FIBROUS DYSPLASIA OF THE SKULL

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GENERAL ASPECTS OF FIBROUS DYSPLASIA

Within recent years, largely as a result of the contributions of Albright and his associates,2,4 of McCune and Bruch,34 Lichtenstein,31 and of Lichtenstein and Jaffe,32 the concept of fibrous dysplasia of bone as a disease entity has become established. The clinical features of this disorder were clearly epitomized in the subtitle of a paper published by Lichtenstein and Jaffe32 in 1942, as “A condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of the skin, premature sexual development, hyperthyroidism or still other extraskeletal abnormalities.” The term, Albright’s syndrome, has been applied to those cases in which disseminated bone lesions are associated with cutaneous pigmentation and sexual precocity in females.

Judging from the literature and from our own experience, it is evident that involvement of the skull is frequently observed in this condition and may, in fact, constitute its only manifestation. It is with this aspect of the disease and its neurosurgical implications that we are primarily concerned. Detailed accounts of a more general nature are available in a number of publications.2,3,8,10,16,17,21,23,26,31,32,46

Pathology. Involvement of osseous structures may occur alone or in association with the endocrine and cutaneous manifestations of Albright’s syndrome. The skeletal lesions may be confined to a single bone (monostotic), or may involve a number of bones (polyostotic). Regardless of the clinical form assumed by the disease, the basic histopathologic changes are fundamentally identical in all cases. Within an affected bone, either flat or tubular, there takes place an accumulation of fibrous connective tissue. This may be cellular, consisting of spindle cells arranged in whorls, or densely collagenous. Dispersed throughout the connective tissue, trabeculae of immature bone may be frequently observed. This new bone is poorly formed, imperfectly calcified and may show evidence of osteoclastic resorption. In some cases the amount of bone laid down may be considerable, so that the connective-tissue element appears relatively insignificant. Islands of cartilage may also be observed within the fibrous tissue and occasionally small cysts, areas of hemorrhage, giant cells or foam cells are to be found. With the ter-

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mination of the active phase of the disease, the fibrodysplastic tissue may become increasingly ossified. In some bones, especially those of the skull, sclerotization of the fibrodysplastic tissue may eventually become extremely marked. As will be indicated later, the roentgenologic manifestations of this disorder are variable, depending on the relative amounts and distribution of fibrous tissue and bone.

Grossly such dysplastic tissue appears yellow or greyish-white, is of variable consistency, though usually firm and rubbery, and often feels gritty owing to the presence of many small bone spicules. It may occasionally contain small cysts filled with brown fluid. The skeletal structures affected by this disease may either retain their shape or become widened and deformed, or even fractured as a result of the expansile nature of the pathologic process.

Etiology. The etiology of this disorder is unknown. As indicated by Albright and his associates, the regional distribution of the lesions would tend to exclude a metabolic or endocrine cause. They suggest that the responsible factor may be either a neurologic disturbance or an embryologic defect. A congenital anomaly of development that may account for both skeletal and extraskeletal features is advocated by Lichtenstein and Jaffe. In keeping with this hypothesis, abnormal activity of the specific bone-forming mesenchyme would be the cause of the osseous lesions. The embryonic defect theory is also favored by Neller. The possibility that the monostotic form of fibrous dysplasia may represent a disturbance of the normal reparative processes following injury is proposed by Schlumberger. Derangement of liver function, hormonal disturbances, hyperemia caused by anomalies of the sympathetic nervous system, and chronic hyperparathyroidism due to a hyperphosphatemia have also been suggested as etiologic factors.

Snapper formerly was of the opinion that fibrous dysplasia represented a variant of Hand-Schüller-Christian’s disease. In the latest edition of his book, however, he has modified this view and concedes that in most cases this interpretation does not appear to have been substantiated. Thannhauser’s thesis that fibrous dysplasia is a form of neurofibromatosis of von Recklinghausen has been critically analyzed by Jaffe and Albright. Both reject this concept. The clinical and anatomic evidence they submit leaves little doubt that the two conditions are indeed separate entities.

Clinical Aspects. Fibrous dysplasia is primarily a disease of childhood, its progress frequently becoming retarded or arrested when adult life is reached and skeletal growth ceases. It is believed that in cases in which the disorder is first encountered later in life, the skeletal lesions originated during childhood. Females are more commonly affected than males. The usual clinical manifestations are limp, deformity, pain and pathologic fracture. In cases with advanced skull lesions, the degree of disfigurement may be considerable. This will be discussed in greater detail subsequently. When more than one bone is affected, the involvement is frequently exclusively or predominantly unilateral. It may be monomelic. Long bones are mainly affected, the proximal parts more than the distal. Thus the upper half of the
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Femur is often involved, resulting usually in an outward bowing referred to as the "shepherd crook" deformity. Other bones that may be implicated include the scapula, pelvis, clavicle, vertebrae, tarsal and carpal bones, ribs, sternum and mandible. In the series of 90 cases collected by Lichtenstein and Jaffe, the extent of the lesion was known in 87, in 15 of which it was limited to a single bone. Probably the incidence of monostotic involvement is considerably greater. In 67 of the 69 cases Schlumberger collected from the Army Institute of Pathology, the lesion was restricted to one bone. Additional instances have been recorded by Elmslie, Freund and Meffert, Wyatt and Randall, and Wells. To illustrate further the probable relative frequency of single lesions, in the recent publications of Proffitt, McSwain and Kalmon, and Russell and Chandler, the monostotic cases outnumbered the polyostotic.

Of the extraskeletal manifestations that are known to occur in fibrous dysplasia, the commonest, according to Jaffe, is cutaneous pigmentation. The affected area of skin is yellow or yellow-brown in color, flat and of variable size. Albright states that the pigmentation in cases of fibrous dysplasia is characterized by an irregular border reminiscent of the "coast of Maine," in contrast to that observed in neurofibromatosis, which possesses a more regular contour likened to the "coast of California." Its location may or may not correspond to that of the fibrodyplastic skeletal lesions. Though apparently uncommon, the occurrence of cutaneous pigmentation in monostotic cases has been reported by Jaffe, Proffitt, McSwain and Kalmon and by Russell and Chandler.

Sexual precocity is found in a small proportion of cases, and in these, the osseous lesions as a rule are marked and widespread. Though most often observed in females, precocious sexual development has occasionally been reported in males.

Accelerated skeletal growth and premature fusion of the epiphyses may occur. In such cases the children may at first appear unusually tall, but their final height is short due to early epiphyseal fusion. As indicated by Jaffe, skeletal precocity has been observed mainly in patients exhibiting the several features of Albright's syndrome. Whether it occurs in cases in which the bony involvement is more limited, is uncertain.

Other extraskeletal manifestations reported in the literature include hyperthyroidism, congenital arteriovenous aneurysms, gynecomastia and other feminine characteristics in a male adolescent, acromegalic features, and coarctation of the aorta together with a rudimentary kidney. A case of diabetes mellitus associated with Albright's syndrome was encountered by Peck and Sage. In one of our patients with fibrodyplastic changes limited to the skull, an impaired carbohydrate tolerance was demonstrable.

Blood chemical studies are usually normal, though elevation of the alkaline phosphatase level has been reported.

The disease runs a protracted, slowly progressive course. Apparently a
relatively stabilized condition may be reached when the period of active skeletal growth comes to an end. Increasing deformity of an involved bone may, however, occur during adult life as a result of structural weakness. Occasionally, as observed by Jaffe, a lesion that appears to have become quiescent may show signs of activity again after a lapse of many years. Four cases are on record in which sarcomas developed in an affected bone.

Roentgen Appearance. When fibrous dysplasia affects a tubular bone, the changes observed on roentgenographic study involve the shaft and metaphyses, rarely the epiphyses. The basic lesion being a replacement of medullary bone by fibrous tissue, areas of decreased density may be seen. Since the involved bone is often expanded, and its cortex thinned, the roentgenographic picture takes on a cystic appearance. There may be ridges on the inner surface of the cortex of the bone giving the impression of a multilocular lesion. The presence of bony trabeculae in many of the apparently cystic areas gives rise to increased densities resembling ground glass or "columns of slowly ascending smoke."

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Cranial lesions are of frequent occurrence in polyostotic fibrous dysplasia. According to Windholz, about half the cases with moderate skeletal involvement show skull changes; in those with marked skeletal manifestations, the skull is invariably affected. Involvement of the skull, on the other hand, occurs fairly frequently in the absence of demonstrable dysplastic lesions elsewhere in the body. Windholz is of the opinion that the cranium is affected in approximately 1 out of every 10 cases of the monostotic variety. Pugh gathered 10 cases in which the disease apparently was limited to the cranium and facial bones, though in only 3 was a complete skeletal examination performed. The calvarium was the site of the lesion in 5 of the 67 monostotic cases reported by Schlumberger. The frontal bone was involved in 2 instances while the parietal, temporal and occipital bones were each affected in 1 case. Localized osteitis fibrosa cystica of the frontoparietal skull in a child, undoubtedly an example of fibrous dysplasia, was recently described by Paget, Fricker and Ver Bruggen.

It has been suggested by a number of observers that many of the cases classified as leontiasis ossea are in reality manifestations of fibrous dysplasia. The view that the two conditions might be closely related was proposed by Falconer, Cope and Robb-Smith and is concurred in by Furst and Shapiro, Dockerty and his associates, Windholz and Cutting, and by Fairbank. Leontiasis ossea has generally been regarded not as a specific pathologic entity, but rather as a syndrome, of uncertain, though presumably diverse etiology. Paget's disease, osteitis fibrosa cystica of von Recklinghausen and inflammatory disease (Virchow's type) have been held responsible. The subject is well reviewed by Windholz and Cutting, who conclude that the majority of cases described as Virchow's and von Recklinghausen's type of leontiasis ossea, in which there were no chemical alterations or dif-
fuse osteoporosis, were in all probability instances of fibrous dysplasia. Reference is also made to the work of Knaggs, who divided the cases of leontiasis ossea into two groups—creeping periostitis and diffuse osteitis. The periostitic form was thought to result from bacterial infection and to originate in the nasal fossae or accessory sinuses. Spread of the infection was believed to take place on the undersurface of the periostium and to be accompanied by an osteitis of the adjacent bone, resulting in subperiosteal bone deposition. The cases of diffuse osteitis, regarded by Knaggs as synonymous with osteitis fibrosa, were further divided into a general diffuse osteitis of the cranial and facial bones, a circumscribed form, and an osteitis beginning in one or both jaws and rarely spreading far beyond them. Histologically, this form of leontiasis ossea is characterized by an accumulation of vascular and cellular connective tissue in which new bone develops through metaplasia of the fibrous tissue. Windholz and Cutting are of the opinion that many of the cases classified by Knaggs as diffuse osteitis were probably instances of Paget’s disease or fibrous dysplasia. Fairbank, who also reviewed Knaggs’ work, goes even further and states that he is not convinced that there is any material difference in the two groups, nor that any of the cases appear to belong in the category of Paget’s disease. He believes that “there seems no reason for regarding leontiasis ossea occurring alone as different and distinct from the hyperostoses of the skull seen in many cases of polyostotic fibrous dysplasia.”

The lesion designated as an ossifying fibroma or fibrous osteoma also appears to be closely related to fibrous dysplasia. This view, originally propounded by Lichtenstein, is also held by Schlumberger and by Jaffe. Jaffe is inclined to regard an ossifying fibroma or fibrous osteoma as a very osseous form of fibro-osseous dysplasia. Such lesions have been observed in the jaw and other bones of the skull. Eden described a group of benign fibro-osseous tumors of the membrane bones of the vault of the skull and face which were unassociated with general skeletal disease, arose in one or more foci usually early in life and grew slowly for many years before becoming stationary. They possessed an essentially similar structure, arising as a result of a transformation of fibrous tissue into bone by metaplasia. To quote Eden, “they range from the ossifying fibromas of the jaws, which contain only small amounts of bone and were formerly regarded as pure fibromas, to the mature bony compact osteomas and include many varieties of intermediate hyperostoses, frequently described as focal osteitis fibrosa.” These fibro-osseous tumors were divided into four groups: the ossifying fibromas, the fibrous or spongy osteomas limited to a part or whole of one bone, the localized compact osteomas, and the diffuse osteomas or hyperostoses involving several adjacent bones. The ossifying fibromas most commonly were observed in the horizontal ramus of the mandible and in the walls of the antra. A case in which a structurally similar process affected the frontal bone was also described. Histologically these lesions consisted of mature fibrous tissue in which there were scattered areas of calcification and ossi-
fication, and well developed blood vessels. They were interpreted to represent the most immature form of benign fibro-osseous tumor involving membranous bone. The localized osteomas were of two varieties, fibrous and compact. Though apt to occur anywhere in the membranous bones of the skull and face, these lesions most commonly arise in the frontal and facial regions. In Eden’s series of 10 cases of localized fibrous osteomas, 5 were maxillary, 2 frontal, 2 mandibular and 1 temporo-occipital. Microscopically these tumors displayed trabeculae of newly formed primitive bone irregularly dispersed in a fibrous stroma of varying cellularity. The compact or ivory osteomas were found to involve any of the membrane bones of the skull and face, arising on either table of the mandible along the alveolar margin, on the hard palate and surface of the zygoma and maxilla, on either side of the bones of the vault of the skull, often in the external auditory meatus and orbit, and in the antra and frontal sinuses. They were composed of mature, dense, laminated bone with small haversian systems. Eden regarded this type as “the most mature and localized form of the fibro-osseous tumors of the membrane bones. It is periosteal and subperiosteal in origin, and although fibrous tissue may be almost absent, the tumor is formed in a manner similar to the more fibrous types, and all stages of transition are found between the two groups.” The diffuse osteomas, comprising Eden’s last type, differed from the localized fibrous osteomas only in that the disease was not limited to a single bone. Such cases have been described under the name of leontiasis ossea, and are synonymous with the second group of Knaggs, referred to previously. The microscopic structure of the bone in these cases was identical with that of the more localized fibrous osteomas, being characterized by a diffuse replacement of the marrow by fibrous tissue in which new bone was deposited. As stated by Eden, “the trabeculae pass in all directions, and may be slender, composed mostly of woven bone and separated widely by fibrous tissue in the more spongy types; and stouter, formed of laminated bone and separated only by narrow tracts of fibrous tissue, in the denser types. Osteoclastic resorption of bone and re-formation of bone by osteoblasts may be active, or the process may appear quiescent with evidence of extensive old remodelling.”

A series of cranial osteomas comparable to the localized osteomas of Eden was reported by Echlin.12 These involved the external surface of the cranium, most often the frontal bone. Spongy and eburnated, as well as intermediary forms, were encountered. It was stressed by the author that these several types represented different stages of the same process, all apparently arising from the deeper layers of the periosteum. The eburnated tumors were composed of quiescent adult cortical and cancellous bone, the spongy tumors of proliferating preosseous tissue, derived from spindle-shaped fibroblasts, and trabeculae of young bone. Most of the osteomas, especially those of the spongy variety, arose at an early age.

Roentgen Appearance. The roentgenographic changes observed in the skull in cases of fibrous dysplasia are not uniform. The cyst-like, translucent
areas typically found elsewhere in the skeleton are less often encountered in the skull. They are usually restricted to the calvarium and are associated with widening of the diploe and thinning of the tables. According to Windholz\textsuperscript{64} such translucencies possess a dense margin and may or may not extend beyond the surface of the outer table. In none of his cases did the cysts extend through sutures. Such lesions have been observed in the occipital, frontal and parietal bones. More commonly the skull is the site of extensive new bone formation which causes an increase in the thickness and density of the affected structures. While bone deposition of a pronounced degree is especially evident in cases in which the base of the skull is involved, the vault may be similarly affected. The localization of the skull and facial lesions may be unilateral and restricted to the side of the skeletal lesions when the latter involve only one side of the body. In the more severe cases, the skull changes are extensive. The calvarium, roofs of the orbits, the wings of the sphenoid bones, the anterior and posterior clinoids, the malar bones, paranasal sinuses and mandible may all be affected. At times, as in some of the cases to be described, the extent of the lesion may be sharply circumscribed.

According to Dyke,\textsuperscript{11} in cases of leontiasis ossea, localized or generalized, thickening of the bones of the skull may be observed. In the localized form, the frontal bone and superior maxillae are affected, resulting in encroachment on the orbital cavities and obliteration of the antra. The vault and base, especially the former, are thickened in the generalized form. Both types may be associated with sclerosis of other skeletal parts.

The localized fibrous osteomas (Eden) are characterized radiographically by a shell of cortical bone continuous with the adjacent outer table surrounding a mass of fine, spongy new bone extending into the diploe. Expansion of the bone may be observed. The inner table may be unaffected or thickened and extend into the cranial cavity.

In cases of what has been referred to as osteitis fibrosa localisata affecting the bones of the face and skull, there usually is also found expansion of the cavity of long bones, which become less dense than normal (Dyke\textsuperscript{11}).

AUTHORS’ EXPERIENCE

Our experience with fibrous dysplasia consists of 5 cases, 2 definitely of the monostotic variety and 3 presumably so. Symptoms referable to the eye led to neurosurgical consultation in 3 instances. The lesion was accidentally disclosed in 1 patient when x-rays were taken following an injury. An operation was performed in 4 cases, in 3 of which the preoperative diagnosis was a meningioma; 1 was diagnosed an osteoma. In the remaining patient the diagnosis was established on clinical grounds and subsequently verified histologically. Unilateral exophthalmos was observed in 3 of the patients subjected to operation, and optic atrophy in 1. The symptoms of the patient not operated upon were deformity of the skull and unilateral impairment of hearing. At the time they were observed in this clinic, 2 of the
patients were in the first decade of life, 1 in the second, and 2 in the third. The roentgenographic appearance in 3 cases was that of a sharply localized calcific mass in the anterior fossa.

CASE HISTORIES


**History.** A 13-year-old girl was admitted on Nov. 29, 1944 because of unilateral exophthalmos of 4 months' duration. This involved the left eye and was progressive in character. It was not associated with any disturbance of vision or with other symptoms referable to the nervous system. Menstruation had not yet begun.

**Examination.** There was a distinct proptosis of the left eye. Exophthalmometer measurements were 17 on the right and 21.5 on the left. Visual fields were normal. The retinal veins, especially those on the left, appeared congested. A slight lid lag involving the left eye was also noted. There was no abnormal cutaneous pigmentation.

**Laboratory Data.** Blood and urine were normal. Blood serology was negative. B.M.R. was −5.5. Roentgenograms of the skull revealed a calcific lesion involving the left orbital plate and sphenoid wing. It extended downward into the orbit and upward into the anterior fossa. The sella turcica appeared normal and there was no evidence of increased intracranial pressure. Diagnosis: Psammomatous meningioma.

**Operation.** On Dec. 4, 1944, under avertin endotracheal anesthesia, a left transfrontal craniotomy was performed. The dura was opened and the frontal lobe retracted in search of an intradural lesion. None was found. It was possible, however, to visualize a purplish-brown extradural mass overlying the orbital plate. The dura was therefore peeled off the floor of the anterior fossa, permitting direct access to the lesion, which involved the middle of the posterior half of the orbital roof. It had

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**Fig. 1. Case 1.** Cellular fibrous tissue containing many trabeculae of immature bone.
expanded the orbital plate and attenuated its walls so that it was contained within a bony shell. This was readily punctured with a blunt instrument. A needle was inserted and a small quantity of dark brown fluid removed. What appeared to be a complete excision of the mass and its capsule was then performed. The tissue removed was moderately firm in consistency and imparted a gritty sensation when sectioned.

**Histology.** The specimen consisted basically of fibrous connective tissue. It was composed chiefly of spindle-shaped cells with fusiform, vesicular nuclei containing small or inconspicuous nucleoli. There was a pronounced tendency for the cells to arrange themselves in small whorls. No mitotic figures were seen. For the most part the spindle cells were separated by only a small amount of fibrillar intercellular material, but in some areas the cells were so closely packed that there appeared to be no intercellular fibers whatever. Scattered throughout the fibrous tissue were numerous, small, newly formed, irregular trabeculae of “coarse fiber bone.” About some of these there was a rim of osteoblasts and osteoid tissue. A few contained foci of calcification. Also present in the fibrous tissue were vascular channels and a few multinucleated giant cells (Fig. 1).

**Course.** The postoperative course was in no way unusual and, at the time of discharge on Dec. 16, 1944, the degree of exophthalmos had diminished considerably. The patient continued to improve until October, 1945 when the left eye began to bulge again. A recurrence of the lesion was suspected and this impression was confirmed by roentgen examination. The medial portion of the sphenoid ridge on the left, including the region of the optic foramen, appeared deformed and displaced downward. In the lateral projection a well defined bony elevation was visualized in front of the anterior clinoid involving the superior orbital wall (Fig. 2). Reoperation was performed on Dec. 11, 1945. The lesion again was located entirely extradurally. The defect left in the orbital roof at the previous operation had become obliterated as a result of new bone formation. Within the orbital plate a mass containing both bony and soft tissue elements was exposed. A gross total removal was accomplished. The orbital fascia was opened, providing for a decompression of the orbital contents. The patient did well and at the time of discharge on the 11th postoperative day, the proptosis had completely receded. The histological appearance of the specimen was identical with that of the tissue removed at the first operation. The patient has remained under observation for 5 years and has shown no further evidence of recurrence.

History. A 9-year-old boy was admitted on Sept. 5, 1941 because of increasing prominence of the right eye for 9 months. There were no other symptoms.

Examination. Exophthalmos of the right eye was the only positive neurological finding.

Laboratory Data. Blood and urine were normal. Blood and CSF serology were negative. CSF protein was 23 mg. per cent. Roentgenograms of the skull disclosed a dense homogeneous mass, 3.5 cm. long and 2 cm. thick, involving the right orbital plate (Fig. 3). No vascular channels were observed leading towards this lesion. A pneumoencephalogram showed no encroachment on the ventricles or basilar cisterns. It was thought that the lesion probably was an osteoma.

Operation. A right transfrontal craniotomy was done under avertin endotracheal anesthesia on Sept. 18, 1941. The dura was retracted from the orbital plate, exposing what at first appeared to be a bony tumor. As soon as the lesion was entered, however, it became evident that it was actually a soft tissue mass infiltrated with calcific deposits. The operator described the feeling it imparted to a sharp curette as similar to that experienced when scraping a piece of ice. The tissue was of uniform consistency, and devoid of large blood vessels. A gross total removal of the lesion was accomplished.

Fig. 3. Case 2. A dense homogeneous mass (arrow) is present over the right orbital plate. Note similarity to Case 1.

Fig. 4. Case 2. Numerous trabeculae of newly formed bone are scattered throughout the fibrous tissue. Care must be taken not to confuse this picture with whorl formation commonly seen in meningiomas.
**Histology.** The lesion was composed of fibrous tissue containing newly formed bone. The fibrous tissue varied in its degree of cellularity, though most of it was rich in spindle-shaped cells. Prominently scattered throughout the fibrous tissue were newly formed trabeculae of primitive bone. These showed no characteristic arrangement, and were represented by irregular islands of pale eosinophilic and somewhat basophilic staining "coarse fiber bone." Foci of calcification were noted in some. In places the trabeculae were surrounded by osteoblasts and osteoid tissue. These immature trabeculae contained very few normal-appearing osteocytes. Multinucleated giant cells and areas of hemorrhage were noted occasionally (Fig. 4).

**Course.** At the time of discharge, 12 days after operation, exophthalmos was no longer evident. During the next 4 years, he remained asymptomatic. No further followup is available.

![Figs. 5 and 6. Case 3. Thickening of roof of left orbit and of sphenoid ridge (arrow). Roentgenographic picture suggests a hyperostosing sphenoid ridge meningioma.](image)


**History.** A 9-year-old boy came under observation on Aug. 29, 1949. On July 1, 1949 he had been struck over the left eye with a baseball. The area became swollen and he was placed under the care of a physician. Roentgenograms of the skull showed changes in the region of the left orbit, and because of these further investigation was advised. The child’s parents denied the presence of a deformity about the eye prior to the accident. Within a few days following the injury, the periorbital swelling subsided. At no time had he experienced headache, visual impairment, diplopia, or other neurologic symptoms.

His past history was not remarkable except possibly for the fact that he had been delivered by forceps and a mark over the left eye, caused by the instrument, had been present for the first few days after birth.

**Examination.** There was a prominence of the supraorbital ridge and temporal side of the orbit on the left side. A hard mass was palpable in this region. The left eye appeared displaced slightly forward and downward. Ocular motility was grossly...
unimpaired. Neither papilledema nor optic atrophy was evident. The retinal veins were full, especially those of the left eye. Visual acuity was 20/25, corrected, bilaterally. Exophthalmometer readings were 11 on the right and 12 to 13 on the left. The pupils were equal in size, and reacted promptly to light and accommodation. The peripheral fields of vision were normal. No pigmented areas were observed.

**Laboratory Data.** Blood and urine were normal. EEG disclosed a diminished alpha amplitude in the left temporal region. Roentgenograms of the skull revealed an eburnation and thickening of the roof of the left orbit as far back as the tuberculum sellae, the lesser wing of the sphenoid, and the reflection of the greater wing of the sphenoid on the lateral cranial vault. The edges of the thickened bone were smooth and the increase in density homogeneous (Figs. 5 and 6). These changes had resulted in a diminution in volume of the left orbit. Undoubtedly the skull changes long antedated the injury. Diagnosis: Sphenoid wing meningioma.

**Operation.** On Aug. 31, 1949 a local craniectomy was performed under endotracheal anesthesia. A semilunar incision was made in the left frontal region and the scalp reflected so as to gain access to the base of the anterior fossa. The entire orbital ridge on the left side and the most mesial portion of the ridge on the right side were involved by the lesion. The presenting abnormal tissue was removed piecemeal and the orbital plate exposed. This too was abnormal, as far back as the margin of the lesser wing of the sphenoid. The superior and lateral walls and the upper part of the medial wall of the orbit were removed in an attempt to eradicate the lesion, but probably a small amount was left behind close to the bridge of the nose. There was no evidence that the intradural contents were implicated by the pathologic process. The ethmoidal sinuses, which had been laid open on both sides, were covered both by gelfoam soaked in penicillin and a transplant of pericranium, after which the wound was closed.

**Histology.** The lesion was an admixture of fibrous tissue and trabeculae of bone.

*Fig. 7. Case 3. Very osseous phase of a fibro-osseous dysplastic lesion.*
Evidence of bone resorption was noted in the form of Howship’s lacunae filled with osteoclasts. In places there was osteoid tissue formation. The fibrous tissue was fairly cellular, its compactness varying. For the most part the fibroblasts were spindle-shaped with ovoid nuclei. Some had hyperchromatic pyknotic nuclei. No mitotic figures were noted. Throughout the fibrous tissue small vascular channels were prominent. Very few giant cells and lipid-laden macrophages were seen. The portion of cortical bone present showed a normal lamellar arrangement. The microscopic appearance of the tissue was that of a very osseous phase of a fibro-osseous dysplastic lesion (Fig. 7).

Course. Postoperatively the child noticed diplopia in all fields of gaze. A skeletal survey was done which failed to demonstrate involvement of other bones. He was readmitted on April 24, 1950 and the skull defect was repaired, utilizing a preformed stainless steel plate. The diplopia at this time had largely disappeared and the eyeball appeared to have receded.


History. A 25-year-old female was admitted Sept. 30, 1948 because of impairment of vision of the left eye. About a year prior to admission, during a routine physical examination, evidence of pressure on the left optic nerve had been found; skull films demonstrated a lesion involving the tuberculum sellae. She became aware of diminished visual acuity only about 6 months before admission. During this time visual failure had not been progressive. She presented no other symptoms. Her menses had begun at the age of 12 years and were normal. Her past history was negative.

Examination. The only significant findings involved the left eye. The left pupil was slightly larger than the right and reacted sluggishly to light. Funduscopic examination revealed a sharply outlined white optic nerve head, indicative of primary atrophy. Visual acuity on the right was normal; on the left it was reduced to finger counting at a distance of 1 ft. in the nasal field. Central and peripheral fields on the right were normal.

Laboratory Data. Blood count, urinalysis and blood chemical studies disclosed no abnormalities. EEG showed a normal pattern. Roentgenograms of the skull demonstrated a bony mass in the posterior medial part of the floor of both anterior fossae. This lesion was not uniformly opaque, its surface being distinctly denser than its inner portion (Fig. 8).

Operation. The nature of this mass was not altogether clear. On the assumption that it might represent a calcified meningioma, a right transfrontal craniotomy was performed under endotracheal anesthesia on Oct. 1, 1948. When the frontal lobe was retracted away from the floor of the anterior fossa, an extradural tumor arising

Fig. 8. Case 4. Bony mass in region of tuberculum sellae. The surface of the lesion is distinctly denser.
FIG. 9. Case 4. Newly formed bone is present in a matrix of fibrous tissue.

FIG. 10 (left). Case 4. Section showing immature bone, cartilaginous and fibrous tissue. FIG. 11 (right). Case 4. Area of hemorrhage showing presence of giant cells.
from the orbital plate in the region of the olfactory groove and extending back to
the anterior clinoid processes was exposed. It possessed a hard shell and contained
gritty material suggesting psammomatous tissue. To the surgeon it appeared more
than likely that the lesion was a calcified meningioma. A subtotal removal was
accomplished, sufficient in amount to decompress the optic nerves and chiasm.
The left optic nerve was found to be about half the size of the right one and grayish
in color. Although the operation presented no great difficulties, the patient expired
48 hours later.

**Histology.** Microscopic examination of the tissue revealed the presence of fibro-
blastic cells arranged for the most part in parallel rows, though occasionally there
was a suggestion of whorl formation. Scattered among these cells were numerous
areas of new bone formation in various stages of development, as well as islands of
cartilage. Osteoblasts were present around many of the new bone fragments. Giant
cells were noted where extravasation of blood had taken place (Figs. 9, 10 and 11).

**Case 5. A.J.** Deformity of skull in a 28-year-old male, resulting from exten-
sive fibrous dysplasia of cranium and face. Duration 21 years. Disease clin-
ically inactive.

**History.** A 28-year-old man was referred for an opinion in August 1949 as
to the nature of a mass in the right tem-
poral region. A lump had been present
in this area since the age of 7 years. It
had slowly become more prominent un-
til 5 or 6 years before admission, when
it had ceased to enlarge. A gradual dimin-
uation in hearing had taken place on
the involved side, beginning at the age
of 14 or 15 years. The patient was
reasonably sure that no further loss of
hearing had occurred in recent years.
He had on occasion experienced pain
during the winter months over the en-
tire right side of the face, but this symp-
tom had not recurred in the past 7 years.
No other complaints were elicited.

His past history was in no way un-
usual. The family history was note-
worthy in that his father had died of a hypernephroma and his mother was a
schizophrenic.

**Examination.** The most conspicuous finding was a hard, non-tender mass involv-
ing the right temporal region and zygoma. Hearing was grossly defective on the
right side, bone conduction being prolonged over air, and a tuning fork placed over
the forehead was lateralized to that side. It was the opinion of the otorhinolaryngol-
ogist that an air conduction deafness existed, caused by an obstruction of the ex-
ternal canal. There was no evidence of defective trigeminal function.

**Laboratory Data.** Blood and urine were normal. Blood serology was negative.
Sedimentation rate was slightly elevated, measuring 23 mm./hr. Blood chemical

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![Fig. 12. Case 5. Extreme degree of bony overgrowth involving vault and base of skull, and bones of face on right side.](image)
findings were cholesterol 184 mg. per cent; cholesterol esters 115 mg. per cent; total serum protein 7.25 gm./100 cc.; albumin 4.1 gm.; globulin 3.1 gm.; calcium 9.0 mg. per cent; phosphorus 4.0 mg. per cent; serum alkaline phosphatase 4.8 units (Bodansky u.); NPN 41.5 mg. per cent; uric acid 4.1 mg. per cent; glucose 1r mg. per cent.

A glucose tolerance test revealed subclinical diabetes mellitus; the blood sugar level rose to 242 mg. per cent at the end of 16 min. and failed to return to normal after 2 hr. B.M.R. was +3.

The entire skeleton was x-rayed but changes were observed only in the skull. These consisted of an intense hyperostosis involving the vault, zygoma, maxilla, petrous ridge, mastoid and supraorbital region on the right side. The frontotemporal region of the calvarium was thickened, its maximum width measuring 3.5 cm. An oval-shaped area of decreased density was visible within the hyperostosis near the surface of the bone in the anteroposterior projection (Fig. 12). Clinical impression: Fibrous dysplasia.

![Image](image_url)

**Fig. 13. Case 5. Biopsy specimen, showing fibro-osseous character of tissue.**

**Histology.** A biopsy was taken from the involved temporal bone. Sections showed fibrous tissue with large amounts of osseous tissue forming a typical pattern of fibrous dysplasia. About the bony trabeculae both osteoblastic and osteoclastic activity was noted. Howship's lacunae were in evidence, indicating active bone resorption. The cement lines of the trabeculae were fairly prominent, but the mosaic structure, characteristic of Paget's disease, was not observed. The fibrous tissue was compact, well vascularized and contained an abundance of spindle-shaped cells. Foci of lipoid-laden phagocytes were present. An occasional small spicule of primitive "coarse fiber bone" was seen (Fig. 13).

**COMMENT**

In a discussion of the paper by Pugh, Sosman stated that the one condition with which fibrous dysplasia of the cranium is most apt to be confused is a meningioma. He further added that at the time the original publication of Albright and his associates appeared, he had already collected 9 such cases.
referred to Cushing as possible meningiomas. That the two conditions may offer a real problem in differential diagnosis is borne out by our experience. This is particularly true of lesions that are relatively localized and involve the base of the skull. In our series the floor of the anterior fossa was frequently the site of the disease, leading to the suspicion of a meningioma in this region in 3 instances. The orbital plate, sphenoid ridge and tuberculum sellae were each thought to harbor such a growth. While the likelihood of a fibrodysplastic lesion may be suspected, it may not be possible to exclude a meningioma by any means short of operation. A most important differentiating clue is the age of the patient. Fibrous dysplasia usually manifests itself in a young person, often during childhood. Meningiomas, on the other hand, occur later in life. One wonders whether the case described recently by MacCarty and Gogela\textsuperscript{33} as a sphenoid ridge meningioma in a 12-year-old child was not actually one of fibrous dysplasia.

Cases in which there is extensive cranial involvement will ordinarily offer no problem in diagnosis. The associated deformity and dense bony deposits will readily identify the nature of the pathologic process. Nor should the differentiation between fibrous dysplasia and the hyperostosis associated with a meningioma be difficult when the vault is the site of the lesion. The bony reaction of a meningioma is circumscribed, and in contrast to fibrous dysplasia, which begins in the diploe, first affects the inner table, resulting in an enostosis. Localized increase in vascularity, characteristic of a meningioma but absent in fibrous dysplasia, is another distinguishing feature. The fact that meningiomas tend to originate at certain favorite sites and are associated with characteristic neurologic syndromes in specific locations may be of additional help. The examiner should keep in mind, moreover, the fact that extraskeletal manifestations, such as cutaneous pigmentation and sexual precocity, may accompany fibrous dysplasia. Furthermore, since the cranial manifestations may be part of a polyostotic process, in suspected cases the entire skeleton should be studied in search of other foci.

In addition to meningioma, there are several other entities which may cause confusion with fibrous dysplasia. Hyperparathyroidism should offer no problem in differential diagnosis since the appearance of the cranium is one of generalized demineralization, without hyperostoses. Moreover, the entire skeleton is involved in this condition, and blood chemical studies disclose characteristic alterations in the phosphorus and calcium levels. Paget’s disease usually occurs later in life and presents a fairly characteristic roentgen picture. The bones of the vault become diffusely thickened due to widening of the diploe and outer table, and develop a “cotton-wool” or “coarse moth-eaten” appearance. It is unusual for the area involved to be circumscribed. The base of the skull is commonly affected also. Windholz and Cutting\textsuperscript{35} observed changes in the facial bones only after the vault and base of the skull were already extensively involved. Lipoid granulomatosis should be readily distinguished by the presence of multiple defects of varying size occurring in the bones of the vault and base. Occasionally only a
solitary lesion is observed in this condition. Frequently similar changes may be demonstrated elsewhere in the skeletal system. Should diabetes insipidus and exophthalmos occur in conjunction with the skull defects, especially in a child, the diagnosis of Hand-Schüller-Christian disease is virtually assured. In doubtful cases a trial of radiation therapy should clarify the issue. Benign giant-cell tumors seldom involve the cranial bones. In the few reported cases the site of the tumor has usually been an intracartilaginous bone. According to Geschickter and Copeland,22 such growths produce a sharply outlined area of bone destruction.

Reference to the osteomas and their possible relationship to fibrous dysplasia has already been made elsewhere in this paper. The compact osteomas arise most often from the outer table, frequently in the frontal region. Roentgen examination reveals a well defined, round, homogeneous, dense shadow. The basilar sphenoidal and ethmoidal osteochondromas occurring in young adults may be recognized by their characteristic radiographic appearance. This consists of a combination of bony erosion and dense or flaky calcification. Their parasellar location often results in a neurologic picture indicative of involvement of this region. Other conditions that conceivably might bear a superficial resemblance to fibrous dysplasia are hemangioma of bone, metastatic malignancy, cholesteatoma and inflammatory disease. Their radiographic appearance is ordinarily sufficiently distinctive to establish their identity. Undoubtedly, at times, a biopsy and histologic examination will be required to establish the correct diagnosis.

With regard to clinical symptomatology, fibrous dysplasia affecting the skull may produce varying degrees of deformity. This may be relatively mild, being evident only as an asymmetry of the face or head, or extremely pronounced. Obstruction of the paranasal sinuses and lacrimal ducts may give rise to symptoms. Ocular manifestations are frequently encountered. These include deformity of the orbit, exophthalmos and displacement of the eye. Proptosis was noted in 3 of our patients, in one of whom the eye was, in addition, displaced downward. Ocular involvement has been reported by other observers. The occurrence of exophthalmos is mentioned, for example, in the reports of Albright, Scoville and Sulkowitch,4 Stauffer, Arbuckle and Aegerter,48 Falconer, Cope and Robb-Smith17 and Pugh.42 Eden13 states that the ossifying fibromas and fibrous osteomas may cause proptosis. Reference to osteitis fibrosa cystica as a cause of exophthalmos is also to be found in the ophthalmic literature (Pfeiffer,40 Reese43). Ocular depression has been reported by Etter and Hurst,15 by Sosman47 and by Schlumberger.46 Disturbance of extraocular motility was observed in the case of Stauffer and his associates. Visual impairment, manifested as optic atrophy in 1 of our patients, has been described by others too. Stauffer et al. observed early unilateral papilledema and a relative central scotoma in their case. A combination of papilledema in one eye and optic atrophy in the other, associated with a central scotoma on the side of the atrophy, was found in 1 of the 2 cases reported by Falconer, Cope and Robb-Smith. Examination of
their second patient disclosed bilateral optic atrophy and bitemporal hemianopic scotomas. Unilateral choked disc was found in 1 of the cases described by Furst and Shapiro.\textsuperscript{21} Ford\textsuperscript{18} mentions a case of osteitis fibrosa in a child, affecting the frontal bone and orbit, which was associated with exophthalmos and optic atrophy. Decompression of the orbit and optic foramen resulted in some improvement.

Hearing was affected and a history of facial pain elicited in 1 of our patients. Such symptoms are known to occur in leontiasis ossea which, as we have already indicated, is believed to be a manifestation of fibrous dysplasia in some cases at least. Kanavel\textsuperscript{28} collected 34 cases of leontiasis ossea, in 11 of which there was a history of neuralgic pains and in 4 of which hearing was impaired. The occurrence of headache, convulsions and mental impairment is also recorded. Mention is made by Oppenheim\textsuperscript{87} of a condition of “diffuse hyperostosis” occurring at an early age and characterized by an increase in the size of all cranial bones, in which a diminution in volume of the cranial fossae and orbits and narrowing of foramina may lead to blindness, deafness, exophthalmos, headache and dementia. Clearly the situation with regard to neurologic symptoms in fibrous dysplasia is analogous in many respects to that of Paget’s disease.

There is no specific treatment for fibrous dysplasia. Just as long bone involvement may require orthopedic treatment for the purpose of dealing with fractures and deformities, neurosurgical intervention may be necessary in cranial cases in order to provide symptomatic relief. Surgical measures will probably be indicated chiefly for the treatment of progressive exophthalmos and compression of the optic nerves and chiasm. Possibly cosmetic considerations may at times justify surgical therapy.

**SUMMARY**

The pathologic, clinical and radiographic aspects of fibrous dysplasia are reviewed, with special emphasis on cranial involvement. The probable relationship of this disease to leontiasis ossea and fibro-osseous tumors of the skull is discussed. Five cases of fibrous dysplasia of the skull observed by the authors are presented. Two were definitely of the monostotic variety and 3 presumably so.

Involvement of the skull is known to occur frequently in polyostotic fibrous dysplasia. At times, however, the skull appears to be exclusively affected by this disease. In cases with cranial involvement, particularly when the base of the skull is the site of the lesion, localized clinical symptoms may be present. Ocular manifestations are especially likely to be prominent.

Confusion may arise in distinguishing between localized fibrous dysplasia and the bony changes associated with a meningioma. One of the most valuable differential criteria is the age of the patient. Fibrous dysplasia is a disorder of childhood and adolescence. Meningiomas as a rule occur during adult life.

The etiology of fibrous dysplasia is unknown and there is no specific
treatment for it. Progressive exophthalmos and compression of cranial nerves may call for neurosurgical intervention.

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REFERENCES

FIBROUS DYSPLASIA OF THE SKULL

27. Jaffe, H. L. Personal communication.
32. Lichtenstein, L., and Jaffe, H. L. Fibrous dysplasia of bone. A condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of skin, premature sexual development, hyperthyroidism or still other extraskeletal abnormalities. Arch. Path., 1942, 33: 777–816.