HYPERPARATHYROIDISM: ITS CLINICAL PRESENTATION AND MANAGEMENT*

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The history of the parathyroid glands and their diseases is briefly as follows:

In 1880 Sandstrom (Sweden) recognised parathyroids as separate structures. He thought they were embryonic thyroid tissue.

In 1891 von Recklinghausen described osteitis fibrosa cystica.

In 1925 Mandl followed Schlagenhaufer's suggestion and reported the first removal of a parathyroid tumour.

The most interesting way to recount my experiences with hyperparathyroidism will be to describe the manner in which the cases presented. Presentation implies symptomatology, which is divisible into 3 groups:

1. Symptoms due to hypercalcaemia. The effect of excess calcium in the blood is: Hypotonia, muscular weakness, lassitude, and chronic constipation.

2. Symptoms due to transportation and excretion of calcium. These are mostly renal, viz. polyuria, which implies nocturia, dysuria, and polydipsia.

3. Symptoms affecting the skeletal system: viz. pain in bones and joints, spontaneous fractures, cysts in long bones and skull, deformity of long bones, kyphosis and sclerosis, and waddling gait and inability to walk.

The most notable change in the blood chemistry is that phosphorus is depressed and calcium is raised; they move apart. Alkaline phosphatase is only elevated when gross bone changes occur; this only happens in a small percentage of cases. Depression of phosphorus levels is not as consistent as increase of calcium in the blood and is therefore not as true an index of hyperparathyroidism.

These manifestations are illustrated by the following cases:

CASE 1

Mrs. Dr. A.M., aged 37, was referred to me by Dr. Malkiel Shapiro, of Johannesburg, in October 1950. The patient dated her symptoms from a septic confinement 12 years before. She complained of intermittent pain in the left elbow, the neck and the left lower limb and in other parts of the body. The areas felt heavy and on occasions the attacks were severe and lasted for days. She had frequent headaches. There had been numerous attacks of dysuria and the passage of black gravel. Occasional bouts of vomiting with pyrexia occurred. She complained of great fatigue and was extremely sluggish, which had not always been the case. The appetite was good.

The patient was generally flabby. The blood pressure was 130/90 mm. Hg. There was the suggestion of a nodule in relation to the left lobe of the thyroid gland. Despite the patient's numerous complaints there was no discoverable clinical evidence to account for them. In discussion with Dr. Malkiel Shapiro it was considered that the flitting body pains, asthenia and sluggishness, together with the dysuria and passage of gravel, warranted a tentative clinical diagnosis of hyperparathyroidism.

I then left for overseas and Dr. Malkiel Shapiro undertook the investigations. The following summarizes the findings:

Serum calcium ..	14·6	13·8	14·0	14·0	mg.%
Serum inorganic phosphate	3·25	5·8	2·7	1·5	mg.%
Serum alkaline phosphate	5	7	5	6	King-Armstrong units

* Paper delivered on 5 August 1958 at the second meeting of the Surgical Forum of the Department of Surgery, University of the Witwatersrand, Johannesburg.

On a low calcium diet the 24-hour urinary calcium excretion on 3 successive days was 0·60, 0·80, and 0·38 g. (the normal being 0·20 g.). There were no kidney stones and no evidence of skeletal demineralization or heterotropic ossification.

The patient was referred to Dr. Allbright at the Massachusetts General Hospital in Boston, Mass., who confirmed the diagnosis of hyperparathyroidism.

Dr. Oliver Cope removed an adenoma of the left superior parathyroid gland, measuring 1·5×2 cm. The lower left parathyroid body was atropic.

Apart from a positive Chvostek sign after operation there was no tetany, and the patient recovered well. Dr. Malkiel Shapiro has continued to follow the progress of the patient. She is cured of her hyperparathyroidism and the blood chemistry is normal.

Comment

Mrs. Dr. A.M. illustrates the clinical picture of hypercalcaemia without gross renal pathology. Von Recklinghausen's disease—osteitis fibrosa cystica—is a relatively rare manifestation of hyperparathyroidism, occurring in 28% of cases; this merely means that gross bone changes are demonstrable by X-rays. Bone is a living substance in which not less than an acre in area of osteoclastic and osteoblastic activity goes on constantly. 70% of cases of hyperparathyroidism have renal stones. The mobilization of calcium because of increase of parathyroid hormone goes on usually constantly, sometimes intermittently, and it is this excess of calcium in the circulating blood which resulted in the clinical picture in this case. The patient is cured of her disease. Her blood calcium and phosphorus are normal.

This patient therefore belongs to the group of cases characterized by hypercalcaemia and illustrates the fact that these cases have the best prognosis.

CASE 2

This case illustrates an extremely rare manifestation of hypercalcaemia—acute parathyroid poisoning. He was referred to me by Dr. B. A. Bradlow,[1] of Johannesburg, who made the diagnosis by a study of the clinical presentation and the electrocardiographic changes. All previously reported cases of this type—before 1956—ended fatally.

Dr. Bradlow's history, abbreviated, is as follows:

A 57-year-old farmer was seen on 4 July 1955. Two weeks before, whilst motoring, he suffered a momentary severe substernal pain which was bad enough to make him stop. For 14 days he felt blown up and suffered epigastric pain. The chest pain recurred several times in this fortnight. He also noted increased weakness and lassitude, with a sense of lameness in his arms. He suffered severely from constipation, sometimes missing a week. Micturition was normal.

Fifteen years ago he suffered backache. Ten years ago a peptic ulcer was found by X-ray and was treated for 4 weeks in a country hospital with milk and alkalis. This treatment made him feel weak and he suffered from pins-and-needles in his hands. He felt worse after treatment, though X-ray showed the ulcer healed. For 2 years thereafter he had paraesthesia and weakness of his legs. Backache recurred on occasions.

His usual diet included porridge with milk daily and cream and cheese on alternate days, with two eggs for breakfast daily. He drank extra milk and often took raw eggs. There was no polydipsia or polyuria. He had lost 10 lb. in weight in the preceeding 2 weeks.

On examination striking pallor and great asthenia were observed. He could barely walk or talk and was extremely depressed. The temperature was just under 100°F and the pulse rate was 100 per minute. He was edentulous. A doubtful fullness was present in the right lower pole of the thyroid. The cardiovascular system was normal. The blood pressure was 160/100 mm. Hg, and later 130/80 mm. The tendon reflexes were brisk and the central nervous system normal. Despite this there was marked muscular hypotonia. The ECG together with the clinical findings indicated the diagnosis of hyperparathyroidism.

On admission the serum calcium was 21 mg. per 100 ml., and the inorganic phosphate 2·7 mg. The blood count was normal. A complete skeletal X-ray showed no demineralization, no extra-osseous calcification and no nephrocalcinosis. He deteriorated alarmingly after admission, and soon became confused. Whilst aphonia and asthenia increased, anorexia became extreme and his condition critical.

By telephone from Boston, Mass., Dr. Oliver Cope, advised that renal function be stabilized before resorting to surgery. A low-calcium (100 mg. daily) and high-phosphorus diet was begun together with intravenous normal saline and dextrose. The blood urea had risen from 54 mg. per 100 ml. to 82 mg. and the inorganic phosphorus to 3·2 mg. These findings, together with a uric-acid level of 11 mg. per 100 ml., a creatinine level of 2·1 mg., and a urea clearance of 25%, indicated a severe degree of renal failure. Progress on this regimen was gratifying and after 12 days the parenteral therapy was stopped. The patient improved so much that after 24 days he was considered fit for surgery. Operation was purposely delayed to allow of improvement of renal function, but had amelioration not occurred surgery would have become necessary much earlier.

On 28 July 1955 an adenoma weighing 3·7 g. (2·6×1·5 cm.) was removed from the right inferior parathyroid gland area. Inspection of the left inferior parathyroid showed no abnormality and there was no reason to suspect the remaining parathyroids. Histology carried out by Prof. James Murray of the South African Institute for Medical Research showed a chief cell parathyroid adenoma with a large cyst of the lower pole.

The convalescence was uneventful. A dramatic decrease in blood and urinary calcium and a negative Sulkowitz test occurred in 48 hours. Ten days after operation the patient was discharged in excellent health. Five months later he had gained 17 lb. in weight, he had lost the constipation of many years' standing, and the blood chemistry was normal. In a note kindly given me by Dr. Bradlow a few days ago he says: 'This patient, 3 months ago, was perfectly well, with normal blood urea and serum calcium, negative Sulkowitz, and normal blood pressure. Six months ago he had a minor myocardial infarction but made a good recovery with bed rest and anti-coagulants.'

Dr. Bradlow refers to Rienhoff's follow-up (1950) of 25 cases of hyperparathyroidism due to adenomata which had been operated on.[2] Nine cases died from hypertension 3-11 years after discharge from hospital. This re-affirms the accepted fact that after removal of the tumour(s) 36% of cases of hyperparathyroidism due to adenoma die from hypertension with or without renal insufficiency. All but one of Rienhoff's cases were between 40 and 60 years old. Half the cases had renal lesions at the time of operation. The other half had skeletal but no renal complications. All these cases were well after operation and the serum calcium and phosphorus became normal. None the less a continuous degenerative renal lesion produced death.

In this case renal function has improved and the blood urea is normal, yet the outlook is uncertain.

Comment

The lessons to be learned from this case are that acute parathyroid poisoning is an extremely dangerous condition and that physicians do not carry their big bags around without a purpose.

The case also illustrates the fact that milk drinkers who have parathyroid tumours do not develop gross bone lesions.

The condition of acute parathyroid poisoning may be anticipated when the serum calcium reaches the figure of 19 mg.%. James and Richards[3] in 1956 reported a case of parathyroid crisis in a 22-year-old female who developed parathyroid poisoning in hospital while she was being prepared for parathyroid surgery. An emergency removal of a parathyroid adenoma was carried out with a successful outcome.

CASE 3

Case 3, chronologically the second in this series, concerns a man ('the Dutchman') who was operated on in hospital in 1942. All efforts have failed to unearth the record, but I remember the salient facts. The housemen of my surgical unit had shown much interest in the case of Mr. R.C.S. (case 4), which we thought to be the first parathyroid tumour removed in the Union. These boys were like bloodhounds off the leash, in their search for parathyroid tumours. Incredible as it sounds, they found one. A poor inoffensive Hollander was picked up in the medical out-patient department. What he was in search of was a bottle of medicine for his cough. He certainly never expected to have his throat cut! However, questioning disclosed that for years he had suffered bitterly from weakness and tiredness and flitting body pains. It was the asthenia which encouraged the houseman to investigate the blood chemistry. Another point was that he had undergone an operation in Holland some years previously for his weakness but was no better for it. The serum phosphorus and calcium had moved apart and the diagnosis of hyperparathyroidism was ultimately established.

During the war years we often had visits to hospital by medical men in transit to other war areas. When we operated on 'the Dutchman' there was a bearded Colonel of the Dutch Army in the theatre. The operation was difficult because of the preceeding exposure. The thyroid lobes were mobilized and quite a large adenoma of the left inferior parathyroid was removed. Over a cup of tea in the doctors' room afterwards, our visitor told us that several years earlier at Leyden, he had watched the operation when the first parathyroid gland tumour was removed in Holland. An adenoma had been removed from the left side and who should the patient have been but the very Dutchman from whom we had removed a second adenoma.

The patient lost his symptoms of hyperparathyroidism.

Comment

This case shows that more than one parathyroid tumour may exist. Multiplicity occurs in less than 10% of cases. What cognizance should the surgeon take of this fact? This will depend on several factors. The first is the condition of the patient. Should he or she be in a grave hyperparathyroidic condition the ideal management of the case is illustrated by Dr. Bradlow's case of acute parathyroid poisoning. Should conservative treatment not have attained this happy result in that case then operation would have been necessary and the surgeon would have had to make a serious decision whether a part of the growth should be left *in situ* to prevent the onset of tetany. If the general condition of the patient is good and the tumour has been removed, should the other parathyroids be visualized? If the case is one of hyperplasia of these glands, then that must necessarily be done. Should the case be one of adenoma then the best plan is to put a few stay sutures in the other inferior pole of the thyroid gland, elevate it and look at (and if necessary feel) the inferior parathyroid area. If a tumour is found, remove it. If not, terminate the operation and await events. It is unwise in these cases to try and visualize the superior parathyroids. They are often most difficult to find and in any case tumours of them are rare.

If hyperparathyroidism continues after operation further search is necessary. This may be a most difficult procedure, which may entail splitting the sternum. In other words, it is poor surgery, having removed an adenoma, to make a half-hearted search for another. It merely complicates greatly a possible second procedure. Churchill and Cope[4] (1936) state that in operating for hyperparathyroidism in cases which have been operated on for this condition before, should an adenoma be found they leave part of it behind. There is no means of knowing how much damage may have been done to the parathyroids at previous operations. Interference with the blood supply may have jeopardized their existence; therefore the risk of inadvertent total parathyroidectomy should be avoided.

The group of symptoms dependent on skeletal changes is illustrated by cases 4 and 5. Case 4 is to the best of my knowledge the first one in this country in which a parathyroid tumour was removed.

CASE 4

This case was referred to me by Dr. E. J. Swirsky in August 1942. Dr. M. M. Suzman was also interested in the case.

Mr. R.C.S., aged 34, married with 4 children, analytical chemist. This patient began to complain 4 years previously of the appearance of swellings on his hands, feet, left arm, left leg, and right side of jaw. They were not tender but were slowly growing. In spite of great increase of appetite he had lost 20 lb. in weight. He complained of polydipsia and polyuria, rising 3 times at night to urinate. There was increasing fatigue. He had seen a number of doctors and had recently been advised to have his left hand amputated.

The blood pressure was 120/80 mm. Hg. There was a suggestion of a fullness under the lower part of the left sternomastoid

muscle. A deformity of the left metacarpus was present, of the type seen in multiple chondromata; also swelling of the tibiae and feet. X-ray showed typical osteitis fibrosa cystica (von Recklinghausen's disease).

The serum calcium was 13·1 mg.% and the serum inorganic phosphate 2·3 mg.%. The alkaline phosphatase was 21 King-Armstrong units at the first analysis and 14 at the second.

Clinical diagnosis: hyperparathyroidism.

In April 1942 operation was performed. The left lower parathyroid gland was found to be enlarged. It was light brown in colour and on removal was seen to be the size of a walnut (normal size 6×3×1 mm.). The pathologist reported it to be an adenoma of the parathyroid gland.

On the night after operation and succeeding ones there was no nocturia. Convalescence was uneventful.

Follow-up. The patient reported to me and Dr. Suzman, and I am grateful to Dr. Suzman for access to his notes. In 1947, i.e. 5 years after operation, X-rays showed recalcification of the bone cysts. Blood phosphorus was 3·3 mg.% and blood calcium 10·9 mg.%. Alkaline phosphate was 4 King-Armstrong units. He had put on weight. In 1950 the blood pressure was 180/140 mm. Hg and he complained of hypertensive headache. At the time of operation 8 years before, the blood pressure was 120/80 mm. Hg. At the time of writing—16 years after operation—the hyperparathyroidism has been cured but hypertension has developed.

Comment

This case combines the symptomatology of the renal and skeletal groups of presentation. He showed the characteristic features of von Recklinghausen's disease. His blood pressure when first seen in 1942—the year of operation—was 120/80 mm. Hg. In 1948 it was 180/140 mm. Hg, at which it remained in 1950. He was subject to headaches of the hypertensive type. There was no polyuria or nocturia, but he was thought to be a candidate for malignant hypertension. The case illustrates the fact that because of the long time which usually elapses before hyperparathyroid tumours are recognized and removed, the kidney has suffered in such a way that the development of hypertension may well shorten life although the original disease is cured.

CASE 5

This lady is another example of the group of cases where the changes in the skeletal system draw attention to hyperparathyroidism. Mrs. E.J.P., aged 62, was referred to me by Dr. N. C. Leiman in July 1952. She had been seen by Dr. M. M. Suzman intermittently since 1936. I am grateful to him for giving me access to his files and for his help with the diagnosis.

In 1946 she began to complain of fairly persistent headaches. At that time there was some intracranial calcification and paraesthesia—pins-and-needles in the hand when lying on the arm. In 1947 she saw Mr. Norman Dott in Edinburgh, who thought the parasaggital intracranial calcification was possibly a healed tuberculoma and advised no surgery.

When I first saw her in 1952 she stated that 4 months previously she noted blockage of the right side of the nose and deafness in the right ear. There was a 'pimple' on the right upper alveolus and sometimes a speck of blood on the handkerchief after forcible blowing of the nose. She was eating poorly and had lost weight. Biopsy of the gum was reported as osteoclastoma Deep-therapy for 6 weeks had not helped. She also complained of muscular weakness and was always tired.

Examination showed the alveolus of the superior maxilla to be bulged inferiorly and laterally. The right half of the palate was depressed and spongy to the feel. The inner wall of the maxillary antrum was pushed medially, blocking that side of the nose. No enlarged lymph nodes were found. The examination was not otherwise noteworthy except for a blood pressure of 230/100 mm. Hg.

Treatment was discussed with Dr. Leiman and removal of the superior maxilla was mooted. However, it was thought wise to discuss the case with Dr. Lester Brown, who had removed an osteoclastoma from the right side of the lower jaw 3 years previously. In view of the rarity of multiple true benign giant-cell tumours, it was resolved at his suggestion to investigate the blood chemistry. Dr. Suzman's help was also invoked.

The 24-hour urinary excretion of calcium after 3 days on a low calcium diet was 102 mg. (normal maximum 300 mg.). The Sulkowitz test was doubtful in 2 instances and in 1 instance it was positive. Serum calcium 11·8 mg.% (normal 9-11 mg.%). Inorganic phosphate 2·8 mg.% (normal 2-3 mg.%). Alkaline phosphatase 5·1 King-Armstrong units. Blood urea (*a*) 53 mg.%, (*b*) 47 mg.%. These findings were equivocal—normal phosphorus, some elevation of the blood calcium and low urinary calcium.

X-ray studies by Drs. Eric Samuel and M. H. Fainsinger showed (1) distension of the right maxilla (osteoclastoma) (Fig. 1), (2) diffuse skeletal decalcification, (3) subperiosteal absorption of phalanges, (4) skull decalcified and woolly, (5) cupping and fraying of the acromio-clavicular joints, and (6) calcified opacities in lungs—heterotopic calcification. This combination of X-ray findings is typical of hyperparathyroidism.

Diagnosis: hyperparathyroidism. The reasons for this conclusion were the following:

(*a*) It was thought that the reason why the blood phosphorus was within normal limits was some impairment of kidney function causing defective excretion of phosphate but for which the blood phosphorus would have been lower.

(*b*) The blood calcium was raised, though only moderately so.

(*c*) The X-ray appearances were those of hyperparathyroidism. It is averred that absorption of the subperiosteal bone of the phalanges is pathognomonic of the condition, especially when

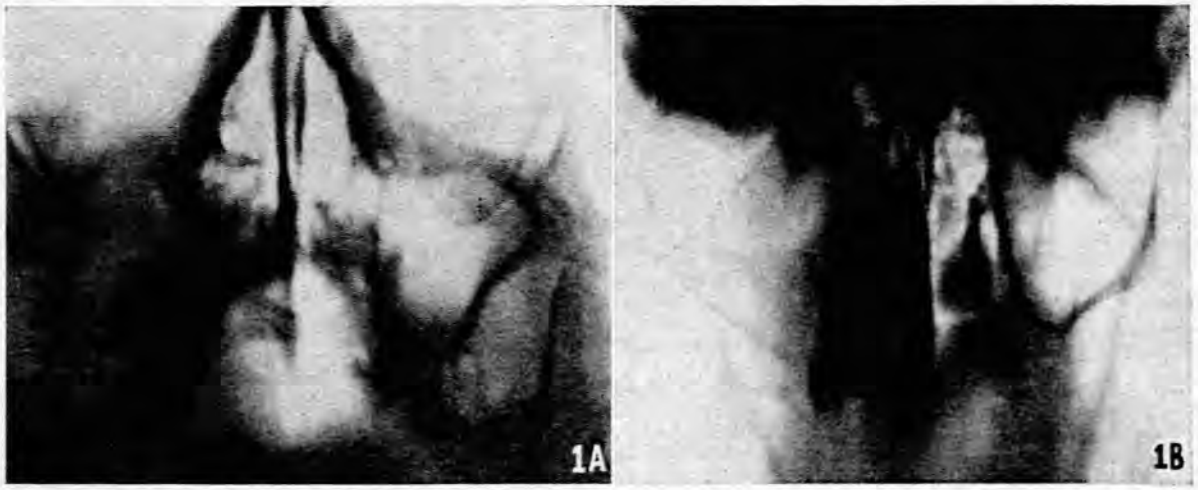

Fig. 1. Hyperparathyroidism. Osteoclastomatous mass in right maxillary antrum. A—Occipito-mental view.—B.—P.A tomogram.

occurring in conjunction with cupping and fraying of the acromioclavicular joints.[5]

(*d*) The occurrence of two osteoclastomata is so unusual that they were considered more likely to be the brown tumours of Jaffe than true neoplasms.

Operation was performed on 15 August 1952. The sternomastoid muscles were mobilized in their lower parts and the ribbon muscles divided. The right lobe of the thyroid gland was seen to be pushed forwards. The middle thyroid vein was divided. The lower part of the gland was elevated by stay sutures used as retractors. A brown tumour the size of the last phalanx of the middle finger was then seen to occupy the position of the right inferior parathyroid gland. The recurrent laryngeal nerve was closely applied to the *lateral* surface of the tumour (reference is made below to the diagnostic importance of this finding). The removal of the tumour presented no difficulty. The tumour was reported to be a clear-cell tumour of the parathyroid by Dr. C. J. Uys of the Department of Pathology. Recovery was uneventful. The serum calcium 14 days later was 10·1 mg.% (normal 9-11 mg.%).

The patient was seen by Dr. Suzman periodically. Fourteen months after operation the inorganic phosphate was 3·0 mg.% (normal 2·3 mg.%), the serum calcium was 8·4 mg.%, and the alkaline phosphatase was 5·1 King-Armstrong units (normal 4·5-9·5). The Sulkowitz test for urinary calcium was negative.

X-rays taken by Dr. Eric Samuel on 7 October 1953 showed (1) the bones of the cranial vault increased in width and density, (2) the right maxillary antrum calcifying and the osteoclastoma resolving, and (3) the jaw itself showing a considerable improvement in the extent of calcification in the mandible.

The hyperparathyroidism was cured. The ultimate death of the patient some years later was, I am informed, due to a cerebral haemorrhage.

Comment

An interesting feature in this case was that it presented as a tumour of the maxilla. Although a proved osteoclastoma, the significance of the finding was not appreciated until, in consultation with Dr. Lester Brown, the possibility of hyperparathyroidism was mooted. In 1948 Thoma *et al.*[6] reported that cystic changes and tumour swelling of the maxilla was sometimes the first clinical indication of hyperparathyroidism. Even after blood and urinary investigations were made the findings in this case were equivocal. However the association of the outcome of the serological and radiological studies together with the history of the removal of an osteoclastoma from another site several years before were felt to justify a firm diagnosis of hyperparathyroidism. The rule has been laid down that there is no place for surgical exploration in the diagnosis of this condition, because the diagnosis can always be made.

CASES 6 AND 7: LARGE CYSTS OF THE PARATHYROID GLANDS

Reference was made above to the importance of the relationship of the tumour to the recurrent nerve. The inferior parathyroid lies usually close to this nerve and in case 5 the nerve was pushed laterally by the tumour growth. We have in 2 cases had to deal with cysts each as large as a medium sized orange which were thought to be of thyroid origin. I make it a practice to expose the recurrent nerve in most cases requiring removal of thyroid tissue. In neither of these cases was the recurrent found at operation in its usual situation between oesophagus and trachea, nor would the cyst shell out from thyroid as thyroid cysts usually do. In each case after a difficult dissection the pedicle of the cyst, not much thicker than a match, was traced to a fibrous area at the junction of oesophagus and pharynx. In both cases the recurrent nerve was ultimately found lying lateral to the cyst. One of the cysts extended into the anterior mediastinum to the level of the angle of Louis. This case was referred to me by Dr. L. I. Braun. The report on the specimen signed by Prof. James Murray reads as follows:

'Sections of this cyst from the region of the thyroid gland show a fibrous-tissue wall in which are embedded masses of cuboidal epithelial cells. The cells are arranged mainly in alveolar masses between which run delicate connective-tissue trabeculae but in some areas there is a tendency to acinar arrangement in which the cuboidal epithelial cells line the acinar spaces. In addition there are foci in which the epithelial cells show more hyperchromatic nuclei, are more deeply oesinophilic and tend to be spindle-shaped with an appearance of whorling suggestive of a change towards a squamous type of epithelium. The cyst is apparently of developmental origin. The majority of the cells resemble those of parathyroid tissue. No evidence of malignancy has been observed.'

Thus the relationship of the recurrent nerve to a tumour growing in relation to the tracheo-oesophageal sulcus gives a pointer to whether the growth is of thyroid or parathyroid origin. I have never seen a mass coming from the thyroid displace the recurrent nerve. Cysts of the parathyroid gland are described in text-books as being small. Larger ones, however, do occur. Only about 14 cases of large cysts of the parathyroid have been reported. Apart from swelling, the only symptom such a cyst is likely to cause is compression of the recurrent nerve.[7]

DISCUSSION

The number of parathyroids is dependent on the enthusiasm of the investigator. Usually there are 2 superior and 2 inferior ones. They are in dimension 6×3×1 mm., coffee brown at puberty and yellowish in middle age. When exposed at operation they look very like fat, which is what determines their colour in later life. The superior ones arise from the epithelium of the 4th branchial pouch. They always lie between the layers of the pretracheal fascia. The inferior glands arise from the lining of the 3rd pouch. If they lie above the inferior thyroid artery they are often deep to the pretracheal fascia and are not visible until this fascia is incised. A tumour of these glands may thus pass into the posterior mediastinum in relation to the oesophagus. If the gland lies below the inferior thyroid artery, it is within the layers of the pretracheal fascia and will, if it descends, pass along the inferior thyroid veins and come to lie in the anterior mediastinum behind the sternum. Here it may be felt from the neck and pulled up. The blood supply is from the thyroid arteries. Whether both are supplied from the inferior or whether the superior artery takes a share, is undecided. It is noteworthy that the blood supply is sinusoidal, like that of the liver. Thus the least injury to the glands leads to its suffusion with blood. This is evidenced to the operator by the swelling and discolouration of the gland if surgically damaged. Under these circumstances it will be out of action during the critical post-operative days. Whether a parathyroid gland ever lies within the thyroid substance is debatable on embryological grounds. It may, however, lie in a cleft in the thyroid, which explains why portions of this gland have on occasions been removed for hyperparathyroidism.

I was taught by Sharpey Schaefer (Sr.) that the function of the parathyroid glands is to control the metabolism of guanidine. The gland produces parathyroid hormone and has no proved relationship to other glands. The excretory function is regulated by the calcium and phosphorus requirements of the body. Parathyroid hormone regulates the electrolyte equilibrium of the body. Its influence is primarily on the calcium and phosphorus metabolism, the greater effect being on phosphorus. A low blood calcium stimulates the secretion. It acts directly on the osteoclastic activity of bone and influences the circulating phosphorus, which in turn stimulates the increase of urinary phosphatase excretion. Also the control of muscular tone is regulated by the metabolism of guanidine, which is influenced by the hormone of the parathyroid. Excess of this hormone in the body, whether due to administration or excessive secretion, is to bring about (1) increased secretion of phosphatase in the urine, (2) decreased secretion of phosphatase in the serum (below

3 mg.%), (3) increased calcium in the serum, and (4) increased calcium in the urine.

Hypercalcaemia causes diminished neuromuscular activity and hypotonicity of muscles. If long continued the excretion of lime salts leads to a deposition of calcium in the kidney tubules, the gastric mucosa and the alveoli of the lungs. The latter was considered to be the cause of the 'bronchitis' which was the presenting symptom of 'the Dutchman' (case 3). As a result of this nephrocalcinosis renal insufficiency ensues. Because of this, phosphorus retention occurs and serum calcium is lowered, producing a compensatory hyperparathyroidism.

It will be observed that in nephrocalcinosis, although the metabolism of calcium and phosphorus is gravely disturbed, none the less the effects are to produce an apparent normality in the serological readings. This was the state of affairs in case 5. At this stage the diagnosis of hyperparathyroidism becomes extremely difficult unless the possibility is envisaged and further evidence exists in the form of bone changes, osteoclastoma, renal calculi or heterotopic ossification. It is of special significance that if the patient fails to ingest as much calcium as is being lost, then osteoclastic activity is increased. This occurs only in a small proportion of cases and thus the classical picture of von Recklinghausen's disease occurs but seldom, and milk drinkers do not suffer from osteitis fibrosa cystica. Of the body calcium 99% is in the form of calcium phosphate and carbonate. Blood calcium occurs in the form of the proteinate and calcium ions, the latter modicum being regulated by the parathyroid hormone—the lower the ionic concentration the greater the demand for the hormone.

Of the serum calcium 45% is combined with protein. One-third of the daily calcium excretion is *via* the urine and two-thirds by the faeces. Vitamin D and A.T. 10 (dihydrotachysterol) diminish the faecal calcium and phosphorus by increasing calcium absorption and urinary calcium excretion.

The grave risk of parathyroidectomy is tetany. There are many causes of tetany—rickets, osteomalacia, steatorrhoea, renal insufficiency and alkalosis. The signs and symptoms are increased neuromuscular activity, with paraesthesia, cramps and carpo-pedal and laryngeal spasm. Positive Chvostek and Trousseau's signs may occur. The treatment is to treat the cause by administration of calcium, parathormone, vitamin D and A.T. 10. The diet should be high in calcium and low in phosphorus; therefore no dairy products are admissible.

Hyperparathyroidism may be secondary, in which excess hormone is produced by a compensatory mechanism such as poor nutrition due to vitamin-D deficiency, pregnancy, lactation, and renal insufficiency with phosphorus retention. Primary hyperparathyroidism is caused by:

(*a*) Idiopathic hyperplasia, which affects one or more of the parathyroid glands and the signs and symptoms of which are indistinguishable from those of adenomata. It occurs in 8% of cases of hyperparathyroidism. I have had one case which was operated on and for reasons of space has not been described here.

(*b*) Adenomata. About half of these are non-functioning for shorter or longer periods. Females account for three-quarters of the cases. The age incidence is 30-60 years. About 3% of the tumours occur in the mediastinum. About 70% of cases have nephrocalcinosis or urinary stones. About a third of the cases show von Recklinghausen's disease.

Of cases presenting with renal stones about 12% suffer from hyperparathyroidism.

Tetany occurs in about half the operated cases, whereas after thyroidectomy the incidence is 1%. The severe form is apt to occur in cases of osteitis fibrosa cystica and those with high serum-phosphatase levels. Phosphatase is an ensyme which plays an important role in the deposition of calcium in osteogenesis. It is therefore increased when active bone destruction and regeneration are going on. The level of the serum phosphatase is therefore a measure of osteoblastic activity.

The ultimate prognosis depends on the degree of renal damage and, as we have seen above, 36% die of hypertension within 3-11 years, even though renal function appears good at the time of operation. Most cases of hyperparathyroidism progress inexorably to a fatal end. They may never be recognized, and thus are never properly treated. The period between the occurrence of symptoms and recognition is usually several years. The prognosis depends on the length of this period.

The physician, the radiologist, and the biochemist are necessary in the recognition of hyperparathyroidism. For the house doctor to suspect the existence of the disease:

1. He must be aware of the entity.
2. He must show a high degree of suspicion in all cases of (*a*) renal stones or insufficiency, (*b*) heterotopic ossification, (*c*) spinal deformities, (*d*) spontaneous fractures, and (*e*) bone swellings and bone pains.
3. In all cases of hypertension he must exclude hyperparathyroidism just as he must exclude pheochromocytoma.
4. Cases of long continued chronic fatigue and loss of energy of unexplained aetiology must claim his especial attention.

SUMMARY

1. Seven cases of parathyroid pathology are reported and analysed. Case 4 is thought to be the first case in the Union in which a tumour of the parathyroid gland was removed.
2. The variability of presentation is illustrated.
3. The pathophysiology and biochemistry are discussed.
4. Operation resulted in 'cure' of all cases.
5. 36% of cases will die in 3-11 years from the complications of hypertension.
6. The attention of the house doctor is drawn to the symptoms and signs which should make him suspicious of the existence of parathyroid pathology.

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