ATYPICAL MULTIPLE MYELOMATOSIS

BY

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McGeown and Montgomery (1956) reported a fatal case of multiple myelomatosis with many features of hyperparathyroidism. A study of the serum proteins, however, would have revealed the true condition in life.

In October, 1955, a similar problem presented itself at this hospital. The results of the investigation of the serum proteins tended to exclude multiple myelomatosis, and biochemical estimations supported a diagnosis of hyperparathyroidism.

The following report may again serve to illustrate the occasional similarity of the two conditions. In this patient the possibility of metastatic carcinoma had also to be considered.

Case Report

In December, 1954, a Rhodesian farmer aged 45 complained of pain in the left upper chest. It was a continuous dull ache at rest and was aggravated by movement. A month later, while stooping, he suffered a violent pain in the middle of the chest and upper part of the back. The pain was severe and continuous, and necessitated his lying flat in bed for three weeks. As this pain subsided he became aware of pain in the loin and difficulty in moving his legs.

He was investigated in South Africa in June, 1955, and a radiograph of his chest showed his bones to be osteoporotic. The serum calcium level was found to be 13.6 mg. per 100 ml. A tentative diagnosis of hyperparathyroidism was made. He came to Britain and was admitted to hospital for further investigation and removal of the suspected parathyroid adenoma.

On admission he complained of pain in the back and thighs, continuous nausea, vomiting, polydipsia, and polyuria. He could walk only with difficulty and great pain. He was anorexic and had lost 24 lb. (10.9 kg.) in weight in the preceding two months. On clinical examination the only positive finding was a large goitre of the soft nodular type, most pronounced at the left lower pole and causing deviation of the trachea to the right. No abnormality was found in the skeleton, abdomen, or pelvis. Radiological examin-

ation showed severe generalized decalcification of the skeleton with collapse of D 6 and L 5. Multiple circumscribed areas of bone destruction could be seen in the femora, pelvis, and skull. The hands showed no abnormality.

Laboratory Investigations.—On September 13 a blood count showed: Hb, 9.8 g. (68%); red cells, 3,600,000; haematocrit, 30%; M.C.V., 83 cubic microns; M.C.H.C., 33%; white cells, 10,000 (neutrophils 62%, lymphocytes 30%, monocytes 6%, eosinophils 2%). The serum sodium was 144 mEq/l., potassium 4.3 mEq/l., chloride 105 mEq/l., CO₂ combining power 26 mEq/l. The blood and urine analysis are shown in Tables I and II.

On the whole the results of the biochemical investigations suggested a parathyroid adenoma.

It was decided to explore the neck, for this operation would reveal a thyroid carcinoma or a parathyroid tumour. If a frozen section of this material proved negative it was proposed to take a biopsy from the left femur, the radiological changes being maximal at this site.

The operation was performed by Mr. Vaughan Hudson on September 20. The neck and superior mediastinum were carefully explored. The whole thyroid gland was exposed, the left lobe was removed, and two normal parathyroid glands were identified. The right lobe was then removed and two normal parathyroid glands were again identified. A frozen section of the excised thyroid was reported on before the neck was closed. Neither carcinoma nor parathyroid tumour was revealed. The histology of the thyroid gland was that of a simple nodular goitre.

The biopsy of the left femur which followed showed plasma-cell myeloma. The patient made an uneventful recovery.

Discussion

The radiologists considered the bony lesions to be those of multiple myelomatosis, or possibly secondary deposits from a thyroid carcinoma. The radiographic appearances did not suggest hyperparathyroidism. Paper electrophoresis of the serum proteins failed to confirm the diagnosis of myelomatosis, but the normal protein pattern did not necessarily exclude it.

Flynn (1954) stressed the importance of investigating the electrophoretic mobility of any urinary protein should the results of the serum study be equivocal. In this way a diagnosis of myelomatosis may be confirmed or refuted in 95% of cases. We have, in fact, seen a patient with proteinuria suffering from a plasma-cell myeloma whose serum pattern was within normal limits, yet the mobility of the urinary protein was that of gamma-globulin. A negative heat test for Bence Jones protein does not exclude myelomatosis, for we have experienced negative heat tests in the face of proteinuria, particularly in the β -type of myeloma.

In the case under discussion, however, the normal protein pattern, together with absence of any detectable urinary protein (before operation), made the diagnosis of multiple myelomatosis seem unlikely, and no examination was made of the bone marrow.

A raised serum calcium level with resulting hypercalcaemia may occasionally be found in patients suffering from myelomatosis. The mechanism is unknown. Hypercalcaemia and hypercalcaemia may also be associated with multiple bony metastases.

The raised serum calcium level and hypercalcaemia were in this case associated with a low serum phosphate level but a relatively high urinary phosphate excretion, suggesting primary hyperparathyroidism. The serum alkaline phosphatase activity was at the upper limit of normal. In retrospect, a higher serum level, reflecting increased osteoblastic activity, might have been expected had such extensive bony changes been the result of a parathyroid adenoma. In view of the high endogenous calcium excretion, it was decided that a calcium balance test was unlikely to furnish further useful information.

The diagnosis of primary hyperparathyroidism can be difficult when complicated by renal insufficiency. Again,

TABLE I.—Blood Analyses

Date	Calcium (mg./100 ml.)	Phosphate (mg. P/100 ml.)	Alkaline Phosphatase (K-A Units)	Acid Phosphatase (K-A Units)	Total Serum Protein (g./100 ml.)	Serum Albumin (g./100 ml.)	Serum Globulin (g./100 ml.)	Urea (mg./100 ml.)	Serum Electro- phoresis
13/9/55	13.8	2.0	12.0		6.8	4.9	1.9	43	Within normal limits
16/9/55									
19/9/55	14.8	1.8		2.3				50	
23/9/55	13.6							69	
26/9/55								70	
4/10/55	15.4								
11/10/55									

TABLE II.—Urine Analyses

Date	Protein (mg./100 ml.)	Calcium (mg./24 hr.)	Phosphate (mg./24 hr.)	Bence Jones Protein (Heat Test)
14/9/55	< 10	600	600	Negative
23/9/55	80			
4/10/55	< 10			

diagnosis may be confused by the excessive phosphate excretion that may occasionally be found in multiple myelomatosis, associated usually with the excretion of myeloma globulin.

FIG. 1.—Relation between plasma inorganic phosphate and rate of urinary phosphate excretion. Control cases. (Herbert, 1951.) ● Miscellaneous disease without renal damage or disturbance of acid-base balance. ○ Non-metabolic diseases of bone. The area within which these points fall defines the normal limits indicated by the two straight lines.

FIG. 2.—Relation between plasma inorganic phosphate and rate of urinary phosphate excretion. Hyperparathyroidism and hypoparathyroidism. (Herbert, 1951.) ● Hyperparathyroidism, untreated. ○ Hyperparathyroidism, post-operative. + Hypoparathyroidism. The continuous lines represent the normal limits as in Fig. 1. The dotted lines connect consecutive data on individual cases, in the sequence indicated by the arrows.

In the absence of complicating features, we placed great reliance upon the relationship of the rate of urinary phosphate excretion to the plasma phosphate level. The normal relationship is shown (Fig. 1) and compared with that found in primary hyperparathyroidism (Fig. 2). Figs. 1 and 2 show that a urinary phosphate excretion of 0.4 mg. a minute falls outside normal limits when the plasma phosphate level is 2 mg. per 100 ml.

Since the diagrams were originally published (Herbert, 1951), phosphate excretions in a number of patients suffering from hyperparathyroidism have been investigated. No unexpected results were found (Herbert, 1956, personal communication).

It would appear from our experience, and that of McGeown and Montgomery (1956), that the interpretation of

urinary phosphate excretions can be difficult. They are not necessarily an index of parathyroid activity, even in the apparently uncomplicated case.

The presence of anaemia did not influence the diagnosis. It occurs in most patients suffering from myelomatosis, but in primary hyperparathyroidism, fibrosis and cyst formation may also be associated with anaemia and leucopenia.

Post-operatively, protein (80 mg. per 100 ml.) appeared in the urine, but the heat test for Bence Jones protein was negative. The proteinuria was transient. A 24-hour urine specimen collected 10 days after operation was examined for protein concentration with a view to investigation of its electrophoretic mobility, but it contained less than 10 mg. of protein per 100 ml.

The biochemical estimations illustrate the manner in which multiple myelomatosis may occasionally simulate hyperparathyroidism. The examination of a sternal-marrow aspirate might have revealed the true diagnosis, and this investigation should be made if a diagnosis of multiple myelomatosis is at all likely.

Summary

A case of multiple myelomatosis is reported, presenting many of the features of hyperparathyroidism. The absence of serum protein changes and proteinuria led to an erroneous diagnosis of parathyroid adenoma. A possible diagnosis of bony metastases from a carcinoma of the thyroid had also to be considered.

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PROPANTHELINE BROMIDE IN PRIMARY DYSMENORRHOEA

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Primary dysmenorrhoea is such a common condition and causes such invalidism that any treatment which promises relief to even some patients deserves investigation. Secondary dysmenorrhoea due to disease of the pelvic organs does not come within the scope of this investigation. In investigating any form of treatment it is essential that the effects of suggestion should be eliminated so far as possible by giving dummy tablets to alternate patients in a control series.

A trial of propantheline bromide ("pro-banthine") was made on these lines. Methanthelinium, then propantheline, were introduced as anticholinergic drugs for treatment of various conditions in which spasm was believed to play a part. Propantheline bromide is used extensively in the treatment of gastric and duodenal ulcers. It has also been used successfully for treatment of spasmodic conditions of the various components of the renal tract. It therefore seemed likely that it would be of value in the treatment of primary dysmenorrhoea.

Malkin (1955), in a preliminary report based on three cases in which methanthelinium was used, felt that the results justified further investigation. Ainsworth (1955) published a most favourable report in which propantheline was used: out of 36 cases all but two obtained