

Primary Hyperparathyroidism in the Primary Care Setting

R. O. Haight, MD, T. E. Temple, Jr., MD,
R. G. Garrett, MD, and D. W. Marsland, MD
Newport News and Richmond, Virginia

A series of 36 patients with surgically proved primary hyperparathyroidism is reported. From this group a clinical profile consisting of obesity, anxiety, and/or depression in a mildly hypertensive, middle-aged female was derived. Women constituted 92 percent of the patients. The serum calcium was confirmed again as the single most valuable test in the evaluation of this disorder.

Classically, primary hyperparathyroidism has been thought of as a syndrome of "bones, stones, and abdominal groans."¹ Considered relatively rare for several decades, hyperparathyroidism is now recognized with greater frequency and in patients with atypical, often deceptive, features.² Because of the routine use of sequential multiphasic chemical analyzers in many hospital laboratories, relatively asymptomatic patients have been identified. Yet, even this group of patients may represent only a minority of the "at risk" population. More frequent use of outpatient screening may lead to earlier recognition of more people with this disease.

Previous reports have indicated that five percent of patients with a single kidney stone and approximately 15 percent of those with recurrent stones harbor a parathyroid disorder.³ On the other hand, the screening of supposedly asymptomatic individuals has been questioned.⁴ The present retrospective study was undertaken to evaluate our experience with the

clinical and laboratory features of patients with proven primary hyperparathyroidism in a primary care setting. From this analysis we have constructed a clinical profile by which the physician may suspect this diagnosis and be guided to appropriate laboratory tests in those patients most likely to derive benefit.

Methods

All the Riverside Hospital records for the years 1967 to 1975 coded as hyperparathyroidism, parathyroid adenoma, parathyroid hyperplasia, and hypercalcemia were examined. Common and uncommon features of the disease were sought. Other problems and diagnoses were listed. Serum calcium, phosphorous, alkaline phosphatase, uric acid, serum creatinine, and creatinine clearance were recorded. The pathologist's report was used as the final major criterion for establishing the diagnosis and the type of hyperparathyroidism.

Results

Of the 39 charts reviewed, 36 were coded correctly and had been confirmed by surgical and histological criteria. Thirty-three of the 36 patients were female. The average age was 53.6 years. Their related laboratory data and associated medical problems are enumerated in Tables 1 and 2. Ab-

normal elevation of serum calcium was the most consistent laboratory finding and hypertension was the most common physical abnormality. Renal calculi and arthralgias were present in 39 percent and 42 percent of the patients, respectively. Obesity and depression, however, were almost as common. Interestingly, peptic ulcer and pancreatitis which are most regularly associated with hyperparathyroidism were distinctly less common in this group of patients than expected. The radiographic features of hyperparathyroidism, while helpful when positive, are not quantitatively of great diagnostic use. The intravenous pyelogram revealed renal calculi in only seven of fifteen patients tested.

Discussion

The results of this study confirm the importance of the carefully obtained history and meticulously performed physical examination in diagnosing hyperparathyroidism. Excluding the history or presence of renal stones, which occurred in only 39 percent of this study group, a profile for the person with hyperparathyroidism may be constructed. A characteristic patient is an overweight, anxious, mildly hypertensive, middle-aged woman with multiple somatic but non-specific complaints, one of which is often low back pain. As a frequent visitor to her physician's office she may be considered a neurotic with depressive symptoms. While most of the pathophysiologic abnormalities of hyperparathyroidism are explainable on the basis of the serum calcium concentration, several of the findings in our profile remain undefined. However, hypertension and anxiety have been reported previously in association with this disorder and documented fully in the study of Mallette et al along with many other signs and symptoms.⁵

From this study one cannot determine the real prevalence of the truly asymptomatic patient with primary parathyroid disease. However, one may surmise that the incidence of the asymptomatic patient is much lower than previously suspected. Since all of the patients in this study were hypercalcemic, at least intermittently, the incidence of the normocalcemic variety of primary hyperparathyroidism may reflect this intermittency. The intra-patient variability of serum

From the Departments of Medicine and Surgery, Riverside Hospital, Newport News, Virginia, and the Department of Family Practice, Medical College of Virginia of Virginia Commonwealth University, Richmond, Virginia. Requests for reprints should be addressed to Dr. T. E. Temple, Jr., Riverside Hospital, J. Clyde Morris Boulevard, Newport News, Va 23601.

Laboratory Test	Number of	
	Patients Positive	% of Total
Ca > 10.5	35	97
P < 3.0	19	53
IVP	7/16	44
Alk Phos > 85	15	42
24 H Urine for Ca	4/11	36
Uric Acid > 8.0	6	17
Bone x-ray	6	17
Serum Cr > 1.6	4	11

Problems - Symptoms	Patients	% of Total
Hypertension	24	67
Depression and/or anxiety	17	47
Obesity	16	44
Arthralgia	15	42
Calculi	14	39
Diabetes	7	19
Gout	5	14
Hypercholesterolemia	4	11
Peptic ulcer	3	8
Renal failure	2	6
Pancreatitis	1	3

Cause	Test
Carcinoma Ectopic PTH production Metastatic to bone Unknown causes	search for primary
Multiple myeloma	protein electrophoresis CBC urine - Bence Jones protein
Lymphomas, leukemias	CBC physical examination
Sarcoidosis	chest x-ray physical examination
Vitamin D intoxication	history of ingestion remove vitamin D
Milk-alkali syndrome	history of ingestion remove calcium source
Thyroid disorder	history physical examination thyroid profile
Adrenal insufficiency	serum electrolytes plasma cortisol
Idiopathic hypercalcemia of infancy	follow serum calciums
Paget's disease	x-rays alkaline phosphatase

calcium in this group does suggest that the time of calcium determination may be an important determinant of patient categorization. Therefore, laboratory confirmation of this disease depends upon repeated determinations of the serum calcium concentration, and a single normal serum calcium in a subject with the above syndrome does not exclude primary hyperparathyroidism.

Along with the serum calcium, several other tests have been employed for the diagnosis of hyperparathyroidism. Strott and Nugent reviewed these in detail and found all significantly less useful than the serum calcium.⁶ Specific assay of parathyroid hormone (PTH) is being accomplished in some laboratories. However, the laboratory reliability of PTH assay is difficult to ascertain due to the immunoheterogeneity of the circulating hormone.⁷ Even when done accurately, the serum PTH may be only minimally, if at all, elevated in primary hyperparathyroidism. In addition, there is variable secretion of PTH by parathyroid adenomas.⁷ Significantly greater levels are found in secondary hyperparathyroidism, however. Even when the PTH and serum calcium are correctly assayed, the etiology of their elevation may not be hyperparathyroidism. It is mandatory that other disorders which cause an elevated calcium be excluded when evaluating these patients. Table 3 lists some of these diseases and suggests diagnostic studies to exclude them.^{6,8}

References

- Howard JE, Thomas WC Jr: Clinical disorders of calcium hemostasis. *Medicine* 42:25-45, 1963
- Yendt ER, Gagne RJA: Detection of primary hyperparathyroidism, with special reference to its occurrence in hypercalcemic females with "normal" or borderline serum calcium. *Can Med Assoc J* 98:331-336, 1968
- Fourman P, Royer P: *Calcium Metabolism and the Bone*. Philadelphia, FA Davis Co, 1968, pp 347-387
- Williamson E, Van Peenan HJ: Patient benefit in discovering occult hyperparathyroidism. *Arch Int Med* 133:430-431, 1974
- Mallette LE, Bilezikian JP, Heath DA, et al: Primary hyperparathyroidism: Clinical and biochemical features. *Medicine* 53:127-146, 1974
- Strott CA, Nugent CA: Laboratory tests in the diagnosis of hyperparathyroidism in hypercalcemic patients. *Ann Intern Med* 1:188-202, 1968
- Arnaud CD, Goldsmith R, Bordier PJ, et al: Influence of immunoheterogeneity of circulating parathyroid hormone on results of radio-immuno assays of serum in man. *Am J Med* 56:785-793, 1974
- Rabinowitz D, Bledsoe T: The parathyroid glands. In Harvey MA (ed): *The Principles and Practice of Medicine*. New York, Appleton-Century-Crofts, 1972