

SECONDARY HYPERPARATHYROIDISM IN URAEMIC PATIENTS ON CHRONIC HAEMODIALYSIS—A CASE REPORT AND REVIEW

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SYNOPSIS

With the advent of haemodialysis and kidney transplantation, the condition of secondary hyperparathyroidism in chronic uraemics is more frequently encountered. A case of secondary hyperparathyroidism occurring in an uraemic patient on chronic haemodialysis is presented. This case illustrates one of the problems encountered by patients on chronic haemodialysis. The current concept of management is discussed. It will be noted that surgery is of importance in the treatment of this condition.

INTRODUCTION

The incidence of secondary hyperparathyroidism following long standing renal insufficiency used to be very low. Castleman and Mallory (1937) found only one case in two and a half years. With the advent of chronic haemodialysis and renal transplantation, many chronic renal failures have a significant prolongation of life. Thus, Pendas (1969) found eighteen cases of secondary hyperparathyroidism amongst his series of sixty four patients with chronic renal failure over a seven year period. In Singapore, since haemodialysis was first introduced in 1968, four cases of clinically overt secondary hyperparathyroidism were seen amongst the thirty-one cases of chronic uraemics on haemodialysis (Lim Pin).

The following is a case of a patient with chronic glomerulonephritis, who had bilateral nephrectomy done for uncontrollable hypertension and was placed on chronic haemodialysis. He subsequently developed secondary hyperparathyroidism. The case serves to draw attention to the problem of bone diseases and abnormal calcium and phosphate metabolism in uraemic patients on chronic haemodialysis.

CASE REPORT

L.P.K., a 30 year old Chinese male was first admitted to hospital in November 1967 with a history of nausea, vomiting, headache and oliguria for 3 days. Positive physical signs revealed an uraemic man with a puffy face and sallow skin. His blood pressure was $\frac{190}{130}$ mm.Hg. His blood urea was 430 mg./100 ml., serum calcium was 7.2 mg./100 ml., serum phosphate was 9.6 mg./

100 ml. and serum alkaline phosphatase 4.4 King-Armstrong units. He was diagnosed as a case of chronic renal failure with hypertension, and was treated with peritoneal dialysis initially.

In March 1968, he was started on chronic haemodialysis. Dialysis was carried out twice a week. His blood urea was checked regularly and it ranged from 45 to 82 mg./100 ml. His blood pressure however gradually climbed to $\frac{250}{190}$ mm.Hg. and became uncontrollable. He also developed Grade IV retinopathy.

In August 1968, bilateral nephrectomy and splenectomy were done with future renal transplantation in mind. His blood pressure promptly came down and varied between $\frac{100}{70}$ to $\frac{130}{100}$ mm.Hg. Histology of both removed kidneys confirmed the diagnosis of chronic glomerulonephritis with hypertensive changes. He was treated with twice-weekly haemodialysis thereafter.

He was well till November 1969, 20 months after the commencement of haemodialysis, when he complained of pain in both hands, and X-rays of his hands showed 'calcification of soft tissues and erosion of bones.' Later in June 1970, he complained of pain in his right hip. His serum calcium was 9.4 mg./100 ml., serum phosphate was also 9.4 mg./100 ml. and serum alkaline phosphatase was 11.3 K-A units. Radiological studies of his right hip showed a pathological fracture of the neck of the right femur. This was treated by a Moores' pinning (See Fig. 1).

It was decided that because of the persistent bone pain and the presence of metastatic calcification and pathological fracture, a subtotal parathyroidectomy would be advisable. This was done on 23rd November 1970. Three and a half glands were excised leaving half of the right upper parathyroid gland behind. Histology of both the lower glands showed hyperplasia of the glandular tissues with chief cells predominating (See Fig. 2).

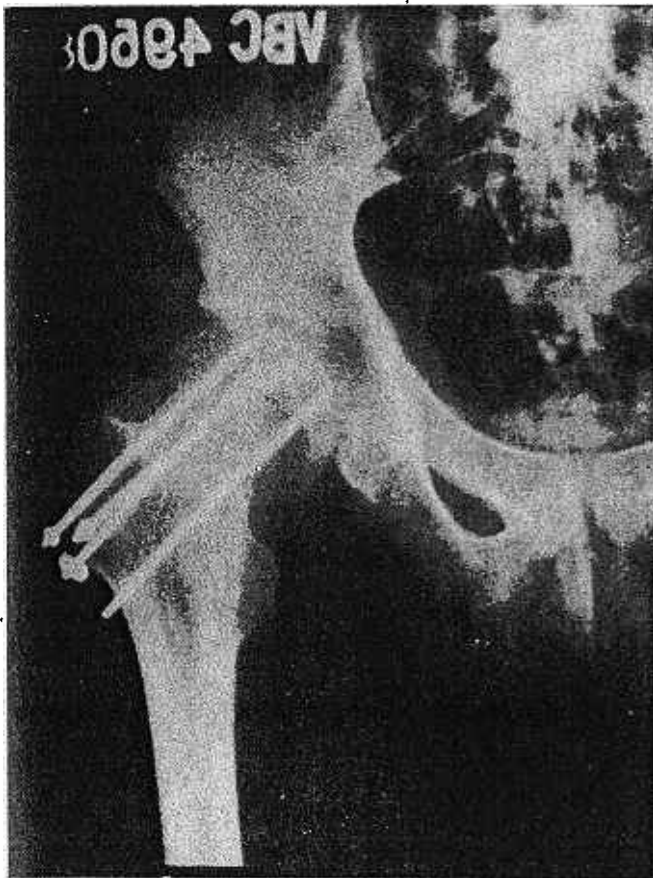


Fig. 1. X-ray of patient's right hip showing pathological fracture of neck of femur treated by Moores' pinning.

The upper glands showed normal parathyroid tissue. Unfortunately the excised glands were not weighed or measured. After the operation, the bone pains in the hands and the right hip disappeared.

From May 1971, he again had pain in the right shoulder and left hip and X-rays again showed osteodystrophy. From then on he continued having these bone pains which greatly depressed him; so much so that he was admitted in May 1972 for suspected opium poisoning. He was placed under the care of a psychiatrist for his depression.

In March 1972, the serum biochemical studies showed that serum calcium was 9.0 mg./100 ml., serum phosphate was 11.7 mg./100 ml. and serum alkaline phosphatase was 12.0 K-A units. In June 1972, repeated estimations of these serum levels were 9.2 mg./100 ml., 7.6 mg./100 ml. and 11.6 K-A units respectively.

His final admission was on the 12th July 1972. He was admitted with pathological fracture of the neck of his right femur for the second time, and was treated with a hip spica. His condition deteriorated. He became breathless and febrile and died on the 24th July 1972, nearly four and a half years after the commencement of his chronic haemodialysis. Relevant serum biochemistry in July were as follows: calcium 9.6 mg./100 ml., phosphate

7.5 mg./100 ml. and alkaline phosphatase 31 K-A units.

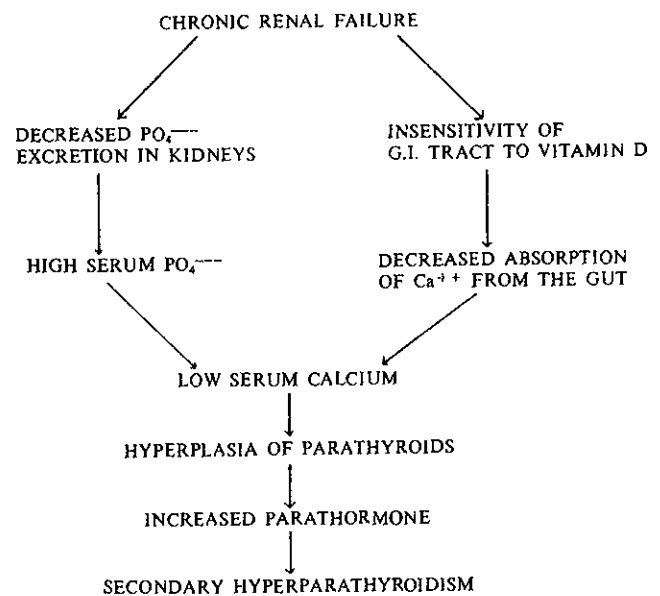
At postmortem examination, no accessory parathyroids were found despite thorough searching in the neck and the superior mediastinum. Bone taken from the iliac crest showed rarefaction with patchy areas of fibrosis. There was also suggestion of increased osteoclastic activity. The immediate cause of death was bronchopneumonia.

DISCUSSION

There is little doubt that the patient had secondary hyperparathyroidism. The average figure for his serum calcium levels estimated regularly over the 57 months period was 9.6 mg./100ml. (Normal being 8.8 to 10.4 mg./100ml.). His serum phosphate level averaged 8.9 mg./100ml., (Normal being 2 to 4 mg./100ml.) and his serum alkaline phosphatase was 11.8 K-A units on the average (Normal being 3 to 13 K-A units).

He had bone pains, subperiosteal bone resorption and soft tissue calcification. He thus had most of the criteria essential for the diagnosis of secondary hyperparathyroidism (See Table I).

Secondary hyperparathyroidism is a metabolic state characterised by an excessive but not autonomous rate of production of parathormone due to compensatory hyperplasia of the parathyroid glands in conditions where there is lowered calcium level. The mechanism of production of secondary hyperparathyroidism in chronic uraemics can be schematically represented by the following diagram:



Secondary hyperparathyroidism should be distinguished from primary and tertiary forms where the parathyroid glands are autonomous and not under the influence of the serum calcium level. The distinguishing features of the three types of hyperparathyroidism are summarised in Table II.

The incidence of secondary hyperparathyroidism in chronic uraemics undergoing haemodialysis is about 28 percent. Pendras (1969) found 18 cases of secondary hyperparathyroidism in his series of 64 chronic uraemics on dialysis. He also noted that the longer the patient was on the dialysis programme, the more likelihood that secondary hyperparathyroidism would develop. In 20 patients who had haemodialysis for 1 to 2 years, only 1 patient, i.e. 5 percent developed secondary hyperparathyroidism; whereas in 5 patients who had dialysis for 4 to 5 years, he found 3, i.e. 60 percent, who had secondary hyperparathyroidism.

Why does chronic haemodialysis lead to secondary hyperparathyroidism?

In uraemia, the skeleton is relatively unresponsive to high levels of parathormone. Dialysis improves the uraemia, resulting in greater responsiveness of the skeleton to parathormone, thus hyperparathyroidism may become overt or a previously existing one may be worsened following long term haemodialysis.

There are two schools of thoughts in the management of secondary hyperparathyroidism. Pendras and others of the conservative school advised medical treatment initially. Vitamin D (Ergocalciferol) 50,000 units per day was given for 2 to 3 months. A decrease in bone pain and a lowering of the serum alkaline phosphatase level indicated good response. Meanwhile, a close watch was made on the patient's serum calcium level to exclude hypercalcaemia. They also advised three-monthly X-rays of the patient's hands, feet and pelvis to exclude further osteodystrophy and metastatic calcification. If the patient was resistant to Vitamin D treatment, surgical treatment was carried out.

If renal transplantation was anticipated within 2 years, subtotal parathyroidectomy with a post-operative course of Vitamin D would be indicated. If renal transplantation was not envisaged and the patient was to be put on chronic haemodialysis for more than 2 years, then total parathyroidectomy with a post-operative course of Vitamin D would be considered.

The results of Pendras were satisfactory. In 18 patients, 16 responded well to Ergocalciferol; 1 patient had subtotal parathyroidectomy with post-operative Vitamin D and the other had total parathyroidectomy plus post-operative Vitamin D. All responded well except the one who had subtotal parathyroidectomy; he again had high serum alkaline phosphatase level 2 years later.

However within the course of his seven years follow-up studies, Pendras found 1 patient who died of cardio-respiratory failure due to generalised

metastatic calcification of the heart and lungs after treatment with Vitamin D, and another died of septicaemia following a pinning operation for a pathological fracture of the femur.

The school of Massry and Katz believed that while mild secondary hyperparathyroidism characterized by osteomalacia or mild metastatic calcification could be treated medically with Vitamin D and calcium supplement, overt cases of secondary hyperparathyroidism with osteitis fibrosa or incapacitating metastatic calcification should be treated surgically. For chronic renal failure patients with secondary hyperparathyroidism not on haemodialysis, Massry advised subtotal parathyroidectomy where three and three quarter glands were to be removed. For patients on dialysis with renal transplantation in mind, he advocated total parathyroidectomy. The results of Massry seem to speak well for this school.

He did 10 subtotal parathyroidectomies and 1 total parathyroidectomy. There was no mortality and all patients had improvement with respect to bone disease and soft tissue calcification. Two patients developed frank tetany in the post-operative period, but it was easily controlled with intravenous infusion of calcium. Katz and Wilson of the Peter Bent Brigham Hospital also did elective subtotal parathyroidectomies on overt cases of secondary hyperparathyroidism in uraemic patients on chronic dialysis, and all their patients showed improvement. Similar observations were reported by Findlay (1961).

The patient under discussion was treated according to the Massry school. When subtotal parathyroidectomy was done, we anticipated renal transplantation for him within two years, hence the decision was correct. His bone pain recurred five months after the operation, probably because too much parathyroid tissue was left behind, or the remaining parathyroid tissue might have hypertrophied again. His condition did not improve because he had been on chronic dialysis for more than four years; and prolonged dialysis does worsen the state of secondary hyperparathyroidism. Perhaps total parathyroidectomy should have been considered when the bone changes recurred after the subtotal parathyroidectomy.

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TABLE I

DIAGNOSTIC CRITERIA: URAEMIC PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

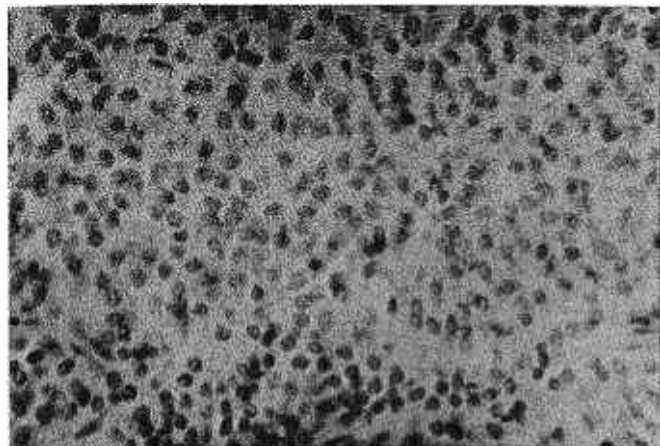


Fig. 2. Histology of excised parathyroid gland showing hyperplasia with chief cells predominating.

- I. **Clinical**
Bone pain
Pruritus unresponsive to Dialysis
- II. **Biochemical**
Serum Calcium normal or low
Hyperphosphataemia
Raised Serum Alkaline Phosphatase
- III. **Roentgenographic**
Osteitis fibrosa or Subperiosteal Resorption
Soft tissue Calcification

Based on Massry, 1969.

TABLE II

FEATURES OF THE THREE TYPES OF HYPERPARATHYROIDISM

	Primary	Secondary	Tertiary
Mechanism	Glands Autonomous ↑Ca ⁺⁺ → Still ↑PN	Glands Under Control of Ca ⁺⁺ ↓Ca ⁺⁺ → ↑PN	Long Standing Secondary Hyperparathyroidism sustained low Ca ⁺⁺ ↓ Glands become Autonomous Function like Primary Hyperparathyroidism
Histology	1. Hyperplasia (water clear cells) 2. Adenoma 3. Carcinoma	Hyperplasia (chief cell type)	May appear as —Hyperplasia —Adenoma —Carcinoma
Serum Ca ⁺⁺ Serum PO ₄ ⁻⁻⁻	Raised Low	Low or Normal Raised	} As in Primary
Serum Alkaline Phosphatase	Normal or Raised	Normal or Raised	
Urine Ca ⁺⁺	Raised	Low	
Urine PO ₄ ⁻⁻⁻	Raised	Low	

Key ↑Ca⁺⁺ — Raised Serum Calcium Level
 ↑PN — Increased Parathormone Secretion
 ↓ — Decrease

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