Fibrous Dysplasia Involving the Skull Base and Temporal Bone

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Objective: To gain a broader appreciation of the clinical presentation, operative treatment, and outcome of patients with fibrous dysplasia involving the skull base.

Design: Retrospective review of a clinical case series.

Setting: A single tertiary academic medical center.

Patients: Twenty-one patients with histopathologically confirmed fibrous dysplasia involving the skull base cared for over a 15-year period (1983-1998).

Main Outcome Measures: Clinical and radiographic location of the fibrous dysplasia lesions within the skull base, clinical presentation, surgical intervention, and clinical outcome were tabulated for each patient.

Results: The ethmoids were most commonly involved (71%), followed by the sphenoid (43%), frontal (33%), maxilla (29%), temporal (24%), parietal (14%), and occipital (5%) bones. The most common presenting features included atypical facial pain and headache, complaints referable to the sinuses, proptosis and diplopia, hearing loss, and facial numbness. Surgical treatment, guided by clinical presentation, ranged from simple biopsy with conservative follow-up to craniofacial resection.

Conclusions: Fibrous dysplasia can present in myriad ways within the skull base. Modern imaging modalities and histopathologic analysis have made diagnosis relatively straightforward. Surgery, particularly in such a challenging region as the skull base, should be reserved for patients with functional impairment or a cosmetic deformity. Because of the benign nature of the condition, the surgery itself should be relatively conservative, with the primary goal being preservation of existing function.


FIBROUS DYSPLASIA is a localized disorder of bone characterized by abnormal proliferation of fibrous tissue interspersed with normal or immature bone, endocrine dysfunction, abnormal pigmentation, and precocious puberty in girls. The entity is not a new one. Although von Recklinghausen, a student of Virchow, is credited with the first accurate pathologic description of the disorder in 1891, characteristic lesions have been identified in prehistoric specimens and in a seventh-century Anglo-Saxon. McCune and Bruch and Albright and co-workers recognized in separate publications in 1937 the entity of osteodystrophia fibrosa disseminata, characterized by endocrinopathies, cutaneous hyperpigmentation, and precocious puberty in females. This severe form of fibrous dysplasia subsequently became known as the Albright triad or McCune-Albright syndrome. The terms fibrous dysplasia and polyostotic fibrous dysplasia were first suggested by Lichtenstein in 1938. Currently, 3 general subtypes of disease are recognized: monostotic, polyostotic, and McCune-Albright syndrome. The monostotic form is the mildest and most common form (approximately 70% of cases), is noted for lesions involving the ribs and craniofacial bones, and is typically diagnosed between ages 20 and 30 years. The incidence of the monostotic form may be even higher than the quoted figure of 70% because these lesions often remain asymptomatic. The polyostotic form (30% of cases) has an earlier onset, typically in childhood, and affected patients tend to have more severe skeletal and craniofacial involvement. The most severe form of the disorder, McCune-Albright syndrome (3% of cases), is more commonly found (although not exclusively) in females, is associated with short stature due to premature closure of the epiphyses, and is associated with endocrine abnormalities and pigmented cutaneous lesions. Although this classification scheme implies a related gradation of severity, the monostotic form is not believed to be a precursor to the...
MATERIALS AND METHODS

All patients with a diagnosis of fibrous dysplasia involving at least a portion of the cranial base in the past 13 years were retrospectively identified through reviews of clinical charts and computerized pathologic records at The Johns Hopkins Hospital. Clinical information was gathered from patient records and included age of onset and presenting symptoms and signs of the skull base lesion, treatment course, and clinical outcome for each patient. Radiologic scans, either computed tomography (CT) or magnetic resonance imaging (MRI), were obtained when possible; radiographic information was otherwise obtained from reports or notations in medical records. All patients had histopathologic confirmation of their diagnosis. Patients were not included in this series if adequate histories and relevant radiographic data, as outlined previously, could not be obtained. Several patients included in this series have been described previously as case reports.6,20

polyostotic form; there are no reports of transition from one to the other, and the two manifest different frequencies and severity toward spontaneous fractures, deformities, and long-term clinical behavior, leading to speculation that the 2 types are not as closely related as their histologic similarity suggests.8,9,10 This dispute of whether the 2 forms are gradations of the same process or distinct diseases with similar pathologic manifestations should in all likelihood be resolved once the genetics of the disorder are elucidated.

The precise etiology of fibrous dysplasia is currently unknown. In 1942, Lichtenstein and Jaffe11 proposed abnormal differentiation of mesenchyme as a cause of the bony abnormalities. In 1957, Changus12 proposed osteoblastic hyperplasia as the underlying pathologic process in fibrous dysplasia. Theories put forward in the 1960s regarding etiology also included arrest of bone at an immature woven stage and a disturbance of postnatal cancellous bone maintenance.13,14

More recent attempts to define the disorder have focused on its underlying genetics and molecular biology. Lee and coworkers15 proposed that abnormal intracellular regulation of cyclic adenosine monophosphate or protein kinase A is a possible etiologic factor in the development of fibrous dysplasia. Several other researchers9,10,16-18 have identified mutations in the Gs-α gene, resulting in altered activity of intrinsic GTPase activity or the Gs protein signal transduction pathway as a cause of fibrous dysplasia. It has thus been postulated that the pattern and distribution of fibrous dysplasia depends on which tissues contain the mutated Gs-α (GNAS1) gene and is in turn affected by such factors as genomic imprinting.19 During the next several years, as the underlying molecular biology of the disorder becomes elucidated, the true etiology of fibrous dysplasia will also be resolved.

Although fibrous dysplasia specifically involving the temporal bone has been described in several case reports and series, its impact on the broader skull base is not as well documented in the literature. In an effort to gain an improved appreciation for the clinical spectrum of this disorder, we performed a retrospective review of all patients with fibrous dysplasia involving the temporal bone and skull base evaluated at The Johns Hopkins University, Baltimore, Md, over a 15-year period (1983-1998). The clinical presentation, evaluation, and recommended treatment of the disorder in light of its benign nature are reviewed.

PATIENT DEMOGRAPHICS

A total of 21 patients were identified with fibrous dysplasia involving at least one aspect of the cranial base (Table 1 and Table 2). Average age at presentation was 22 years (range, 8-54 years). Thirteen patients were younger than 20 years at presentation. There was a 2:1 male-female ratio (14 males and 7 females).

Six patients were classified as having monostotic fibrous dysplasia based on involvement of only a single bone; these patients had an isolated skull base lesion without manifestations of fibrous dysplasia in the remainder of the body. Fifteen patients were classified as having polyostotic fibrous dysplasia because of involvement of multiple bones throughout the skull base or remainder of their body. Of the 15 patients with polyostotic disease, 2 (both males) were designated as having McCune-Albright syndrome based on associated systemic cutaneous and endocrine anomalies.

ANATOMIC LOCATION OF LESIONS

Anatomically, the most commonly involved area of the skull base was the ethmoid bone (71% of patients) (Tables 1 and 2). In only 1 patient was the ethmoid solely involved (Figure 1); the remaining patients with ethmoid disease had involvement of adjacent areas of the skull base.
including the sphenoid (most common), followed by the maxilla (Figure 2) and frontal (Figure 3) bones. The next most common area of skull base involvement was the sphenoid bone (43%), followed by the frontal bone (33%) (Figure 4) and maxilla (29%). Similarly, no patient presented with isolated maxillary disease; all had at least some radiographic involvement of the ethmoids. Taking into account all bones making up the sinus cavities, overall the sinus bases were involved in 17 (81%) of 21 patients.

Five patients had fibrous dysplasia involving the temporal bones: 2 were totally asymptomatic from their temporal bone lesions and had radiographic involvement only (Figure 5), 1 had McCune-Albright syndrome with widespread skull base involvement, and 1 had polyostotic disease with primarily frontal sinus symptoms. Of the 3 patients with symptomatic temporal bone involvement, 2 had true monostotic forms of fibrous dysplasia, with the temporal bone lesion being the only manifestation of the disease in the body (Figure 6). The third patient had McCune-Albright syndrome and widespread skull base involvement (Figure 7).

Three patients presented with parietal skull involvement: 1 with monostotic disease had an isolated bony lesion in the parietal skull and the 2 other with parietal involvement had widespread involvement of the entire base of the skull (Figure 7 and Figure 8). Similarly, the patient with occipital bone involvement had widespread disease throughout the skull base (Figure 7).
CLINICAL FEATURES

The most common complaint at presentation was atypical facial pain or headache (57%), followed by sinus congestion or infection that was initially interpreted as sinusitis (43%) (Tables 1 and 2). Orbital involvement, manifested as proptosis, diplopia, or visual changes, was identified in 43% of patients. The presence of an expanding facial or skull mass led to the diagnosis in 24% of patients. Hearing loss and facial numbness were identified as presenting symptoms in 2 patients each (10%).

All patients underwent some form of surgical biopsy or excision for diagnosis. Of patients with extensive sinus involvement (ethmoid, frontal, maxillary, and sphenoid), surgery was performed to relieve diplopia or proptosis resulting from impingement on orbital contents in 5 (patients 5, 6, 10, 11, 18 in Table 2). In all 5 patients, surgery was performed via an external ethmoidectomy or lateral rhinotomy–type approach. One of these patients also required facial degloving and craniofacial resection for extensive orbital rim involvement. The symptoms of proptosis were improved in 4 of the 5 patients and stabilized during follow-up. Of the 6 patients with maxillary sinus involvement (patients 4, 5, 10, 15, 17, and 19 in Table 2), 2 underwent a medial maxillectomy and 3 underwent limited transantral resection of the disease. Another patient with McCune-Albright syndrome and widespread skull base disease and a large aneurysmal bone cyst involving the frontal sinuses (Figure 4), impinging on the frontal lobe, required a cranioplasty with cystoethmoidostomy and pericranial closure of the defect.

Of the 5 patients with temporal bone involvement (patients 1, 4, 7, 12, and 21 in Table 2), 3 required surgical intervention due to the temporal bone disease. Two of these patients had lesions that were primarily manifest as external auditory canal stenosis (patients 1 and 7). These 2 patients underwent canalplasty, metaplasty, and placement of Silastic stents in the external auditory canal with subsequent periodic curettage, which has controlled the canal stenosis for the 17 to 30 years they have been followed up. One of these was a patient with McCune-Albright syndrome with a previous history of bilateral radical mastoidectomies 20 years previously. The third patient had a large cystic lesion expanding into the middle cranial fossa and, because of concern for the presence of a neoplastic lesion, underwent a middle fossa approach for diagnosis and excision of the lesion (patient 12 in Figure 6). The lesion has not recurred during 10-year follow-up.

Of the 3 patients with parietal skull involvement (patients 2-4 in Table 2), only 1 presented undiagnosed with a solitary lesion. This patient underwent surgical biopsy and excision and did well, with no recurrence in the subsequent 13 years. The other 2 patients did not require surgical intervention as a result of their parietal lesions and have been managed conservatively by observation.

COMMENT

This clinical series demonstrates the numerous ways in which fibrous dysplasia involving the skull base can present. In many respects, the series differs from previous reports on fibrous dysplasia. Determining the true incidence of fibrous dysplasia, particularly for the more prevalent monostotic form, is difficult because many patients are asymptomatic and are often diagnosed incidentally after radiographic evaluation for other reasons.
Onset is typically in adolescence or late childhood, although more severe forms can arise in infancy. Average age at presentation in this study was 22 years, and the median age was 17 years. Whereas both monostotic and polyostotic forms occur with equal frequency in males and females, McCune-Albright syndrome has a clear female predilection. It is therefore somewhat unusual that there was a 2:1 male-female ratio in this series and that both patients with McCune-Albright syndrome in this study were male. However, the high percentage of children in this series may account for the male predilection we identified; as Spjut and coworkers noted, among young adults, more males than females are affected.

The relative numbers of patients with monostotic vs polyostotic disease in this study are also different than those reported in the general fibrous dysplasia literature, where the polyostotic form typically represents only about one third of patients. In this study, 6 patients were classified as having monostotic fibrous dysplasia and 15 had the polyostotic form. This difference is probably due to the focus on skull base disease in this study. The craniofacial bones are typically involved in approximately 10% of patients with the monostotic form and in 50% with the polyostotic form, although in severe polyostotic cases, craniofacial involvement can approach 100%. This difference is probably due to the focus on skull base disease in this study. The craniofacial bones are typically involved in approximately 10% of patients with the monostotic form and in 50% with the polyostotic form, although in severe polyostotic cases, craniofacial involvement can approach 100%.

Thus, the inclusion of only patients with skull base disease would account for the higher number of patients with the polyostotic form seen in this study.

This study also differs from previous studies with regard to the location of fibrous dysplasia lesions involving the skull base. Van Tillburg analyzed skull lesions from 144 patients identified in the literature and noted that the frontal bones were most commonly involved, followed by the sphenoid, ethmoid, parietal, temporal, and occipital bones. This is in contrast to our findings, which identified the ethmoid as the most commonly involved bone, followed by the sphenoid, frontal, maxilla, temporal, parietal, and occipital bones. This difference can probably account for the higher number of patients with the polyostotic form seen in this study.

This 40-year-old man with a history of severe polyostotic fibrous dysplasia presented with an expanding mass of his left frontal bone after mild head trauma. The patient complained of a bulging left eye, made worse by manually compressing the mass. On examination, compression of the obvious frontal mass caused increased proptosis. The patient underwent left frontal craniotomy, cyst drainage, cystoethmoidectomy, and closure with a pericranial flap, which resulted in alleviation of the proptosis and flattening of the forehead deformity. A follow-up scan 2 years after the drainage procedure demonstrated no change in size of the decompressed cystic mass, and the patient remained asymptomatic with regard to the lesion. This patient has been described previously by Wojno and McCarthy.

Figure 3. Axial computed tomographic scan of a patient with fibrous dysplasia involving the frontal (A) and ethmoid and sphenoid bones (B).

Figure 4. Axial computed tomographic scan of a large 5-cm extra-axial fibrous dysplasia aneurysmal bone cyst of the frontal bone (arrow). In addition, the calvarium is diffusely thickened with a heterogeneous, "ground-glass" appearance, consistent with fibrous dysplasia.
be most readily attributable to improved radiographic diagnosis using CT and MRI (the study by Van Tillburg was published in 1972, before our current standard imaging modalities). These newer modalities are not only able to identify asymptomatic involved areas of the skull base with improved accuracy, they are also superior at diagnosing ethmoid and sphenoid lesions compared with plain radiographs. Consequently, the anatomic breakdown offered here is probably more accurate than in studies before the inclusion of CT or MRI analysis.

Clinically, atypical facial pain and headache were the most common presenting features, followed by symptoms suggestive of sinusitis. This is not surprising given the overwhelming number of patients in the study who presented with fibrous dysplasia involving the sinuses (81%). The fact that 9 of 21 patients also had visual changes, including proptosis and diplopia, also relates to the preponderance of ethmoid, sphenoid, and frontal bone involvement in many patients. Through progressive enlargement, the lesions most commonly cause symptoms in the orbit by pressure and displacement of orbital contents. Facial numbness was noted in 2 patients at presentation, both of whom had maxillary lesions, with the dysethesia due to involvement of the infraorbital nerve.

Of the 5 patients with temporal bone involvement, only 3 were symptomatic at presentation; 2 patients had only radiographic involvement. Two of the symptomatic patients had conductive hearing loss related to external auditory canal stenosis, and the third had headaches. These are typical presenting symptoms of fibrous dysplasia involving the skull base that have been noted by other authors. 34

Three classic radiologic findings of fibrous dysplasia are described: pagetoid, sclerotic, and myxoid. 30 However, these classic radiographic descriptions are based on plain films, which have little relevance with the nearly universal access to modern imaging techniques such as CT and MRI. In this series spanning the past 15 years, plain films played no role in the diagnosis, management, or follow-up of any patients. Computed tomography is the study of choice for diagnosis and follow-up because of its superior bony detail and accurate assessment of the extent of the lesion. Furthermore, CT can often assist with differentiating fibrous dysplasia from other osteodystrophies of the skull base, including otosclerosis, osteogenesis imperfecta, Paget disease, and osteopetrosis. 25 Distinguishing features of fibrous dysplasia on CT include (in order of significance) "ground-glass" appearance, symmetry, involvement of the paranasal sinuses, thickness of the cranial cortices, involvement of the sphenoid bone, orbital involvement, nasal cavity involvement, presence of a soft tissue mass, maxillary involvement, and the presence of cystlike changes (Figures 1-8, Figure 9). 26 There is often a clear margin between affected and unaffected bone. Aneurysmal bone cyst formation is also readily apparent on CT. These lesions appear cystic with a bony shell, with either a fluid or soft tissue–appearing center (Figures 2, 5, 6, and 9). Magnetic resonance imaging is an additional useful modality that can help distinguish fibrous dysplasia from meningioma, osteoma, or mucocele and define the extent of soft tissue involvement, particularly if central nervous system structures are impinged on. Lesions are typically low to isointense on T1- and T2-weighted im-

Figure 5. Axial computed tomographic scan of an extensive fibrous dysplasia lesion involving the sphenoid and temporal bones (arrows). The patient presented with symptoms of orbital compression and proptosis. There were no symptoms related to the temporal bone involvement.

Figure 6. Axial computed tomographic scan demonstrating an aneurysmal bone cyst of the temporal bone (arrow). The patient underwent a right middle cranial fossa approach for biopsy of the lesion, and diagnosis of fibrous dysplasia was made histopathologically.
ages and show moderate to marked enhancement with gadolinium (Figures 8 and 9). Fibrous dysplasia within the skull base is frequently complicated by aneurysmal bone cyst formation (Figures 2, 5, 6, and 9). In the present series, bone cyst formation occurred in 5 patients (24%). Clinically, this entity can often be confused with a malignant lesion. This was the case with a patient in this study with a large cystic lesion expanding into the middle cranial fossa who underwent a middle fossa approach for diagnosis (Figure 6). Although the development of aneurysmal bone cysts is a well-
known occurrence throughout the skeletal system, they have not been frequently described within the skull base. As this study demonstrates, an aneurysmal bone cyst is a lesion that is frequently seen in patients who have fibrous dysplasia of the skull base. However, in contrast to its formation in the long bones throughout the body, because of the confined space within the base of the skull, their expansion can quickly lead to clinical symptoms, with increased morbidity. All 5 patients in this series with aneurysmal bone cyst formation required surgery because of the expansile nature of the lesion. Fibrous dysplasia is thought to be particularly susceptible to bone cyst formation because of the vascularity of the lesion. Radiographically, the lesions appear as expansive cystic lesions with a bony shell, with either a fluid or soft tissue–appearing center.

Pathologically, fibrous dysplasia lesions are characterized by expansion of cortical bone with gradual replacement by fibrous tissue that is firm, rubbery, and gritty. Lesions within the skull tend to have a firmer consistency than their counterparts in the long bones of the body due to a greater amount of bony spicules. Cystic lesions can often be filled with an amber fluid and can occasionally be vascular. Microscopically, the lesion is readily identifiable, with an irregular trabeculae of woven bone intermixed with a connective tissue stroma. Lesions will vary in the amount and distribution of bone and in the cellularity and vascularity of the fibrous stroma.

Within the skull base, a known variant of this classic pathologic picture is a distinct histologic pattern of “cementicles,” small bony spicules resembling pieces of a puzzle, interspersed throughout the lesion (Figure 10). These lesions are characterized by a loose fibrous background and darkly stained cemented ossicles surrounded by reactive bone. Although these lesions, referred to within the literature with such diverse terms as ossifying fibroma and cementifying fibroma, present with subtle clinical, radiographic, and histologic differences, we have traditionally regarded these differences as slight variations of the same underlying pathologic process. Although some pharmacologic agents exist for treating patients with osteodystrophies, their effects have been limited in patients with fibrous dysplasia. These medications include bisphosphonates, which inhibit osteoclastic bone resorption. Other medications, such as aromatase inhibitors (ie, testolactone) and tamoxifen citrate have proven successful in the treatment of precocious puberty in patients with McCune-Albright syndrome.

In the absence of curative medicine for fibrous dysplasia, surgery remains the mainstay of therapy. However, it must be remembered that fibrous dysplasia is a benign process, and therapy should be guided by the patient’s clinical presentation. As such, lesions discovered incidentally and that are asymptomatic may be followed conservatively by serial CT or MRI scans. More often, however, the surgeon is faced with a lesion and without a diagnosis. If a lesion cannot be readily classified by radiologic studies, open biopsy and surgical excision are warranted. If a fibrous dysplasia lesion is suspected and surgery is determined to be the most appropriate course of action, complete extirpation of the lesion may not be required, particularly if important or vital structures (such as cranial nerves or the carotid artery) are placed at risk. In this scenario, subtotal resection with close follow-up is often adequate to control the clinical symptoms. Radiation therapy is ineffective and contraindicated because of the possibility of malignant transformation.

Lesions involving the sinuses can range from a small isolated lesion of the ethmoid or maxilla to massive lesions causing frontal lobe compression. Most lesions can be approached anteriorly, either endoscopically or via a more traditional transfacial approach. Small, isolated lesions of the sinuses, such as in patient 3 in this study, who presented with an isolated lesion of the ethmoid, can be approached endoscopically. Because symptoms are mainly due to compression of adjacent structures, marsupialization and subtotal resection are often adequate to control symptoms in these limited cases. The diagnosis is often not made until after the operation, however, when the pathology report is reviewed. If a subtotal resection was performed in these cases, patients can often be watched conservatively with serial scans and with a planned return to the operating room should the patient’s symptoms recur.

Fibrous dysplasia involving the temporal bones has been well documented in the literature. With tem-
poral bone involvement, the primary indications for surgery are canal stenosis leading to hearing loss, as seen in 2 patients in this study, and the presence of a cholesteatoma behind a stenotic external auditory canal. During canaloplasty, diseased bone is typically spongy, soft, and easily shelled out by curette. Recurrence is likely, however, with approximately half of all patients requiring 2 or more operations. Placement of a simple Silastic stent can often assist with keeping a canal open between outpatient curettage treatments, as was done in both patients in this study. Another option to prevent restenosis of the external canal is skin grafting. Sensorineural hearing loss secondary to impingement on the acoustic nerve within the internal auditory canal is a well-described feature in advanced cases. There have been cases of reversal of the loss after decompression of the internal auditory canal.

Other lesions of the skull base, such as of the parietal or occipital bones, should also be treated according to the patient's presentation. Nonsymptomatic lesions that are not cosmetically disfiguring can be watched conservatively. As solitary lesions expand and compress intracranial structures, such as with aneurysmal bone cyst formation, they may require operative intervention. In patients with widespread skull base involvement, where the occipital and parietal skull is involved, the diagnosis is clear and lesions can often be followed conservatively for years. A common scenario, however, was as seen in one patient in this study (patient 12 in Table 2), where a patient presents with a solitary unknown lesion and undergoes an operative biopsy and excision. Although this patient underwent complete excision of the lesion, even if a subtotal resection has been performed, a patient can usually be conservatively followed for years with serial scans and close attention to recurrence of symptoms.

In summary, fibrous dysplasia involving the skull base can present in myriad ways. Modern imaging modalities and histopathologic analysis have made diagnosis relatively straightforward. Surgery, particularly in a challenging region such as the skull base, should be reserved for patients with functional impairment or a cosmetic deformity. Because of the benign nature of the condition, the surgery itself should be relatively conservative, with the primary goal being preservation of existing function.

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