Hyperparathyroid Crisis

Clinical and Pathologic Studies of 14 Patients

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A study is presented of 14 patients with hyperparathyroid crisis treated at the Massachusetts General Hospital between 1964 and 1978. These patients showed diverse clinical manifestations that were indistinguishable from those in patients with pseudohyperparathyroidism. Their symptoms varied from progressive fatigue, malaise, and weakness to those related to the gastrointestinal and urinary tracts. The one biochemical alteration commonly found among these patients was the rapid increase in the serum calcium. There was a concomitant rise in the BUN in 50% of the patients and in the creatinine in 80%. The diagnosis was established by an elevated immunoreactive parathyroid hormone (PTH) level in all eight patients (100%) who had the radioimmunoassay; by the presence of subperiosteal resorption of the phalanges in six of the eight patients (75%); and in three of four patients (75%) by the loss of the lamina dura of the teeth. The 12 patients who had surgery all survived; the two who did not died. Thirteen patients (93%) had a neoplasm—an adenoma in 12 and a carcinoma in one. One patient had hyperplasia (7%). Nine patients (64%) received hypocalcemic drug therapy. The serum calcium temporarily fell to 12 mg/100 ml in five patients (56%) but failed to budge in four (44%). Simultaneous treatment with saline infusion, furosemide and with hypocalcemic drugs over a prolonged period compounded the difficulty at operation by increasing interstitial edema. Our findings from this study show prompt surgical intervention as the ideal treatment for hyperparathyroid crisis, preferably, within 72 hours of the acute onset of symptoms.

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THE TOXICITY OF the parathyroid hormone (PTH) was clearly demonstrated as early as 1926. Collip[7] in his experiment found that dogs who were injected with multiple large doses of parathyroid extract invariably died within two or three days. Death was preceded by anorexia, vomiting, and a rise in the serum calcium level to 20 mg/100 ml, concomitant with the retention of blood urea nitrogen (BUN).

Hyperparathyroid crisis, also known as acute parathyroid poisoning, acute hyperparathyroidism, parathyrotoxicosis, and acute parathyroid intoxication, was not recognized in man until 1932, when a 5-year-old boy was given repeated injections of parathyroid extract for the treatment of purpura.[14] The boy vomited persistently and became lethargic, presenting a clinical picture similar to that of Collip's dogs. As his serum calcium rose to a level of 19 mg/100 ml, he was on the verge of dying, but he recovered, as the injections of parathyroid extract were discontinued. Since then, sporadic accounts of hyperparathyroid crisis have appeared in the literature.[8,9,11,15,16,19,22,24,27]

Of the first 882 patients with surgically confirmed hyperparathyroidism who were treated at the Massachusetts General Hospital between 1930 and 1978, 14 (1.6%) had hyperparathyroid crisis. The following presentation is based on a clinical and pathologic study of these 14 patients.

Clinical Manifestations

Eight of the 14 patients were men and six, women. Their ages ranged between 20 and 73 years. The mean age was 52.

The clinical manifestations were extremely diverse (Table 1). At the outset, the majority of these patients experienced progressive fatigue, malaise, and weakness, associated with the loss of mental acuity and memory, culminating in lethargy, disorientation and, for a few, the lapse into coma. Eleven of the 14 presented with one or more of these symptoms at the time they were first seen.

Simultaneous with or prior to these mental derangements, symptoms related to the gastrointestinal tract became manifest. The more frequent were anorexia and nausea, associated with constipation and dyspepsia. These symptoms occurred in seven patients in our

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0003-4932/79/1200/0782 $00.95

TABLE 1. *Clinical Manifestations of Hyperparathyroid Crisis in 14 Patients*

Patient No.	Sex	Age	Manifestations	Duration
1	M	73	Fatigue, loss of memory; polyuria; constipation. Anorexia, polydipsia, weight loss (10 lbs). Right neck mass.	1 year 6 weeks
2	M	57	Polyuria, nocturia, hematuria. Fatigue, weakness; anorexia, nausea; constipation, abdominal pain. Right neck mass.	1 year 1 month
3	M	68	Duodenal ulcer. Fatigue, malaise. Polyuria, nocturia. Anorexia, nausea, vomiting Right neck mass.	30 years 3 weeks 1 week 5 days
4	M	40	Fatigue, lassitude; constipation. Peptic ulcer pain. Anorexia, nausea, vomiting, weight loss (20 lbs).	2 years 5 months 2 months
5	F	62	Anorexia, nausea, vomiting. Fatigue, weakness, listlessness after eye surgery. Abdominal pain; lethargy.	1 week 4 days 2 days
6	F	39	Fatigue, weakness; polyuria, polydipsia, hematuria; constipation; renal stone. Anorexia, nausea, vomiting; abdominal pain after parathyroid exploration. Somnolence; comatose; cardiac arrest after selective venous catheterization study.	2 years 7 days 8 hours
7	F	20	Renal stone, cystitis, polyuria, hematuria. Anorexia, nausea, vomiting; severe bone and muscle pain. Right ureterolithotomy. Right neck mass.	2 years 2 days 5 days
8	M	65	Back pain. Disabling muscle pain. Mental confusion, depression.	4 years 3 months 3 days
9	F	32	Polyuria, nocturia, pyuria, cystitis. Polydipsia. Right ureterolithotomy, renal stone. Right neck mass.	2 years 3 months 1 week
10	F	42	Polyuria, polydipsia, nocturia, hematuria, constipation, renal stone. Right and left pyelonephrotomy, renal stone. Right neck mass.	1 year 2 weeks
11	M	63	Lethargy, disorientation. Comatose; nephrocalcinosis, hematuria. Left neck mass.	4 days 12 hours
12	M	61	Lethargy; Cheyne-Stokes respiration, unconsciousness; premature ventricular contractions.	1 week
13	F	65	Renal stone, polyuria, pyuria; bone pain. Muscle pain. Lethargy, confusion.	6 years 1 year 1 week
14	M	45	Lethargy, weakness, loss of memory; loss of weight (10 lbs).	3 weeks

series. Three patients complained of abdominal pain, which mimicked acute surgical abdomen. In addition, five had acute vomiting, which was intermittent in two and persistent in three. Vomiting was invariably projectile, often occurring early in the morning. Characteristically, the vomitus was bilious at first, later becoming unproductive.

Many of these patients had had urinary symptoms for months or even years. Polyuria, nocturia, and polydipsia occurred in eight patients, and in six, hematuria and pyuria were associated with renal calculi. The presence of renal stones or nephrocalcinosis in acute hypercalcemia attests to the chronicity of the disease process, and these complications serve as important diagnostic clues for hyperparathyroid crisis.

Other clinical manifestations of the disease, although rare, were intense pain of bone and muscle and cardiac arrhythmias. In three patients, the pain was so severe that it could not be alleviated by the common analgesic

TABLE 2. *Serum Chemistries in 14 Patients with Hyperparathyroid Crisis**

Patient No.	Ca	P	Alk. P'tase	BUN	Cr	Cl	CO_2
1	12.5–17.6	3.0–2.8	6.6	11	1.8	—	—
2	18.0–18.4	2.3–4.4	10.6	47–64	3.4	99	23
3	17.0–18.2	5.4–5.1	18.0	22–48	4.2	96	32
4	15.8–17.6	1.8–2.4	11.7	10–5	—	99	26
5	15.0	5.1–6.6	4.9	135–150	2.6	86	26
6	16.8–20.1	5.0–7.0	8.9	33–50	2.0	96	26
7	13.0–15.0	1.7–2.7	6.9	13	1.9	103	24
8	16.0–17.2	2.5–3.0	11.9	30–40	2.4	106	24
9	15.4–19.6	2.7–4.1	5.5	34	2.1	100	30
10	11.7–15.7	2.2–3.3	8.2	18–44	2.3	109	23
11	16.0–18.7	3.2–3.9	8.2	36	2.3	95	26
12	15.8–18.8	4.1–7.5	5.0	47–59	1.7	83	24
13	13.6–15.4	2.5	10.7	40	—	99	20
14	19.2–19.0	2.6–2.3	8.0	11	1.3	104	24

* Normal values of Ca = 8.5–10.5 mg/dl. P = 3.0–4.5 mg/dl. Alk P'tase = 2.0–4.5 Bodansky units (BU). BUN = 8.0–25.0 mg/dl. Cr = 0.7–1.5 mg/dl. Cl = 100–106 mEq/l. CO_2 = 20–26 mEq/l.

drugs. Excision of the diseased parathyroid, however, provided instantaneous relief. Cardiac arrhythmia in the form of premature ventricular contractions occurred in one patient. Again, conventional medical therapy was unsuccessful in restoring normal cardiac rhythm, until the hyperparathyroidism had been surgically corrected.

Cachexia was not commonly seen, and, despite their deteriorating mental conditions, these patients seldom seemed gravely ill. However, dehydration was common. It was manifest in sunken eyes, a coated tongue, and dry chapped lips, and it was made worse by acute vomiting.

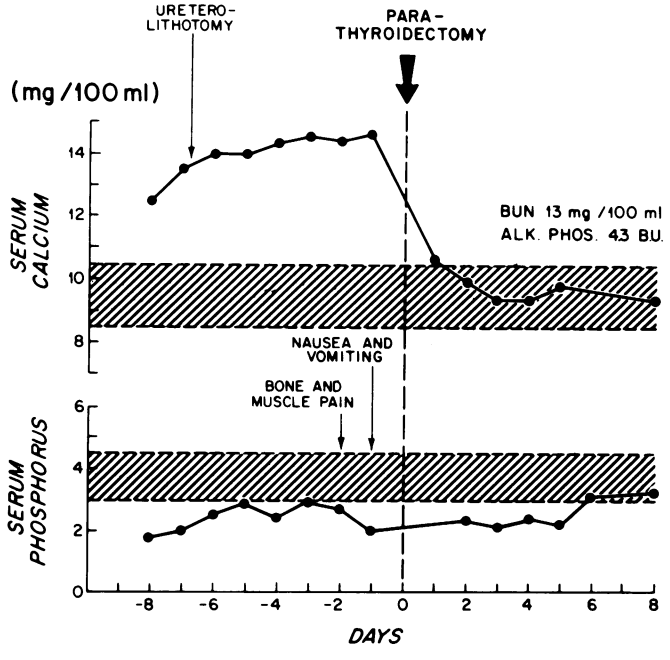

FIG. 1. Rapid acceleration of hyperparathyroid crisis evidenced by rise of serum calcium accounted for acute onset of symptoms in Case 7. All symptoms abated after removal of parathyroid carcinoma.

In seven patients (50%), a palpable mass found in the neck could not be distinguished from a solitary thyroid nodule. By radioactive iodine (RaI) scintiscanning, it appeared to be a nonfunctioning thyroid nodule, but, in each of the seven patients at surgery, the mass proved to be the diseased parathyroid gland.

Contrary to what might be expected in a hypercalcemic patient with malignancy, very few of the 14 patients lost much weight. Only three lost between 10 and 20 pounds within a period of one to four months, as two had persistent vomiting and one had severe anorexia.

Laboratory Data

A progressively rising serum calcium was the rule, although the critical level varied widely among these patients (Table 2). As it rose to 17 mg/100 ml or higher, clinical manifestations became increasingly apparent in ten patients. In three others, even before the serum calcium had reached 17 mg/100 ml, the symptoms had already become severe. There was evidently a close correlation between the level of the serum calcium and the severity of the symptoms. Nonetheless, the rapidity with which the disease progressed also played an important role. The clinical course in one of our patients illustrates this point (Fig. 1). Five days after an uneventful ureterolithotomy for ureteral stone, the patient, a 20-year-old girl, experienced the acute onset of intense muscle and bone pain, followed a day later by persistent projectile vomiting. At the same time, her serum calcium rapidly rose from 13 to 15 mg/100 ml. Hyperparathyroid crisis was diagnosed. Within 48 hours, the patient underwent emergency exploration of the neck, and a 3.5 cm parathyroid carcinoma was removed. Postoperatively, the patient immediately became asymptomatic. Bone and muscle pain dis-

TABLE 3. *Hematologic, PTH, and Urinary Findings in 14 Patients with Hyperparathyroid Crisis*

Patient No.	Hct (%)	Hgb (g/dl)	PTH*		Urine		
			Preop	Postop	pH	sp g	Ca/24°
1	—	14.3	—	—	7.0	1.000	780
2	27	9.7	—	—	5.5	1.006	486
3	38	10.8	—	—	6.0	1.006	—
4	29	—	—	—	5.5	1.007	474
5	48	—	—	—	5.5	1.013	—
6	30	—	—	—	7.5	1.002	—
7	39	14.0	150	3.5	7.0	1.005	222
8	31	12.0	157	3.5	—	1.010	632
9	34	11.5	150	6.3	—	—	222
10	41	10.7	45	—	6.0	1.010	498
11	36	13.0	90	4.0	5.0	1.006	194
12	47	15.9	49	3.5	5.0	1.015	—
13	—	13.7	150	3.0	6.0	1.008	190
14	30	10.5	80	—	6.5	1.009	—

* Normal PTH less than 10 microliter equivalent per ml/plasma.

appeared, vomiting abated. The acute onset of her symptoms was evidently attributable to the rapid progression of the disease, as evidenced by the accelerated rise of the serum calcium.

Eight patients had hypophosphatemia; three had hyperphosphatemia; and three had normophosphatemia. The serum phosphorus was normal or low initially, but, as the disease progressed, it invariably rose, concomitant with the impairment of renal function, as evidenced by the rise of the BUN and creatinine.

In all 14, the alkaline phosphatase was elevated, reflecting active resorption of the bones. The BUN level was normal in six and elevated in eight. In seven, it rose simultaneously with the rise of the serum calcium. In the 12 patients in whom the serum creatinine was determined, the level was elevated in all but one patient.

There was little or no change in the serum sodium, potassium, total protein, albumin, globulin, and electrophoresis in these patients, but, in the 13 who had profile screening, the serum chloride was 102 meq/l or below in nine patients and above 102 meq/l in four.

The carbon dioxide level in all but one of the 11 patients remained within a normal range. A slightly elevated carbon dioxide level in Patient 3 could be attributed to the excessive use of antacids for the relief of pain from a duodenal ulcer.

The hematologic and urinary findings are shown in Table 3. A moderate amount of anemia with a hematocrit below 38% was observed in eight of the 14 patients in the series. Normochromic, normocytic anemia with a hematocrit of 30% or lower was present in four patients in whom bone marrow studies were found to be normal.

Urinalysis revealed a low specific gravity (between 1.000 and 1.015) in each of these patients; in ten, the urinary acidity (pH) ranged from 5.5 to 7.5. The amount of calcium excreted in the urine over a 24 hour period was determined in nine patients, and it ranged between 190 and 780 mg. In two, although the level of serum calcium was high, the urinary calcium was surprisingly low.

The immunoreactive parathyroid hormone (PTH) was determined in eight patients, and in each, the PTH level was considerably elevated (Table 3). The PTH was not available for the first six patients.

Roentgenographic Findings

Roentgenographic evidence of demineralization of one or more bones was present in most of the patients (Table 4). Especially noteworthy was the subperiosteal resorption of the phalanges seen in six of the eight patients (75%) whose hands were examined. In three of the four who had x-ray examination of the teeth, there was partial or complete loss of the lamina dura. Intravenous pyelography revealed the presence of either renal stones, nephrocalcinosis or both in six patients. Upper gastrointestinal examination demonstrated a duodenal ulcer in two.

Twelve patients had a cervical esophagographic study. An indentation of the esophageal wall was

TABLE 4. *Roentgenographic Findings in 14 Patients with Hyperparathyroid Crisis*

	Patients Examined	Positive	Negative
Subperiosteal resorption	8	6 (75%)	2
Lamina dura of teeth (absent)	4	3 (75%)	1
Renal stones	14	6 (43%)	8
Duodenal ulcer	14	2 (14%)	12
Cineesophagram	12	9 (75%)	3

TABLE 5. *Management of 14 Patients with Hyperparathyroid Crisis*

Patient No.	Preoperative Therapy	Days Treated	Condition	Surgery
1	Hydration.	3	Improved	Successful
2	Hydration.	2	Improved	Successful
3	Hydration.	1	Improved	Successful
4	Hydration.	2	Improved	Successful
5	Hydration. Lasix, prednisone, Neutra-Phos.	8	Patient died	No surgery
6	Hydration. Lasix, Neutra-Phos.	7	Patient died	No surgery
7	Hydration.	2	Improved	Successful
8	Hydration. Lasix, Neutra-Phos.	8	Improved	Successful
9	Hydration. Lasix, calcitonin, Neutra-Phos, mithramycin.	10	Improved	Successful
10	Hydration. Lasix, Neutra-Phos, mithramycin, calcitonin.	8	Worse	Successful
11	Hydration. Lasix, Neutra-Phos, Hydrocortisol.	8	Improved	Successful
12	Hydration. Lasix, prednisone, mithramycin, calcitonin. Dialysis.	8	Worse	Successful
13	Hydration. Lasix, Neutra-Phos.	13	Improved	Successful
14	Hydration. Lasix, Neutra-Phos.	14	Improved	Successful

TABLE 6. *Pathologic Findings of Hyperparathyroid Crisis in 14 Patients*

Patient No.	Pathology	Diseased Gland		Biopsied Gland(s)
		Size (cm)	Weight (g)	
1	Adenoma (RU)*	4 × 2.5 × 2	—	RL
2	Adenoma (RU)	4 × 3 × 2.5	10	RL LU
3	Adenoma (RU)	4 × 3 × 4	10	RL
4	Adenoma (LL)	3 × 1.5 × 1.5	5	RL
5†	Adenoma (RU)	5 × 5 × 6	—	—
6†	Adenoma (LU)	—	14	—
7	Carcinoma (RL)	3.5 × 2.5 × 2.5	7	RU
8	Hyperplasia (RU, RL, LL)	—	10	LU
9	Adenoma (RU)	5 × 4 × 1	—	RL
10	Adenoma (RU)	3 × 1.5 × 1	—	RU
11	Adenoma (LU)	7 × 5 × 3	35	RU LL
12	Adenoma (RU)	3.2 × 1.2 × 1	—	RL
13	Adenoma (LU)	5 × 4 × 3	—	LU
14	Adenoma (LU)	7 × 5 × 2	—	LU

* RU, RL = right upper, right lower gland. LU, LL = left upper, left lower gland.

† Uncovered at postmortem examination.

noted in nine (75%), and in each, it coincided with the location of the large parathyroid gland uncovered at surgery.

Treatment and Results

Prompt saline infusion was initiated in each of these patients in an attempt to combat dehydration and lower the serum calcium. Additionally, three patients received corticosteroids as a diagnostic aid in the differentiation of hyperparathyroid crisis from pseudohyperparathyroidism, but in none did the drug lower the serum calcium to any degree.

After having had adequate fluid replacement, five patients underwent successful emergency exploration of the neck within 24–72 hours of the acute onset of symptoms. In the remaining nine patients, surgery was deferred. In addition to hydration and diuresis, each was given one or more of the hypocalcemic drugs (Table 5). Five patients responded to the treatment, and, as their conditions improved, successful surgery was performed on an elective basis. Four failed to respond to the medical therapy which they had received for as many as eight days. As their conditions became progressively worse, two of the four underwent emergency surgical intervention and recovered. The other two patients did not have surgery and eventually died.

Pathologic Findings

Thirteen of the 14 patients had neoplasms. There were 12 adenomas and one carcinoma. Only one patient had primary hyperplasia (Table 6).

Unilateral exploration was performed in seven patients for an adenoma and in one for carcinoma. Bilateral exploration was performed in four patients: in one patient, for hyperplasia; in one, by intent because the pathologic diagnosis of the diseased gland

had been equivocal; and in two patients, for an adenoma in the second side explored.

All the diseased glands were unusually large, weighing from 5 to 35 g and measuring from 3 to 7 cm.

Postoperative Course

The 12 patients who underwent exploration all showed an immediate improvement of symptoms. Lethargy disappeared, nausea and vomiting subsided, and the appetite improved. Cardiac arrhythmia spontaneously abated. The response to surgery was dramatic.

Postoperatively, with few exceptions, the serum electrolytes returned to normal. However, three to four days were generally required for the serum calcium to reach a normal level (Fig. 2). Presumably, it takes time for the large calcium pool in the interstitial space to be mobilized for excretion. Hypocalcemia was seldom a problem. The serum phosphorous, regardless of whether it had been high or low, also reverted to a normal level. Contrary to expectation, both the BUN and the creatinine often remained high in the immediate postoperative period. In some patients, they rose even higher by the second or third postoperative day (Figs. 3a and b). Such sustained or peak elevation might easily be ascribed to progressive or irreversible renal impairment. It is not clearly understood why this happened, but the explanation could be that more time is required for the kidney to resume its normal function.

In each case, the plasma PTH fell promptly after surgery to a normal level (Table 3). Simultaneously, the symptoms improved dramatically. The immediate disappearance of the symptoms and the reversion of the PTH to a normal level lend support to the premise that the primary cause of the symptomatology may be the elevated PTH and the effect of the serum calcium, secondary. Similarly, anemia, which had stubbornly resisted conventional medical therapy, also showed signs of ameliorating, although it often took weeks or even months to resolve completely. The specific gravity and the pH of the urine generally became normal soon after the operation.

Our long-term follow-up studies indicated that it took from three to six months before roentgenologic study showed demonstrable improvement in the condition of the bones.

Postmortem Examination

Two patients died without having surgery. In each, a large parathyroid gland was found in the lower part of the neck. One of these diseased glands measured 5 × 5 × 6 cm, and one weighed 14 g. Examination of the lungs, kidneys, and gastric mucosa revealed extensive calcified deposits in one patient and nephrocalcinosis and renal stones in the other.

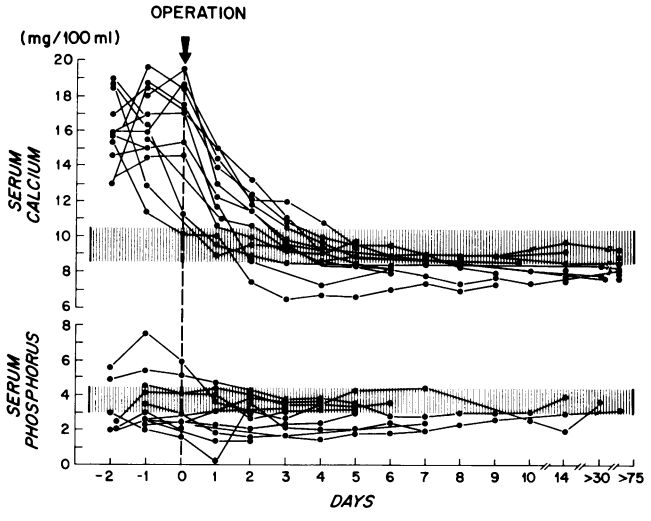

FIG. 2. Eventual but slow return of serum calcium to normal, seldom before third or fourth day. Slowness of return caused concern over thoroughness of exploration, but time may be needed to mobilize immense calcium pool for excretion from interstitial to intravascular space.

Discussion

Hyperparathyroid crisis is a rare disease. Fewer than 100 cases have been reported in the literature.[16] The disease affects both sexes. While it may occur at any age, it is more frequently encountered in the older age group.

Many hyperparathyroid patients with a relatively high serum calcium remain asymptomatic without ever having any of the acute symptoms of hyperparathyroid crisis. At the other extreme, a patient may present a clinical picture of hyperparathyroid crisis with a serum calcium level as low as 15 mg/100 ml. According to Fuller Albright, the danger signs which suggest the onset of hyperparathyroid crisis are a rapid escalation in the serum calcium to a level of about 17 mg/100 ml; a sharp decline in the output of urine; and a continuing rise in serum phosphorus and BUN.[2] To these, we have added a fourth, a marked elevation of the plasma PTH.

In making the diagnosis, the most difficult task is to differentiate hyperparathyroid crisis from pseudohyperparathyroidism. Neither the clinical manifestations nor the biochemical alterations characterize this disease exclusively, as similar findings may be noted in hypercalcemic crisis of an origin other than the parathyroid glands.[13]

The serum chloride level has been generally regarded as useful in differentiating the two diseases,[6,10,26] but we have not found it helpful in making

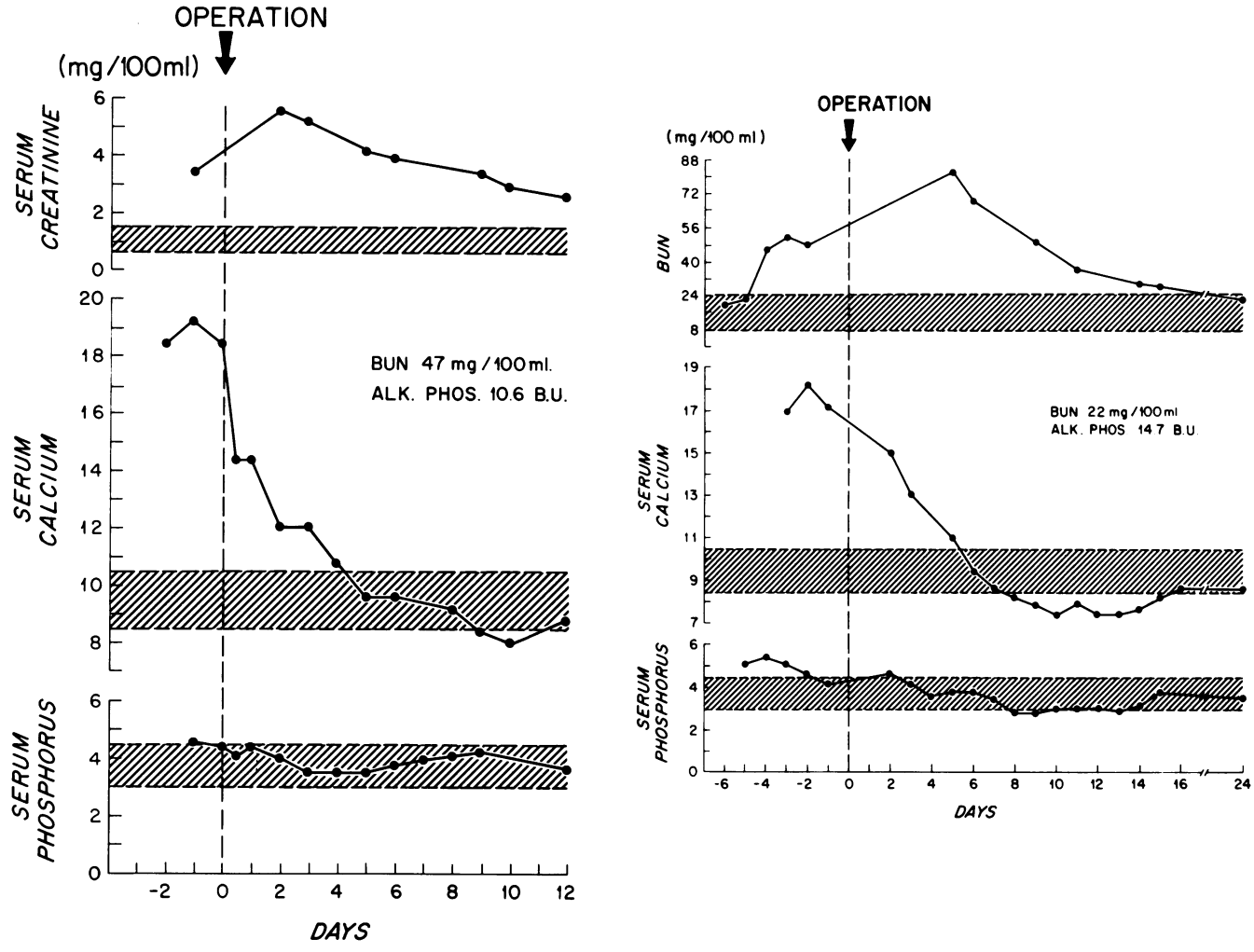

FIG. 3a and b. Continuing high levels of BUN and creatinine after surgery sometimes reached peaks which gave impression of irreversible or worsening renal damage. They eventually returned to normal as the serum calcium leveled off as seen in a) Case 2 and b) Case 3.

the diagnosis. Contrary to the general belief that the serum chloride level is usually higher in hyperparathyroidism and lower in pseudohyperparathyroidism, the serum chloride level was lower than 102 meq/l in nine patients and higher in four of the 13 who had profile screening.

There are, however, a few subtle differences between the two diseases (Table 7). One is in the general appearance of the patient. Patients with hyperparathyroid crisis, unlike those with malignancy, are usually well nourished. In spite of the critical nature of their disease, they seldom lose much weight or are emaciated. Only three of our 14 patients lost up to 20 pounds during the course of the illness. All three had had acute vomiting and anorexia. In contrast, patients suffering from pseudohyperparathyroidism almost always appear chronically ill.

Anemia may be present in either disease, but, in hyperparathyroid crisis, it is rarely associated with hypoproteinemia. In contrast, this association is common in pseudohyperparathyroidism.[4] Eight of our patients had a hematocrit of 38% or lower, but none had associated hypoproteinemia or hypoalbuminemia.

TABLE 7. *Differential Diagnosis of Hyperparathyroid Crisis from Pseudohyperparathyroidism*

	Hyperparathyroid Crisis	Pseudohyperparathyroidism
General appearance	good	poor
Anemia with hypoproteinemia and hypoalbuminemia	no	yes
Metabolic complications	present	absent
Previous hypercalcemia	present	absent
Immunoreactive PTH	elevated	undetectable or low
Subperiosteal resorption of phalanges	present	absent
Lamina dura of teeth	absent	present

The presence or absence of metabolic complications is a second diagnostic clue in the differentiation between the two diseases. Renal stone, peptic ulcer, and skeletal changes are often associated with hyperparathyroid crisis, but they are seldom seen in pseudohyperparathyroidism. Six patients in our series had renal stones or nephrocalcinosis, and two had peptic ulcer. In a patient with severe hypercalcemia, the presence of any one of these complications favors a diagnosis of hyperparathyroid crisis.

A past history of hypercalcemia is presumptive evidence for a diagnosis of hyperparathyroid crisis and thus presents a third dimension in making the diagnosis. Five patients in our series were known to have had hypercalcemia from three months to four years, and the diagnosis of hyperparathyroidism was documented or had been suspected.

A high level of immunoreactive parathyroid hormone PTH strongly suggests hyperparathyroid crisis and is a fourth consideration in making the differentiation. The elevation of immunologically assayable parathyroid hormone-like activity has been reported in some patients with malignancies.[5,12,20,23] However, it has almost always been at a lower level than is usually found in patients with primary hyperparathyroidism.[3] In all eight of our patients who had radioimmunoassay, the PTH was considerably elevated, as much as five to ten times above normal, but, after surgery, it returned promptly to a normal level. It appears that a marked elevation of the PTH in association with acute hypercalcemia further confirms the diagnosis of hyperparathyroid crisis.

Other signs presumably diagnostic of hyperparathyroid crisis are the presence of subperiosteal resorption of the phalanges and the loss of the lamina dura of the teeth. Subperiosteal resorption of the phalanges was present in 75% of our patients, but none had been encountered in pseudohyperparathyroidism. In hyperparathyroid crisis, moreover, subperiosteal resorption is invariably associated with an elevated serum alkaline phosphatase. While the alkaline phosphatase may be elevated in either malignant or benign hepatic disease, only in hyperparathyroid crisis is it associated with subperiosteal resorption of the phalanges or with the loss of the lamina dura of the teeth.

The treatment of hyperparathyroid crisis is primarily surgical and should be promptly undertaken. Dehydration is expeditiously corrected and the serum calcium brought down to a level of 12–13 mg/100 ml. If this level is not achieved within 48 hours, one of the hypocalcemic drugs may be judiciously used, preferably mithramycin. The long-term effectiveness of the hypocalcemic drugs, however, is often debatable.[17,21] Of the nine patients in our series who were treated with one or more of these drugs,‡ the serum calcium fell in only five; in four it failed to respond to the therapy. While these drugs may have brought about a temporary improvement, the prolonged use of saline infusion and furosemide associated with these drugs invariably resulted in increased interstitial edema. As a consequence, identification of the uninvolved parathyroid glands at surgery was often rendered extremely difficult, a technical point that is seldom appreciated by our medical colleagues.

If the serum calcium has fallen to a reasonably safe level, one may proceed with preoperative localization studies. Our first preference is noninvasive cervical esophagraphy. Since the diseased gland in each patient was exceptionally large, one might expect that cervical esophagography would demonstrate an impressive indentation as it did in nine of our 12 patients.

Other sophisticated invasive localization studies are seldom needed for these patients. We have found that selective venous catheterization and arteriography are time-consuming and not without risk, especially in a patient who is already acutely ill. It is best to reserve these procedures for complicated cases which require reexploration. One patient, Number 6, died from cardiac arrest a few hours after undergoing a venous catheterization examination.

A correct intraoperative pathologic diagnosis is imperative, for it dictates the extent of the operation to be undertaken.[25] If the exploration is unnecessarily extensive or if too many glands are indiscriminantly removed, hypoparathyroidism is bound to ensue, but, if the procedure is inadequate, hyperparathyroid crisis may well continue. To treat hyperplasia, the excision of three whole glands and part of a fourth is required. In 13 patients in our series, however, the diseased gland was a neoplasm, and there is thus a 93% chance for a cure in these patients without extensive exploration, simply by excising the diseased gland. We contend, therefore, that routine bilateral cervical exploration is not only unjustified but also invites needless surgical and anesthetic risk.

In conclusion, it cannot be overemphasized that hyperparathyroid crisis is one of the few endocrine emergencies that demands prompt surgical intervention. We have achieved the best results by undertaking exploration as soon as possible, preferably within the first 72 hours of the acute onset of symptoms. We believe that surgery should not be postponed beyond the seventh or eighth day, unless the hypocalcemic drugs, given alone or in conjunction with hydration and diuresis, are successful in lowering the serum calcium

‡ Some of the hypocalcemic drugs used were mithramycin, calcitonin, and Neutra-Phos.

level to 12 or 13 mg/100 ml. Hyperparathyroid crisis is curable whereas hypercalcemic crisis, caused by pseudohyperparathyroidism or other diseases, seldom is. For this reason, emergency exploration of patients with severe hypercalcemia is justified, even if the diagnostic evidence for hyperparathyroid crisis is only presumptive. Should hypercalcemia prove to be associated with an incurable malignancy, surgery will not compromise the prognosis, but should the diagnosis be hyperparathyroid crisis, surgery may well save the patient's life.

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