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PARATHYROID ADENOMA

EXPERIENCE WITH THREE CASES PRESENTING CLINICALLY

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부갑상선 선종

- 임상증례 3예 보고 -

전주 예수병원 외과

설대위 · 오성수 · 박윤규

전주 예수병원 병리과

정 동 규

- 국문초록 -

저자들은 부갑상선 선종 3예를 임상고찰과 함께 보고하는 바이다. 부갑상선 기능 항진증이 있는 환자에서 임상증상들이 각각 서로 달랐으며 증상의 다양성과 여러기관의 침범을 볼수 있었다. 제 1 예는 심한 근 쇄약을, 제 2예는 좌 경골의 낭포성골병변을, 제 3 예는 상복부동통, 관절통 및 정신장애를 나타냈다. 全例 모두에서 骨의 鑛物質 消失(demineralization) 을 보였고 두 예에서는 경부 종괴가 촉지되었고 나머지 한 예만 전형적인 낭포성 섬유성 골염(Osteitis fibrosa cystica) 을 보였다. 3예중 2 예는 주세포 선종 (Chief cell adenoma) 이었으며 나머지 한 예는 혼합성 세포형(mixed cell type) 이었다.

저자들은 본 질환에 대한 진단기준, 외과적 수술방법 및 수술 성공 여부 판정에 대한 지침을 제시하고저 한다.

INTRODUCTION

As noted by Dr. chinan Wang of Harvard, [1] the clinical presentation of hyperparathyroidism has changed greatly since 1960 in the United States. The reason is undoubtedly the introduction of the simultaneous autoanalyzer, or serum multiple analyzer, to that country, where by the determination of serum calcium has become part of the routine laboratory examination. Prior to 1961, only 6% or patients with hyperparathyroidism were asymptomatic at the time of diagnosis; since that time the incidence has risen to 28% and 36% since 1971.

Unfortunately the medical economy in Southwest Korea does not yet support such profile screening of the serum in routine physical check-ups or in admission work-ups. The three cases here in presented all had symptoms caused by the quiet progression of the disease.

Case 1:

A seventeen-year-old boy was brought to the hospital complaining of walking difficulty and weakness of all extremities present for 1 1/2 years. The symptoms had begun with aching pain in the right knee. The weakness was such that the boy could not stand up without "climbing up on himself", that is, using his arms to reinforce his legs by grasping the ankles, knees, and thighs alternately until he reached erect position.

Physical examination revealed diffuse atrophy of the musculature of all extremities. Despite decrease in muscle tone, the deep tendon reflexes were increased. Examination of the neck revealed a palpable mass in the left thyroid region. Laboratory studies of note were serum calcium levels varying from 13.3 to 14.6 mg%, and phosporus levels of 3.2 mg%. Radiologic studies showed extensive demineralization of the skeleton, osteoporosis at the metaphyses of the long bones, lacy trabecular pattern of the phalanges, and indentation of the left side of the trachea. No cystic lesions were seen.

After appropriate hydration the neck was explored on May 5, 1965. A lobular tumor measuring 3.5 cm was found on the posterior surface of the upper pole of the thyroid lobe. The tumor was removed. Pathologic diagnosis was parathyroid adenoma, cell-types mixed. The postoperative course was benign. Seven years after surgery, on out patient examination, he was found to be clinically normal and fully developed.

Case 2:

A 29-year-old farmer's wife came to the hospital complaining of swelling and pain at the medial aspect of the left tibia for 3 months. She had noted mild fever and chilliness at onset. The pain in the left leg caused limping, but in addition she complained of backache.

Physical examination revealed deformity of the left tibial anterior surface with tender swelling on the anterior aspect of the tibial shaft. Examination of the neck revealed a thumb tip-sized mass in the right thyroid area. Laboratory studies of note were serum calcium level of 17 mg%, phosphorus or 4.2 mg%, alkaline phosphatase elevation of 37 Bodansky Units, cystic area in the shaft of the left tibia and generalized decalcification of the entire skeleton.

On February 7, 1962, the thyroid area was explored through a collar incision. Two masses were identified: a cystic brownish mass at the right lower pole, and a second mass imbedded in the posterior aspect of the right lobe of the thyroid gland. Normal parathyroid glands were identified on the left side. The abnormal mass at the lower pole was resected and a right thyroid lobectomy was performed. Pathologic diagnosis of the imbedded mass in the thyroid was chief cell adenoma; the cystic lesion at the lower pole was also diagnosed as chief cell adenoma.

The postoperative course was benign with calcium levels returning to normal and allowing gradual discondinuation of supplemental oral calcium.

Case 3:

A 47-year-old farmer's wife came to Medicine Clinic complaining of epigastric pain and of pain in both knee joints. On physical examiantion the only

findings were tenderness over the lower rib cage bilaterally and tenderness over both knee joints. Routine studies were normal. Radiologic studies of the skeleton were ordered but were not done for economic reasons. Liver function studies were normal except for an alkaline phosphatase level of 750 I.U., the significance of which was not appreciated. She was treated with antiarthritics and ataraxics, but did not improve. In the face of normal gastrointentinal radiographs she was admitted to the Neuropsychiatric Service with the diagnosis of involutional melancholia. During the admission a liver screen again demonstrated an elevated alkaline phosphatase lever of 582 I.U. She was treated as an out patient for six months and readmitted with the diagnosis of somatization disorder. During this admission to the Neuropsychiatric Service the alkaline phosphatase was reported to be 1,629 I.U. and X-rays of the right knee revealed diffuse osteoporotic changes. After discharge the symptoms, both gastrointestinal and arthritic, continued to get worse. Eighteen months after first visiting the hospital the diagnosis of hyperparathyroidism was made on the Medicine Service. At this time serum calcium levels of 11.5 mg% and 12 mg% were found, and phosphorus levels were 1.9 and 1.8mg%. Alkaline phosphatase elevation was to 1,099 and 1,309 I.U. Radiologic studies revealed diffuse osteoporosis with osteolytic changes in the phalanges of both hands and osteolytic destruction of bone in the right femoral neck. Bone marrow studies suggested hyperparathyroidism. Computerized tomography demonstrated a lesion on the right paratracheal area behind the right lobe of the thyroid.

On February 6, 1986, the neck was explored and removal of a parathyroid tumor was accomplished. The pathological diagnosis was parathyroid adenoma. The tumor was composed of well defined, moderately pleomophic large chief cells with clear perinuclear cytoplasmic areas. (Fig 1) The pathological diagnosis was parathyroid adenoma. The postoperative course was benign, chemistry findings returning toward normal as shown in Fig 2.

DISCUSSION

Felix Mandl, of Vienna, first recognized hyperparathyroidism in 1925.[2] His first patient had typical osteitis fibrosa cystica and removal of a parathyroid tumor was successful. Six months after Maldl's case the first case in the United States was recognized by Dubois at the Massachussetts General Hospital, in Boston. However, six neck explorations were futile and the parathyroid tumor was not found until the mediastinum was explored almost seven years later, in 1932.[3] Since that time thousands of cases have been reported, but the variety of clinical presentations, the numerous organ systems which may be affected by overproduction of the parathyroid hormone, and the resulting plurality of complications is not fully appreciated, as was evident in the third case presented.

The parathyroid hormone is normally released by the chief cells of the parathyroid gland in response to a fall in the ionized calcium in the serum. It acts to promote absorption of dietary calcium in the duodenum and proximal jejunum, to promote tubular absorption of calcium and excretion of phosphorus (i. e. phosphate ion) by the kidney; and to promote the release of calcium from bone matrix. In the first and third of these actions PTH works hand-in-hand with Vitamin D. In the third of these actions it is opposed by thyrocalcitonin, which is released by the parafollicular cells of the thyroid gland in response to hypercalcemia.

The clinical manifestations of hyperparathyroidism may produce symtoms of general nature or related to any one or more of five organ systems.[5] The general symptoms of hypercalcemia are polydipsia and weight loss. Renal symptoms produced by calculi and nephrocalcinosis include colic, hematuria, back pain, and polyuria. Musculoskeletal symptoms are the result of osteoporosis and bone cyst formation; bone pain, arthritis and pathologic fractures. Gastrointestinal symptoms may include peptic ulcer disease and pancreatitis

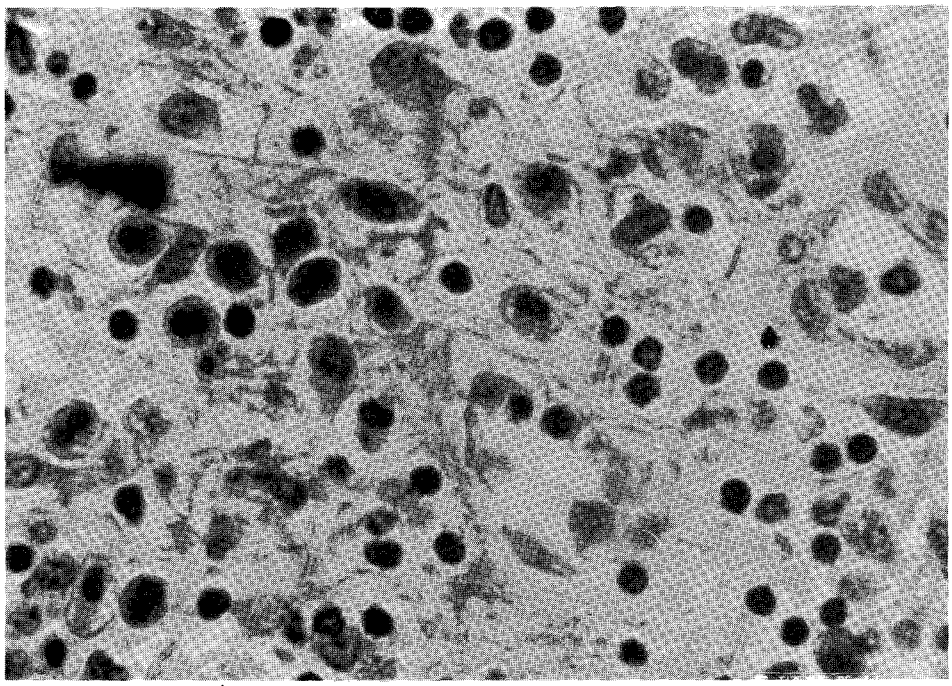

Fig. 1. Parathyroid adenoma composed of well defined, moderately pleomorphic large chief cells with perinuclear clear cytoplasmic areas (×450).

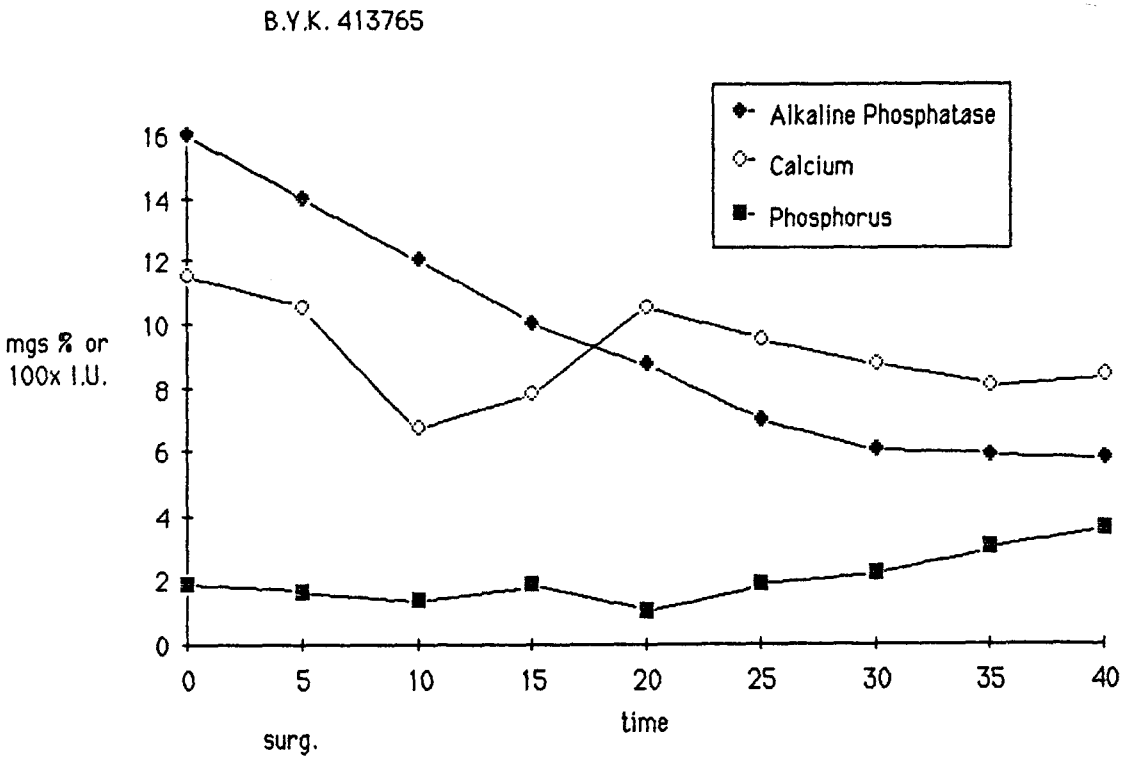

Fig. 2. Postoperative course of patient B.Y.K.

but even in their absence dyspepsia, epigastric or upper abdominal pain, anorexia, nausea, vomiting and constipation may occur. The neurologic symptoms include depression, lethargy, weakness, confusion, neurosis, phychosis, insomnia, headace and apathy. Hypertension and heart block may be seen in the cardiovascular system. Finally, the parathyroid may be involved in multiple endocrine adenopathy Type 1 (Wermer's Syndrome) or in multiple endocrine adenopathy Typ 11 (Sipple's Syndrome).

Case 3 had symptoms involving three of the five organ systems above, and this so confused the clinicians in charge of her case that a delay of 18 months took place before surgery was performed.

Primary hyperparathyroidism is most commonly the result of a single adenoma. Multiple adenomas, as in our Case 2, are very uncommon, comprising 2.5% to 5% in various series. Chief cell hyperplasia appears to be increasing as a pathological entity, and is probably now more common than water-clear (wasser-helle) hyperplasia. Carcinoma of the parathyroid now constitutes 1% or less in most series. A recent review by Holmes[5] indicates that until 1969 only 50 true carcinomas could be confirmed in the literature.

Secondary hyperparathyroidism is most commonly associated with chronic renal failure, and is always of the chief cell type. Tertiary hperparathyroidism is a name given to the senondary type which has become autonomous even after the renal causation (i. e., the hyperphosphatemia) has been corrected.

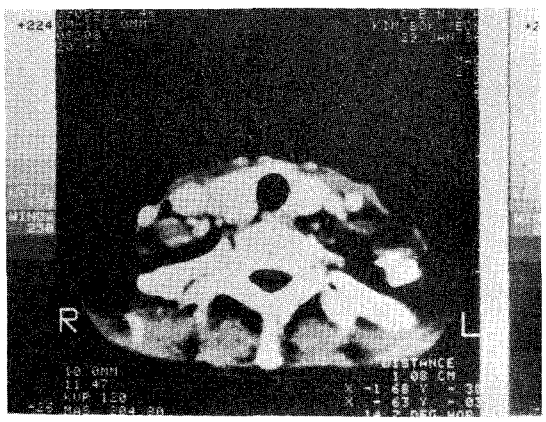

Fig. 3. Preoperative localization of parathyroid adenoma using computerized tomography in case 3. The lesion may be seen adjacent to the right thyroid lobe.

The traditional diagnostic triad of hypercalcemia, hypophosphatemia, and hypercalciuria is inadequate for final diagnosis, in as much as metastatic bone disease, multiple myeloma, cancers arising in certain organs (lung, breast, bone, ovary and prostate), and several other clinical entities can produce the triad. Today the criteria are persistent hypercalcemia, elevated PTH and increased urinary calcium level. Further, localization efforts with ultrasonography, computerized tomography, and—if available—dual parathyroid imaging with ^{99}technetium and ^{201}thallium may reveal the tumor (Fig. 3).

Wang[6] has emphasized that it is not possible histologically to distinguish adenoma from chief cell hyperplasia. "Only the presence of more than one diseased gland is a reliable diagnostic feature of primary chief cell hyperplasia. For this reason it is imperative for the surgeon to identify and prove by biopsy at least one other gland." He recommends both a density test at the operating table, and frozen section. If both biopsies are found to show the same process of chief cell hyperplasia, exploration of the opposite side is mandatory and at least 3 1/2 glands must be removed, lest the problems of hypercalcemia remain unresolved.

Success of the surgery will be readily apparent by a drop in the serum calcium level of 2 to 3 mg% in the first 48 hours. This was our experience in Case 3, the level dropping from 11.5 to 7.5 immediately after surgery (see Fig. 1).

Two of the three cases in this paper were reported previously[6] but are included in the discussion to illustrate the variegated clinical patterns this disease may assume. The third case appears to be the fifteenth case of hyperparathyroidism formally reported in Korea. Park, S. J. and his associates at Chung-Ang University reviewed the Korean literature in 1983 and found 13 cases including the first two in this discussion.[7] Since that time Lee, I. H. and his associates at Kyung-

Hee University have reported one further case of an adenoma presenting in the thoracic inlet.[8] All cases were caused by adenoma. It may be assumed that cases of primary hyperparathyroidism will soon enter the Korean literature as the use of profile screening of the serum is popularized.

SUMMARY

Three cases of hyperparathyroidism are presented from our experience at Presbyterian Medical Center in Chonju in the hope that this will alert us all to the variegated patterns of clinical presentation. In the first case the principal symptom was muscular weakness. In the second a bone cyst (which was part of the syndrome of osteitis fibrosa cystica); and in the third case rib cage tenderness, backache, and persistent epigastric pain. All three had adenomas, but in Case 2 the adenomas were multiple. All three responded to surgical resection and remain well.

REFERENCES

1) Wang C: *Surgery of Hyperparathyroidism. Clinical Problems in surgery, November 1985*

2) Mandl F: *Therapeutischer Versuch bei Ostitis fibrosa feneralisata mitteis Exstirpation eines Epithelkorpercheuntumors. Wien Klin Wochenschr 50: 1343, 1925*

3) Cope O: *The story of hyperparathyroidism at the Massachusetts General Hospital. N Engl J Med 272: 1174, 1966*

4) Clark OH and Way LW: *The Hypercalcemic Syndrome: Hperparathyroidism, Chapter 16 in Surgical Endocrinology: Clinical Syndromes Friesen, SR, Editor, Lippincott, Philadelphia 1978*

5) Holmes EC Morton DL and Ketcham AS: *Parathyroid carcinoma. A collective review. Ann Surg 169: 631, 1969*

6) Lee YT, Seel David J, Lee KY and chung DK: *Two Cases of Hyperparathyroidism in Koreans. Journal of the Korean Surgical Society 13: 846, 11971*

7) Park SJ, Park SI and Chang ST: *A Case of Primary Hyperparathyroidism and Clinical Analysis of Primary Hyperparathyroidism in Korea. Journal of the Korean surgical Society 25: 430, 1983*

8) Lee IH, Lee KY, Koh SH and chun JY: *Primary Hyperparathyroidism. Journal of the Korean Surgical Society 25: 1529, 1983*