

## OSTEOCLASTOMA OF FRONTAL BONE IN HYPERPARATHYROIDISM

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SINCE Mandl's original account (1926) of the relationship between osteitis fibrosa cystica and parathyroid tumours, the signs and symptoms of hyperparathyroidism have been widely recognized, and numerous authoritative accounts, of which that of Hunter and Turnbull (1931) is noteworthy, have been published discussing the relation of this syndrome to other diseases of bone. In most of the published accounts, the patients have sought advice on account of bone pains or other general symptoms referring to the skeleton, or because of multiple and recurring fractures. In the following communication we report a case of parathyroid adenoma in which the symptoms were localized to the frontal bones; as we have not found in the literature any similar case, an account of the clinical and pathological features of such unusual manifestations of hyperparathyroidism is of interest.

*Clinical History.*—The patient, a woman of 40, first attended the Ear and Throat Department of Dundee Royal Infirmary on *July 1st, 1937*, complaining of swelling over the left frontal sinus region of rapid onset about three months previously; she had no pain or headache and no nasal discharge or obstruction to breathing at any time. In view of the later findings it is probably significant that for several months prior to the appearance of the frontal tumour she had felt tired and very easily fatigued. There was a slight degree of "stiffness" and disability on walking and she noticed tenderness in her feet, especially in the heels, which she attributed to unsuitable shoes. A change of footwear, however, brought no relief. She also admitted later that occasionally there had been mild pains in the bones, but never sufficient to cause her any great anxiety. These facts were not volunteered by the patient but were elicited afterwards only by close questioning.

Examination showed a diffuse slightly prominent swelling over the left frontal sinus but extending upwards more than the ordinary limits of an average-sized frontal sinus. The swelling was not obvious from the front view but was distinctly visible from the lateral aspect. Palpation revealed a certain softness, not amounting



FIG. 1.

X-ray plate of skull, lateral view showing tumour-like growth replacing frontal sinus.



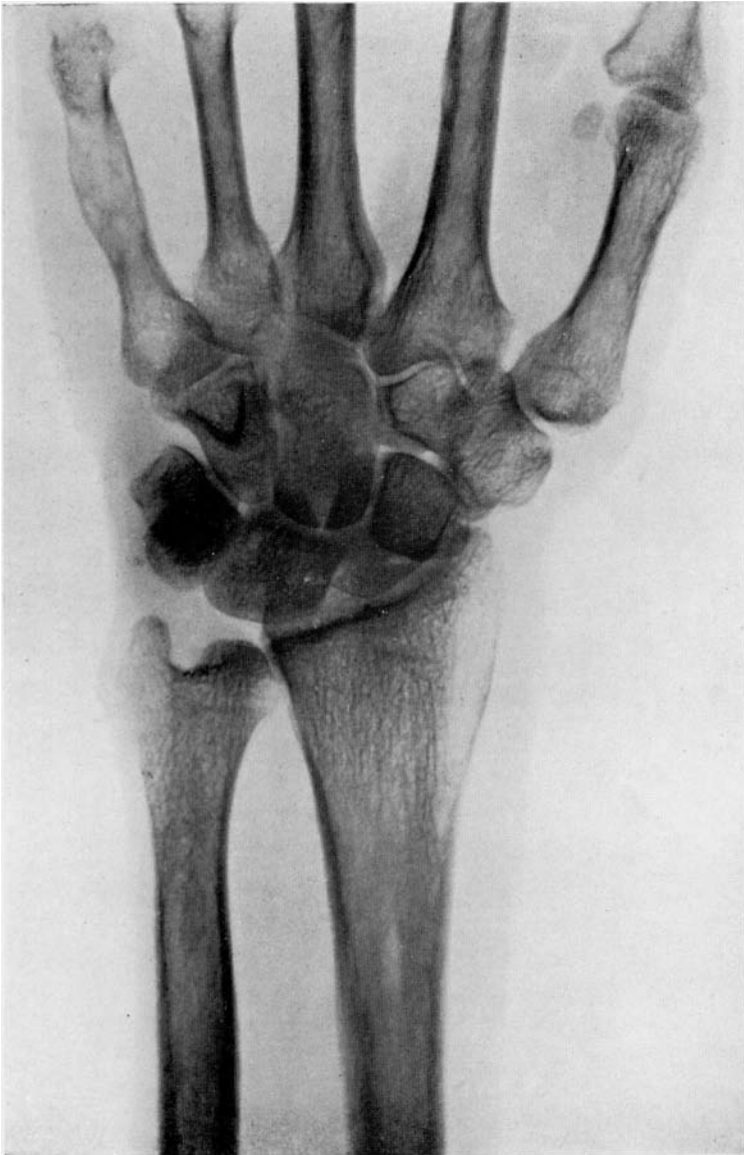


FIG. 2.

X-ray plate of right hand and forearm showing rarefied lesion of the 5th metacarpal with expansion of the shaft, slight general osteoporosis and focal translucencies in the radius.



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to fluctuation, but with a suggestion of elasticity, and firm pressure caused pain. Nasal examination was negative; the passages were clear and the turbinates normal.

Radiographic examinations were made and the reports stated that there was abnormality of the left frontal sinus with lack of transparency and unusual outline. The frontal bones showed a peculiar worm-eaten appearance suggesting a specific lesion. The other nasal sinuses were clear.

Wassermann tests on two occasions were negative. As the patient was unwilling to have any operative treatment, she was asked to report at frequent intervals. During the next six weeks no change was seen in the size or shape of the swelling and no further symptoms developed, but later X-ray films showed definite erosion of bone in the frontal region and on *August 19th, 1937*, arrangements were made to explore the sinus. On *August 23rd* under general anæsthesia, the left frontal sinus was exposed by incision through the left eyebrow. The anterior wall of the sinus was thinned and easily penetrated. A soft friable dark-red material at once bulged through the opening. Severe bleeding occurred on grasping this growth with forceps. The frontal sinus was found to be filled with similar material, which had penetrated across the mid-line into the right frontal sinus. From its appearance and consistency it suggested a tumour of sarcomatous type. While removing it, part of the posterior wall of the left frontal sinus came away, exposing the dura mater, which appeared to be of normal colour and appearance. Two days later 21 mgm. of radium were inserted into the remaining portion of tumour in the sinus and a dose of 2,060 mgm. hours was given.

Microscopical examination of the portions removed surgically showed the changes of multicentric osteoclastoma superimposed on osteitis fibrosa. (See later.) Repeated chemical analysis of the blood showed great elevation of the calcium with reduction of the inorganic phosphorus (see Table) and a diagnosis of generalized osteitis fibrosa (von Recklinghausen's disease) secondary to parathyroid tumour was made.

Radiological examination of the other bones confirmed the diagnosis, and the appearances throughout the skeleton are dealt with later.

Examination of the neck revealed an ill-defined and inconspicuous swelling about the lower pole of the left lobe of the thyroid gland. The patient was therefore transferred to the surgical ward under the care of Mr. F. R. Brown, and, as a preliminary to exploration of the neck, was given a high calcium diet with radio-stoleum for a week prior to operation.

On 20.9.37 under ether anæsthesia, Mr. Brown explored the neck by a transverse incision, and revealed an encapsulated tumour

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lying below and behind the inferior pole of the left lobe of the thyroid gland. The tumour was of reddish-yellow colour and appeared to be partly cystic. It was removed without difficulty and was immediately bisected for examination to exclude the possibility of a concurrent thyroid adenoma.

On sectioning the tumour a few c.cs. of rather sticky fluid escaped; the cut surface presented areas of solid yellowish tissue suggestive of parathyroid tissue and reasonable certainty was felt that the growth which had been diagnosed was the parathyroid tumour. Careful examination of the region exposed including

TABLE I  
ESTIMATION OF SERUM CALCIUM AND INORGANIC PHOSPHORUS

Date.	Mgms. per 100 c.c.	
	Ca.	Inorganic Phos.
3. 9.37	14.7	—
9. 9.37	16.3	—
17. 9.37	17.2	0.7
20. 9.37	Operation: Removal of parathyroid tumour.	
21. 9.37	14.2	1.6
25. 9.37	11.0	0.5
27. 9.37	10.4	—
29. 9.37	10.2	0.7
1.10.37	9.6	2.0
11.10.37	7.8	2.6
18.10.37	8.5	2.8
20.10.37	8.6	2.6
4.11.37	9.0	2.8
19. 5.38	10.8	2.3

the retromanubrial space, failed to reveal any other structure resembling an enlarged parathyroid gland and the wound was therefore closed in layers. Healing of the neck wound was satisfactory, but the frontal wound filled only slowly and continued to discharge for some weeks, necessitating repeated dressing. The diet was arranged to include calcium-rich foods and, in addition, calcium lactate was given daily in 15 gr. doses with radiostoleum by mouth. After some weeks, in order to facilitate drainage and promote healing, a wide opening was made from the frontal sinus into the nose. This greatly helped the condition of the wound and the patient was discharged at her own request with instructions to have the wound dressed regularly. Healing was still unsatisfactory, however, and on the supposition that

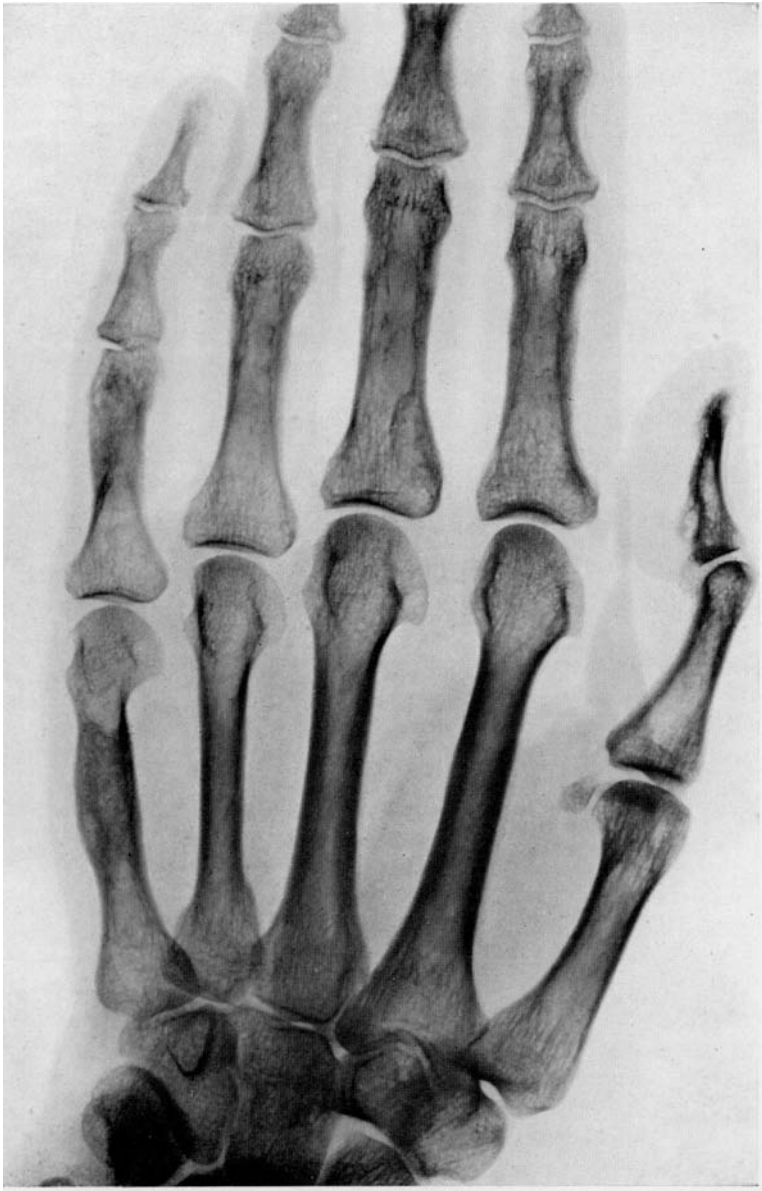


FIG. 3.

X-ray plate of right hand ten months after removal of parathyroid tumour. Note the heavy calcification of the lesion on the Vth metacarpal bone and increased density of other bones.





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there was a portion of necrosed bone due either to the initial operation or the subsequent radium treatment, she was re-admitted and a further operation was undertaken. The frontal sinus was again opened widely and several pieces of necrosed bone embedded in vascular granulation tissue were removed, the right and left frontal sinuses being thrown into one and both into free communication with the nose. Thereafter the wound drained well and healing was satisfactory. The patient was, however, left with an unsightly depressed scar and this has now been repaired by a plastic operation.

Menstruation, which had been normal until the removal of the parathyroid tumour, then ceased and remained in abeyance for almost a year, after which it returned and continued normally.

*Radiological Appearances.*—X-ray examination of the frontal tumour was carried out when the patient first presented herself at the Out-Patient Department and the left frontal sinus showed lack of translucency and was of unusual outline; at the same time a curious worm-eaten appearance of the frontal bone was observed, but the significance of this was not suspected. Further examination after three weeks showed progressive erosion of the frontal bone and four weeks afterwards the anterior wall of the frontal sinus was seen to have been destroyed and the frontal cells replaced by a more translucent tissue (Fig. 1). After the initial exploratory operation and pathological report suggesting von Recklinghausen's disease, radiological examination of the remainder of the skeleton was carried out and a mild degree of generalized osteoporosis was detected, with some loss of definition of the cortical layers in the long bones, notably the radius and ulna, but these changes were slight and evidence of previous fracture was lacking. A few small areas of increased rarefaction were noted, most pronounced in the ribs, iliac bones and in the Vth metacarpal bones; and the latter, especially, were very suggestive of focal osteoclastomata (Fig. 2). Multiple pin-point translucencies were also observed in films of the cranial vault, together with general blurring of its architecture. These findings were consistent with the pathological diagnosis of osteitis fibrosa. No evidence of renal calculi was observed.

After removal of the parathyroid tumour the abnormal excretion of calcium ceased and under the influence of the high calcium diet + radiostoleum, the skeleton became remineralized and the rarefaction disappeared. Films of the hands taken eight weeks after removal of the parathyroid tumour showed increased density of the translucent areas in the metacarpal bones and phalanges, and further examination about six months later clearly demonstrated that these areas had become heavily recalcified and had largely lost their cystic appearance (Fig. 3), thus confirming the view that these lesions were probably little giant-cell tumours rather than

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cysts. At this time the skull was found to have lost the pin-point translucencies observed earlier and the defect in the frontal region was filling up, especially in the right half, with bone of increased density. It is thus apparent that the skeletal changes generally have undergone retrogression and that a degree of remineralization of the skeleton has occurred, though it is to be noted that the increased porosity was only slight in the first instance.

### *Pathological Examination. (a) Bone.*

1. *The Frontal Tumour.* About 20 grammes of tissue consisting of fragments of dark red soft tumour-like substance mingled with portions of cancellous bone was received for pathological examination, the proportion of bony and tumour-like substance varying in different fragments. A flake of more compact bone from the posterior wall of the sinus adjoining the dura mater was also submitted. Portions were fixed in Zenker-formol, Susa, Bouin's fluid and formol saline. The softer portions were embedded in paraffin and cut without decalcification; other parts were first decalcified in De Castro's mixture. Numerous blocks were cut and stained by a variety of methods.

Sections were first prepared from the red sarcoma-like tissue and the appearances were typically those of osteoclastoma (Fig. 4). The lesion consists of numerous large multinucleated cells with rather basophil cytoplasm and central nuclei, embedded in a vascular spindle-celled tissue in which there is abundant recent hæmorrhage and also numerous macrophages containing altered blood pigment. It was apparent, however, that the giant-cell tumour occurred in multiple foci separated by areas of fibrous marrow in which the remains of bony trabeculae could be seen undergoing osteoclastic lacunar absorption. This observation, together with the site of the lesion in a membrane bone, at once suggested the diagnosis of osteitis fibrosa. Further examination of sections from all the fragments submitted and from the bone of the inner table forming the posterior wall of the sinus, confirmed the histological diagnosis.

In the portion of bone thought to be from the inner table the changes are well shown. The bone consists almost entirely of newly formed woven bone of rather fine fibred type (Fig. 5) and here and there are a few fine lamellae upon the surface of the trabeculae (Fig. 6). The spaces between the bony trabeculae are filled with fibrous marrow which, in the outer portions towards the diploe is more abundant, the bony trabeculae being much smaller here and less numerous. In many places groups of osteoclasts lying in Howship's lacunae indicate the activity of the resorptive process (Fig. 7) and in the fibrous marrow the blood vessels show an extreme degree of dilatation and engorgement. Throughout the more fibrous parts, multiple small groups of osteoclasts are seen, often in

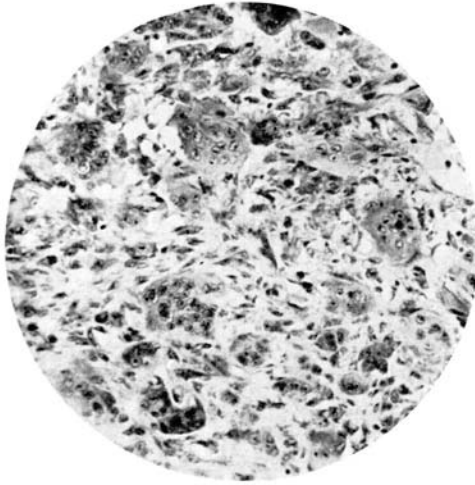


FIG. 4.  
Osteoclastoma of left frontal bone showing typical giant-cell structure.  $\times 190$ .

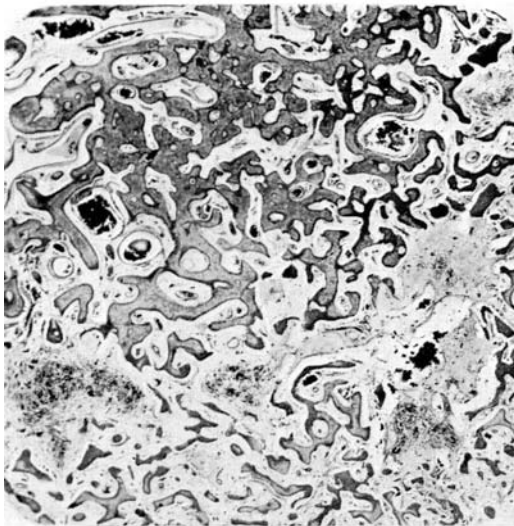


FIG. 5.  
Bone from posterior wall of frontal sinus showing newly-formed bone with fibrous marrow containing widely dilated blood channels. Four small foci of giant-cell proliferation are seen.  $\times 12.5$ .



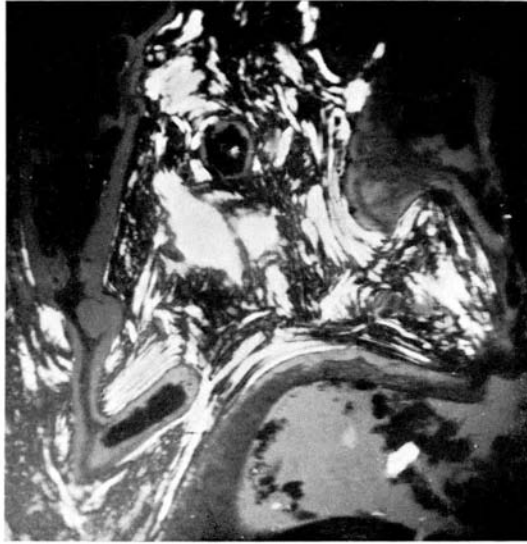


FIG. 6.

One of the new long trabeculae photographed by polarized light to show the architecture of the newly-formed bone.  $\times 49$ .

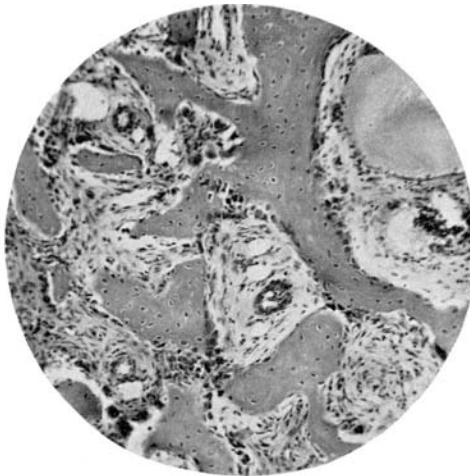


FIG. 7.

Bone showing active osteoclastic lacunar absorption.  $\times 85$ .



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association with extravasated red cells and, as the tissue is traced outwards towards the obliterated frontal sinus, the osteoclastic tissue becomes more abundant, eventually forming considerable masses of the soft reddish tissue seen at operation. Even in the most cellular parts, however, there are scattered remnants of bony trabeculae, the appearances clearly indicating a fusion of multiple centres of osteoclastic proliferation. It seems curious that such a massive formation of giant-cell tissue should have developed giving the clinical features of an osteoclastoma of the frontal bone at a time when the disease appears to have been at a relatively early stage of development.

2. *Bone after removal of parathyroid tumour.* About six months after the first opening of the frontal sinus a further operation was undertaken for the removal of suspected dead bone, and numerous fragments from the operation area were submitted to microscopic examination. These showed clearly the presence of portions of dead bone embedded in dense fibrous tissue in which foci of plasma cells occurred. The left frontal sinus was relined partly by squamous epithelium and partly by poorly developed granulation tissue; the right showed a more columnar lining. From the numerous portions received it seemed that the curettage of the bone had successfully removed all the sequestra and had reached healthy bone.

In the deeper parts, away from the immediate site of operation, the bone now shows no evidence of active resorption, osteoclastic giant-cells being conspicuously absent. There is also very little evidence of lamellar apposition of new bone, and lines of osteoblasts along the surface of the trabeculae are scanty. In the fibrous marrow spaces the blood vessels are much reduced in size thus contrasting very strikingly, in their extremely engorged and dilated condition, with the fragments removed six months previously. The marrow spaces are filled with fibrous tissue, somewhat less cellular than before, and there is a complete absence of the hæmorrhagic and osteoclastic foci formerly present. It was noted that, whereas the bone from the first operation was soft and some portions were cut without decalcification, on the other hand the fragments removed six months later were much harder and required much more vigorous treatment with acid before sectioning.

(b) *The parathyroid tumour.*—The specimen is an ovoid cystic adenoma measuring  $3.5 \times 2.5 \times 1.1$  cm. and weighing 10.9 gm. after the escape of the small amount of fluid in the operating theatre. The growth is well encapsulated and is of soft cystic consistency. Externally it presents a coarsely lobulated surface and in its fibrous capsule a branch from the inferior thyroid artery runs across the anterior surface. On section it shows a variegated structure, the upper pole and the periphery being of solid, dull



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yellowish appearance (Fig. 8). The centre is more vascular and hæmorrhagic and shows several small cysts filled with pale yellowish-brown sticky fluid and lined by pale yellowish cellular tissue, while the lower pole is intersected with bands of dense fibrous tissue amongst which there are masses of more bright yellowish cellular tissue resembling parathyroid substance.

Portions were fixed in Zenker-formol, Bouin's fluid, Susa, Regaud's formol-bichromate mixture and one half of the tumour was preserved in Pick's solution.

Microscopically the tumour is readily identified as a parathyroid adenoma. It is surrounded by a thin sheet of collagenous connective tissue which in places contains small groups of thyroid acini showing atrophy and fibrosis with patchy round-celled infiltration around and between them. From the capsule trabeculae carrying arteries and veins pass into the interior of the adenoma which is thus broken up into rather poorly defined lobules. Two main types of architecture are present, viz. (a) solid nodules consisting of trabeculae of parathyroid cells separated by a very delicate stroma, and (b) areas in which cystic spaces are formed, lined by one or more layers of epithelium and filled with pale-staining secretion. The solid portions consist of closely-packed masses of polygonal cells separated by delicate collagenous septa along which the cells in places assume a columnar shape, the nuclei tending to be at the pole away from the stroma (Fig. 9). Where septa are cut transversely there is thus a tendency to a rosette arrangement. The cells are of variable size but the majority lie between  $12\mu$  and  $20\mu$  in diameter. Their nuclei are oval or round, measuring  $6-8\mu$  and the cytoplasm of practically all the cells is bounded by a very distinct cell membrane which is stained intensely by chromotrope 2R and by the anilin blue in Mallory's and Masson's trichromic methods, after fixation in Bouin's fluid, Susa, or other strongly acid fixatives; with methyl-green-pyronin after formalin fixation the cell membranes are pink. The nuclei by such methods show a fine chromatic network and one or two relatively inconspicuous nucleoli. After fixation in neutral Zenker-formol or in Regaud's fluid, however, followed by phosphotungstic acid hæmatoxylin or eosin-azure, the nucleoli are much more conspicuous and one or two can be seen prominently in each nucleus. The majority of the cells correspond to the principal cells of the parathyroid glands, but are larger. They contain abundant glycogen and fat and their cytoplasm shows numerous eosinophil granules which are coloured red by methyl-green-pyronin, bluish-purple by eosin-azure and are unstained by phosphotungstic acid hæmatoxylin. Here and there are to be seen cells with more deeply coloured fine oxyphil granules which correspond to the pale oxyphil cells of the normal gland (Fig. 10); these are deeply blue-stained in phosphotungstic

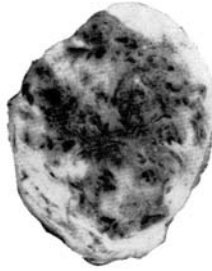


FIG. 8.  
Parathyroid adenoma. Natural size.

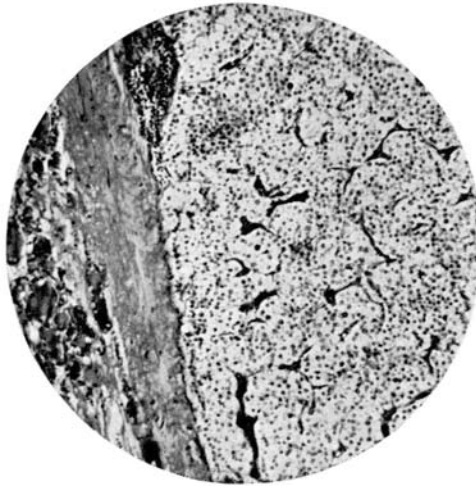


FIG. 9.  
Solid portion of encapsulated parathyroid tumour composed of principal cells.  $\times 85$ .



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acid hæmatoxylin preparations and are brilliant red by Dominici's method and eosin-azure. In other parts the granules lie more discretely in a rather empty-looking cytoplasm, which is rich in glycogen and fat. Principal cells of the ballooned water-clear type are seen here and there, isolated or in small groups throughout the trabeculae of the solid portions of the adenoma, but they tend to be more abundant just beneath the capsule and along the collagenous septa.

A striking feature is the presence within the fibrous capsule around the margin of the tumour, of groups of acini arranged in lobular fashion; these consist almost entirely of principal cells considerably smaller than those of the adenoma, and usually with small, darkly staining nuclei lying close to the outer margin of the cell next the stroma, while the centre of each acinus shows a reticulated structure due to the contiguity of the deeply staining cell membranes. Among these occur groups of pale oxyphil cells and occasional smaller, more darkly-staining oxyphil cells. The anatomical situation of these lobules and the more normal appearance of the cells suggests that they are probably the remains of the left inferior parathyroid body stretched out by the expansive growth of the adenoma owing to their incorporation within its capsule.

The cystic spaces appear to be of two kinds; true glandular lumina, and spaces formed by degeneration of the stroma. Some of the solid masses of epithelial cells open out at one end into a space lined at one side by a single layer of plump cubical cells with rather basophil cytoplasm, while the opposite wall of the space is covered by several layers of principal cells (Fig. 11). Hæmorrhage into these spaces is frequently present, both recent and old, and granules of altered blood pigment are seen in phagocytes around the walls. The cystic glandular spaces are usually filled with pale-staining acidophil coagulum which presents a reticulated or bubbly margin and the epithelial cells are usually well-preserved; only occasionally are the appearances suggestive of cyst formation by central degeneration of the cells seen. In some parts the collagenous septa appear to be œdematous, the individual fibres becoming separated by fluid but retaining their staining qualities, but elsewhere the stroma becomes swollen and hyaline and fades gradually into a homogenous faintly-staining coagulum in which for a time the vessels persist. Finally the vessels disappear and spaces which according to their plane of section may appear as pseudo-glandular lumina within masses of the epithelial cells are left.

### DISCUSSION

Within recent years the disease hyperparathyroidism has been separated from other symptom-complexes in which fibrotic

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and cystic changes in the bones are an important feature. Formerly it was a matter of controversy as to how far Von Recklinghausen's disease of bone differed from Paget's osteitis deformans and the local forms of fibrocystic disease were not sharply distinguished from the generalized variety. Enlargement of one or more parathyroid glands had long been observed in certain cases of generalized osteitis fibrosa cystica but since a degree of enlargement was also sometimes found in other bone diseases, such as renal rickets and osteomalacia, the primary importance of the parathyroid changes in generalized osteitis fibrosa was for a time not recognized. Mandl (1926) was the first to record clinical improvement following removal of an enlarged parathyroid gland, though it is curious that in this case the improvement was not so complete as in many subsequent cases and the condition in Mandl's first case has since recurred and has proved resistant to further surgical measures (Bauer, 1934). Since the publication of Mandl's paper, many successful examples of parathyroidectomy for osteitis fibrosa have been recorded and the subject has been well reviewed by Hunter and Turnbull (1931) and by Cuthbertson and Mackey (1935). Shelling (1935) has also reviewed the whole subject of the parathyroid glands in health and disease.

The therapeutic value of operative removal of a parathyroid tumour in osteitis fibrosa is now generally accepted and the procedure should be undertaken as soon as the diagnosis is satisfactorily established. For this purpose, repeated estimation of the blood calcium and inorganic phosphorus is essential and if the results of such investigations are equivocal, the plasma phosphatase activity should be investigated and the calcium balance should be estimated after a period of stabilization on a low calcium intake.

In hyperparathyroidism, the serum calcium is raised while the inorganic phosphorus of the blood is lowered and it seems clear that the increase in blood calcium represents a draining of calcium from the skeleton into the blood with subsequent excretion of the excess calcium, chiefly in the urine. The exact means by which the excess parathyroid secretion brings about the mineral depletion of the skeleton is not yet clear. The high urinary calcium is an important part in the diagnosis and is characteristic of hyperparathyroidism. The persistence of high urinary calcium over a long period may lead to the precipitation of calcium salts in the renal pelvis resulting in calculus formation, and serious results to the kidneys may follow. The high blood calcium may also lead to deposition of calcium in other organs and tissues—metastatic calcification. It is therefore of the utmost importance that the diagnosis of hyperparathyroidism be reached as soon as possible and the necessary operative measures carried out. There is a considerable danger of post-operative tetany since, owing to the

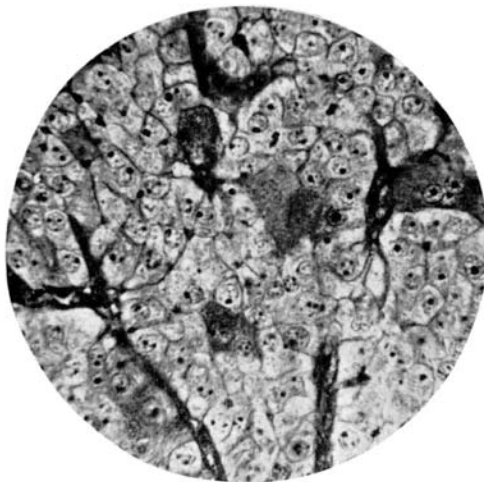


FIG. 10.

Portion of parathyroid tumour showing solid alveolar masses of principal cells with scattered darkly-stained oxyphil cells.  $\times 380$ .

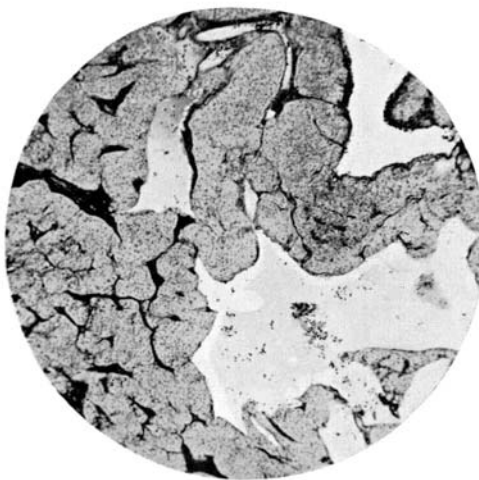


FIG. 11.

Cystic portion of tumour showing spaces filled with colloid.  $\times 40$ .



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functional activity of the enlarged parathyroid, the other glands may have undergone a degree of functional atrophy. Such tetany may be troublesome and even fatal. Accordingly, prior to operation and for some time thereafter, the patient should be given a diet rich in calcium with the addition of vitamin D to promote absorption from the intestine.

Cuthbertson and Mackey quote Telfer in recommending the addition of dilute hydrochloric acid to the milk of the diet in order to promote absorption of calcium. If tetany supervenes and is severe, it may be controlled by the administration of calcium by the intravenous or intramuscular route, supplemented in severe cases by the administration of parathormone. The use of parathormone should, however, be restricted to emergencies, as the effects tend to be transient and the hormone may become less effective if administered continuously over a period.

In the present case, the chief point of interest lies in the unusual first manifestation of the disease and the opportunity to observe the skeleton before the changes have progressed far. We have not found in the literature any record of a similar case in which the primary manifestation was in the skull alone, and it is noteworthy that at a time when a large giant-cell tumour was present in the frontal bones, there was no complaint of general bone pains, usually amongst the earliest of symptoms. In Cuthbertson and Mackey's first two cases the disease declared itself by the development of osteoclastomata in the mandible, but operation on the neck was not performed until several years afterwards and by that time numerous other lesions had appeared. Such cases are not uncommon. In our case it is clear from X-ray examination that multiple lesions, mostly at an early stage, were present but only the frontal tumour had attracted the patient's notice. Doubtless had removal of the enlarged parathyroid been delayed, general symptoms would have occurred later. The opportunity has been afforded to observe radiologically over a period of ten months the changes in the skeleton following removal of the parathyroid tumour. The areas of rarefaction have become recalcified and the lesions in the meta-carpal bones have subsided and become recalcified.

It is generally recognized that single osteoclastomata occur only in bones developed in cartilage and that such a tumour in a membrane bone, would be exceptional. Geschickter (1936) states that of 300 giant-cell tumours reviewed at Johns Hopkins Hospital, only four were in the skull and all four arose in parts of the skull-base developed in cartilage. In the very extensive series of giant-cell tumours and bone cysts investigated by Geschickter, not a single case was localized to the purely membranous parts of the skull. In this case, therefore, the unusual localization in a membrane bone, i.e. the left frontal, of a tumour having the general characters



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of an osteoclastoma, suggested that the growth was not of the usual type. In the bony fragments accompanying the portions of growth, the changes typical of osteitis fibrosa were found and confirmation of the diagnosis was then obtained from estimations of the calcium and phosphorus in the blood; these changes clearly showed that the cranial lesion was part of a general affection and was not one of the localized varieties of osteitis fibrosa. In generalized osteitis fibrosa, however, the skull is usually less affected than the long tubular bones and the changes in the skull are more likely to be patchy and of osteoporotic nature. Widespread involvement of the skull with marked general thickening may occur as in Dawson and Struther's case (1923), but this is unusual, though, when present, the appearances may closely resemble those of Paget's disease. The occurrence of a giant-cell tumour of the frontal bone is, therefore, exceptional and one could scarcely have anticipated the microscopical diagnosis. There is little doubt, however, that the patient would have been spared much suffering had the diagnosis been reached and the parathyroid tumour removed before operation on the frontal bone was performed. It is highly probable that the frontal tumour would have disappeared and the bone undergone healing and recalcification, as has happened in the lesions of apparently similar nature in the metacarpal bones.

It would, therefore, seem advisable to investigate the calcium metabolism in any obscure and unusual tumour of bone, and if the findings are suggestive of hyperparathyroidism, exploration of the neck should be undertaken before any radical operation upon the bone is performed.

### SUMMARY

A case is reported of giant-cell tumour (osteoclastoma) of the left frontal bone as the first manifestation of osteitis fibrosa generalisata.

The skeletal changes were accompanied by marked elevation of the calcium and reduction of the inorganic phosphorus content of the blood, the importance of which in diagnosis is emphasized.

The primary lesion was an adenoma of the left inferior parathyroid gland, causing hyperparathyroidism, and removal of the tumour was followed by reduction of the blood calcium and healing of the skeletal changes with remineralization of the bones.

There was no evidence of post-operative tetany.

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