the previous operation, partial resection of the ureter with reimplantation into the bladder was necessary. The procedure lasted about 5 hours and following this she was quite ill. On Aug. 24, she complained of upper abdominal pain with nausea and vomiting. It was believed that she was probably developing pancreatitis. Serum amylase level was 288 units (high normal 160) which, on the following day,

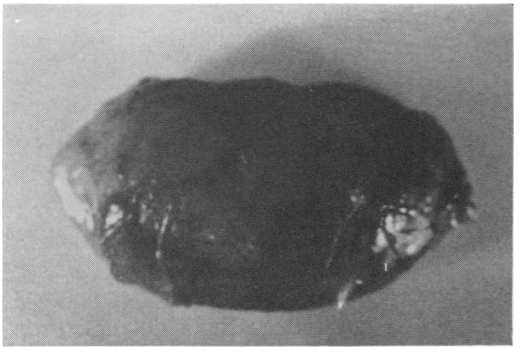

FIG. 4. Parathyroid adenoma measuring 3.0 × 1.6 × 1.5 cm. and weighing 4.2 Gm. (Case 2).

TABLE 2. *Pathologic Diagnosis*

	Cases
Single adenoma	55
Two adenomas	5
Hyperplasia	7
Carcinoma	2
Iatrogenic	1
Total	70

rose to 380. Pancreatitis was treated conservatively with some improvement. On Aug. 24 serium calcium level rose to 17.2 mg./100 ml. and phosphorus to 3.7 mg./100 ml. The possibility of a parathyroid crisis was considered. BUN rose slowly from 17 mg./100 ml. on Aug. 21 to 24 mg./100 ml. on Aug. 28. On Aug. 27, calcium level was 19.1 mg./100 ml. and on the 28th, 18.9 mg./100 ml. She was believed to be in hyperparathyroid crisis and operation was performed on Aug. 29. A single parathyroid adenoma was removed from the left superior pole of the thyroid. The remaining three parathyroids appeared normal. Serium calcium fell slowly during the postoperative period, on Sept. 3, to 7.9 mg./100 ml. and on this day she developed tetany. This was treated with calcium gluconate intravenously, and she was also given oral calcium gluconate and dihydrotachysterol. Additional intravenous calcium gluconate was necessary for the following 2 days because of tetany. After this, however, she improved steadily and was discharged from the hospital on Sept. 8. She continued to take calcium gluconate and small doses of dihydrotachysterol for about 2 weeks after discharge. Since that time she has remained well. BUN returned to normal.

The parathyroid tumor measured 3 × 1.6 × 1.5 cm. and weighed 4.2 Gm. It proved to be a parathyroid adenoma and consisted mostly of chief cells.

Discussion

In the reviewed cases of hyperparathyroid crisis there were 37 females and 33 males. This is in contradistinction to chronic hyperparathyroidism in which the ratio of females to males was at least two to one. Nelson and Cantrell [47] noted that most adenomas were of the chief cell variety. In this review, of 60 patients with adenomas, 33 were designated as the chief cell type. Where the anatomic location of the tumor was specified, 34 occurred on the right side of the neck, 14 on the left side, and seven in the mediastinum.

The only patient who survived without operation had iatrogenic disease.[39] Of 35 operative cases, 28 (80%) survived. Table 3 summarizes seven cases which failed to survive after operation. In three the primary cause of the disease was not found prior to death.

The majority of patients with hyperparathyroid crisis have had chronic hyperparathyroidism prior to the onset of the acute symptoms. Evidence indicates that acute exacerbation is due to excessive amounts of parathyroid hormone in the body.[14, 26, 31, 41] Presumably a parathyroid adenoma begins to secrete more parathyroid hormone. Two main actions of parathormone are mobilization of calcium from the skeleton and inhibition of reabsorption of filtered phosphate by the renal tubules.[24] These two functions are apparently independent. Tubular reabsorption of phosphate is greatly lowered in patients with hyperparathyroidism. Lowering of serum phosphorus level through renal loss is accompanied by increased mobilization of calcium from the skeleton. As increased amounts of the hormone are secreted, serum calcium concentration rises rapidly. Albright [1] estimated that the critical level of serum calcium was 17 mg./100 ml. and when calcium rises above this level there is a direct depressing effect on kidney function and oliguria. Whether oliguria is due to the increased amount of parathormone or to the high level of serum calcium is not known. Once oliguria ensues, phosphorus rises from a low level to normal and then to high as uremia sets in.

Increased serum calcium concentration is also thought to be directly injurious to tissues. The kidneys become infiltrated with calcium which is probably one of the causes of renal failure. Heart muscle also becomes infiltrated with calcium [41] and produces abnormalities in the electrocardiogram and arhythmias and eventually the

TABLE 3. *Summary of Fatal Operative Cases*

Case	Author	Year Reported	Operation	Result
3	Wanke	1930	Excision two adenomas	Died 19 days after operation—autopsy
45	Derbyshire & Angle	1960	Excision adenoma	Died 18 hours after operation—autopsy showed diffuse aspiration pneumonia
52	Fink & Finfrock	1961	Negative exploration of neck	Died—autopsy showed adenoma in mediastinum
56	Veenema	1961	Excision adenoma of neck	Died—autopsy showed second adenoma in mediastinum
63	Wilson *et al.*	1964	1. Negative exploration neck and anterior mediastinum 2. Negative exploration neck and entire mediastinum.	Died—adenoma found on pericaridum at autopsy
64	Wilson *et al.*	1964	1. Exploration neck, biopsy two glands 2. Negative exploration mediastinum	Died—two hyperplastic glands found with thyroid at autopsy
68	Lemann & Donatelli	1964	Excision adenoma of neck	Died; did not survive operation—no autopsy

heart fails. A number of early cases were reported as dying with heart attacks.[16, 29] The central nervous system is also susceptible to increased serum calcium concentration.[20] Varying degrees of psychic disturbances, and mental depression with lethargy, and coma occur. The gastro-intestinal tract is also affected. Nausea, vomiting and abdominal pain are frequent symptoms. The relationship between hyperparathyroidism, duodenal ulcer [5, 12] and pancreatitis [13, 16, 28] has been noted.

It has been suggested that certain factors during the course of chronic hyperparathyroidism might throw the patient into an acute episode.[47] A number of cases have followed a minor operation or anesthetic, such as a cystoscopy.[31, 56, 63] Some cases occurred after trauma or after undue manipulation of structures in the neck, such as frequent physical examinations.[28] This suggests that it is possible to massage the parathyroid adenoma and increase its secretion. A final factor that has been suggested is increased intake of calcium. Some patients were actually given calcium because of central nervous system symptoms, and a number of others were receiving milk and alkali for gastro-intestinal symptoms.[12] Certainly a sudden increase in calcium intake might elevate the serum calcium.[38]

Because of the high mortality of acute hyperparathyroidism, early recognition is important. The following signs should be looked for in all cases of hyperparathyroidism: 1) rapidly rising serum calcium concentration, especially above 15 mg./100 ml., 2) low serum phosphorus levels which rise as oliguria ensues, 3) rising blood urea nitrogen level, 4) acute gastro-intestinal, cardiovascular or central nervous system symptoms.

Once the patient is in crisis, the emergency nature of the situation must be recognized. The only way of overcoming the crisis is surgical removal of the offending

parathyroid tissue. Hydration of the patient with normal saline is probably the only worthwhile preoperative preparation. As pointed out by Lemann and Donatelli,[38] the value of medical measures for the treatment of calcium intoxication are unproved.

Summary

Two cases of hyperparathyroid crisis have been reported. In both it is believed that a fatal outcome was prevented by rapid surgical intervention. Sixty-eight cases collected from the literature are surveyed. Mortality is 59 per cent in the 70 cases. The salient features of the condition have been discussed. Most patients developing acute crisis have had previous signs of chronic hyperparathyroidism. A sudden rise in serum calcium concentration is usually followed by oliguria and uremia. Once acute crisis develops, surgical operation as an emergency procedure is necessary.

References

1. Albright, F., P. C. Baird, O. Cope and E. Bloomberg: Studies on the Physiology of the Parathyroid Glands. IV. Renal Complications of Hyperparathyroidism. Amer. J. Med. Sci., **187**:49, 1934.
2. Alexander, H. B., J. J. Pemberton, E. J. Kepler and A. C. Broders: Functional Parathyroid Tumors and Hyperparathyroidism. Amer. J. Surg., **65**:157, 1944.
3. Anderson, T. R. and C. A. McWhorter: Carcinoma of the Parathyroid Gland. A Report of a Case. Amer. J. Clin. Path., **21**:952, 1951.
4. Arnold, W., Cited by Millgren, J.: Acute Fatal Hyperthyroidism. Acta Path. Microbiol. Scand., **20**:693, 1943.
5. Atsmon, A., M. Frank, P. Nathan and A. DeVries: Recurrent Acute Hyperparathyroidism with Severe Gastrointestinal Manifestations. Gastroenterology, **39**:83, 1960.
6. Bergstrand, H.: Osteitis Fibrosa Generalista Ricklinegausen mit Pluriglandularer Affektion der Innerschetorischen Drusen und Roentgenologisch Nachweisbaren Parathyroideatumor. Acta Med. Scand., **76**:128, 1931.
7. Berne, C. J.: Discussion of Papers by Jarvis, F. J., E. R. Sanderson and R. C. Coe: Hyperparathyroidism. Amer. J. Surg., **94**:292, 1957.
8. Bogdoroff, M. D., A. H. Woods, J. E. White and F. L. Engle: Hyperparathyroidism. Amer. J. Med., **21**:583, 1956.
9. Bottino, C.: On a Case of Embolic Occlusion of the Central Artery of the Retina in the Course of Acute Hyperparathyroidism. Ann. Ottal., **87**:583, 1961.
10. Bradlaw, B. A. and N. Segel: Acute Hyperparathyroidism with Electrocardiographic Changes. Brit. Med. J., **2**:197, 1956.
11. Carlson, K. P., H. Bates and W. Boyce: Death Due to Parathyroid Crisis. J. Urol., **84**:219, 1960.
12. Carpenter, H. M. and E. P. Paulter: Hyperparathyroidism with Renal Insufficiency: Report of a Case Confused with the "Burnett Syndrome." N. Engl. J. Med., **250**:453, 1954.
13. Coffey, R. J.: Hyperparathyroidism and Calcific Pancreatitis. Amer. Sur., **25**:310, 1959.
14. Collip, J. B.: The Parathyroid Glands. Medicine, **5**:1, 1926.
15. Cope, O.: Pancreatitis, A Diagnostic Clue to Hyperparathyroidism. Ann. Surg., **145**:857, 1957.
16. Dawson, J. W. and J. W. Struthers: Generalized Osteitis Fibrosa with Parathyroid Tumor and Metastatic Calcification. Edinburgh Med. J., **30**:421, 1923.
17. Derbyshire, R. C. and R. M. Angle: Acute Hyperparathyroidism: Case Report. Amer. Surg., **26**:166, 1960.
18. Dowlatobodi, H.: Acute Fatal Parathyroid Poisoning with Necrosis of the Parathyroid Adenoma Prior to Death. J. Clin. Endocr., **19**:1481, 1959.
19. Fink, W. J. and J. D. Finfrock: Fatal Hyperparathyroid Crisis Associated with Pancreatitis. Amer. Surg., **27**:424, 1961.
20. Fitz, T. E. and B. L. Hallman: Mental Changes Associated with Hyperparathyroidism. Arch. Int. Med., **89**:547, 1952.
21. Gassmann, R. and H. E. Hass: Acute Hyperparathyroidism. Schweiz. Med. Wschr., **90**: 67, 1960.
22. Gershberg, H., S. Jonas and D. P. Stiff: Hyperparathyroidism with Uremia in a Seventy-Seven Year Old Man. J.A.M.A., **182**:136, 1962.
23. Goldberg, E. and R. Torack: Combined Primary and Secondary Hyperparathyroidism. Two Case Reports and a Review. Ann. Int. Med., **52**:87, 1960.
24. Goldman, L., E. S. Gordon and E. L. Chambers, Jr.: Changing Diagnostic Criteria for Hyperparathyroidism. Ann. Surg., **146**: 407, 1957.
25. Goldman, L.: Unusual Manifestations of Hyperparathyroidism. Surg. Gynec. & Obstet., **100**:675, 1955.
26. Hanes, F. M.: Hyperparathyroidism Due to Parathyroid Adenoma with Death from Parathormone Intoxication. Amer. J. Med. Sci., **197**:85, 1939.
27. Harmon, M.: Parathyroid Adenoma in a Child. J. Dis. Child., **91**:313, 1956.
28. Henrikson, C.: Acute Hyperparathyroidism and Acute Pancreatitis. Acta Path. Microbiol. Scand., **50**:42, 1960.
29. Herzenberg, H.: Ueber einen Fallvon Osteodystrophia Fibrosa Generalisata mit Eigenartig Klinischem Verlauf. Zbl. Allg. Path., **57**: 232, 1933.
30. Hewson, J. S.: Parathyroid Crisis: A Cause of Sudden Death. Arch. Int. Med., **102**:199, 1958.
31. Horowitz, W. and A. A. Berenbaum: Primary Hyperparathyroidism Due to a Parathyroid

Adenoma: Antemortum Diagnosis with Termination in Possible Acute Parathyroid Hormone Intoxication. Ann. Int. Med., 49:181, 1958.
32. Howard, J. E., R. H. Follis, Jr., E. R. Yendt and T. B. Conner: Hyperparathyroidism. Case Report Illustrating Remission Due to Necrosis of Adenoma. J. Clin. Endocr., 13: 997, 1953.
33. James, P. R. and P. G. Richard: Parathyroid Crisis. Arch. Surg., 72:553, 1956.
34. Kimberly, Robert C.: Two Unusual Tumors of the Parathyroid Gland. Southern Med. J., 50:609, 1957.
35. Klein, L., K. Albertsen and P. H. Curtiss, Jr.: Urinary Hydroxyproline in Parathyroidism. A Study of Three Cases With and Without Bone Lesions. Metabolism, 11:1023, 1962.
36. Kretschmer, H. L.: Parathyroid Adenoma and Renal Calculi. J. Urol., 63:947, 1950.
37. Lee, C. M., Jr., W. T. McElhenney and E. A. Gall: Unusual Manifestations of Parathyroid Adenoma. Arch. Surg., 71:475, 1955.
38. Lemann, J., Jr. and A. A. Donatelli: Calcium Intoxication Due to Primary Hyperparathyroidism. Ann. Int. Med., 60:447, 1964.
39. Lowenberg, H. and T. M. Ginsburg: Acute Hypercalcemia: Report of a Case. J.A.M.A., 99:1166, 1932.
40. McClure, R. D. and C. R. Lam: End Results in the Treatment of Hyperparathyroidism. Ann. Surg., 121:454, 1945.
41. McJunkin, F. A., W. R. Tweedy and H. C. Brenhans: The Parathyroid Hormone: Its Regulatory Effect on the Parathyroid Glands and Toxic Effect on the Tissues of the Rat. Arch. Path., 14:649, 1932.
42. Mansberger, A. R., Jr., H. Lovice and J. S. McLaughlin: Intermittent Acute Hypercalcemic Crisis. Amer. Surg., 30:167, 1964.
43. Mellgren, J.: Acute, Fatal Hyperparathyroidism. Acta. Path. Microbiol. Scand., 20:693, 1943.
44. Mellgren, J.: Acta Soc. Med. Upsal., 42:35, 1936.
45. Morelle, J.: Hyperparathyroidie A Forme Digestive. J. Chir. et Ann. Soc. Belge Chir., 33:178, 1934.
46. Murphy, T. R., W. R. Remine and M. K. Burbank: Hyperparathyroidism Report of a Case in which Parathyroid Adenoma Presented Primarily with Profound Muscular Weakness. Proc. Mayo Clin., 35:629, 1960,
47. Nelson, A. R. and J. R. Cantrell: Acute Parathormone Poisoning Complicating Parathyroid Adenoma. Arch. Surg., 83:1, 1961.
48. Oliver, W. A.: Acute Hyperparathyroidism. Lancet, 2:240, 1939.
49. Reinfrank, R. F. and T. L. Edwards: Parathyroid Crisis in a Child. J.A.M.A., 178:468, 1961.
50. Rogers, H. M.: Parathyroid Adenoma and Hypertrophy of Parathyroid Glands. J.A.M.A., 130:22, 1946.
51. Schneider, H. O.: A Case of Hyperparathyroidism with Unusual Deformity of the Thoracic Cage. Ann. Int. Med., 39:357, 1953.
52. Schrumph, A. and H. F. Harbitz: A Case of Hyperparathyroidism with Nephrocalcinosis and Azotemia. Acta Chir. Scand., 80:199, 1937.
53. Selye, H., G. Gabbiani and B. Tuchweber: Protection by Calciphylaxis Against Otherwise Fatal Parathyroid Hormone Intoxication. Endocrinology, 73:825, 1963.
54. Silvestrini, F., G. Faglia, P. Bregani and F. Costa: Su due Casi di Crisi Iperparatiavidea ad Esito Letali. Folia Endocr. (Pisa), 13: 217, 1960.
55. Smith, F. B. and R. T. Cooke: Acute Fatal Hyperparathyroidism. Lancet, 2:650, 1940.
56. Smith, L. C., H. H. Bradshaw and I. L. Holleman: Hyperparathyroid Crisis: A Surgical Emergency. Amer. Surg., 29:761, 1963.
57. Snapper, I.: Parathyroid Tumor and Changes of the Bones. Arch. Int. Med., 46:506, 1930.
58. Spinner, S.: Primary Hyperparathyroidism with Acute Parathyroid Hormone Intoxication. Postgrad. Med., 28:368, 1960.
59. Staub, W., D. M. Groyzel and P. Rosenblatt: Mediastinal Parathyroid Adenoma: Report of Case with Unusual Fatal Course. Arch. Int. Med., 85:765, 1950.
60. Templeton, T. B.: Parathyroid Crisis Successfully Treated by Surgery. N. Carolina Med. J., 23:22, 1962.
61. Thomas, W. C., J. G. Wiswell, T. B. Conner and J. E. Howard: Hypercalcemic Crisis Due to Hyperparathyroidism. Amer. J. Med., 24:229, 1958.
62. Turchi, J. J., R. H. Flandreau, A. L. Forte, G. N. French and G. D. Ludwig: Hyperparathyroidism and Pancreatitis. J.A.M.A., 180:799, 1962.
63. Veenema, R. J.: Parathyroid Tumors: Intermittent Function, A Pitfall in Diagnosis. Calif. Med., 95:83, 1961.
64. Waife, S. O.: Parathyrotoxicosis: The Syndrome of Acute Hyperparathyroidism. Amer. J. Med. Sci., 218:624, 1949.
65. Wanke, R.: Reitrag zur Stoffwechsel Untersuchung der Osteodystrophia Fibrosa Deutsch. Z. Chir., 228:210, 1930.
66. Watanabe, M., S. Baxter and J. C. Bell: Hyperparathyroidism Due to Late Recurrence of Parathyroid Adenoma. Amer. J. Med., 31: 498, 1961.
67. Wilson, R. E., W. F. Bernhard, H. Polet and F. D. Moore: The Problem of Acute Parathyroid Intoxication. Ann. Surg., 159:79, 1964.
68. Young, J. H. and K. Emerson, Jr.: Parathyroid Carcinoma Associated with Acute Parathyroid Intoxication. Ann. Int. Med., 30:823, 1949.
69. Young, M. O. and B. Halpert: Parathyroid Adenoma with Generalized Metastatic Calcification. Arch. Path., 44:628, 1947.

Discussion

Dr. Kenneth W. Warren (Boston): I think it is important to point out, as Dr. Coffey has, that there has been a trend in earlier diagnosis of hyperparathyroidism and, as a result of this, we see less advanced disease, especially in terms of bone pathology. Nevertheless, bone pathology, regardless of whether it be just lack of calcification