BONE TUMORS

Diagnosis, Treatment and Prognosis

ANDREW G. HUVOS, M.D.

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PREFACE

"Few books today are forgivable," says R. D. Laing, and this one may not be an exception. It is written about a relatively obscure but important subject in which a few are interested and even fewer care to master.

This book is intended to be authoritative but not authoritarian, balanced and lucid, reflecting my inherently conservative philosophy influenced by the teachings and long-term association with Dr. Henry L. Jaffe, who stimulated my interest in the diseases of bone. This interest was fostered by many former and present colleagues at Memorial Hospital for Cancer and Allied Diseases who pioneered the diagnosis and treatment of bone tumors not only as a science but also as an art. Among these, Dr. Ralph C. Marcove should be especially mentioned for his infectious enthusiasm and many original ideas.

I should like to acknowledge the cooperation of several people in the writing of this book. Dr. Norman L. Higinbotham gave me ready access to his files, a treasure-trove of clinical and pathological information, which were of great help to me. Particular appreciation is due to the many members of the Medical Illustration Department at Memorial Hospital for Cancer and Allied Diseases for the preparation of illustrative material and reproduction of the many radiographs. Miss Lynn B. McDowell, M.A., deserves special thanks for designing the innovative skeletons and age and sex distribution prototypes and for making me aware of the importance of good visuals. Mr. George C. Vilk, Associate Medical Editor, and the staff at W. B. Saunders Company were most helpful during the production of this book.

My wife, Phyllis, patiently typed and meticulously prepared the entire manuscript from the very beginning to the end, in addition to offering innumerable helpful suggestions for improving it. Without her help and untiring efforts this book would never have been completed. My gratitude to her cannot be totally expressed.

ANDREW G. HUVOS

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1

OSTEOMA AND GARDNER'S SYNDROME

OSTEOMA

DEFINITION

Osteomas are benign bone lesions characterized by bony excrescences usually arising in membranous bones.

They are benign lesions in which a major component is mature, lamellar, or woven bone. They are well-circumscribed and localized and appear to be sessile or pedunculated with expansile, not infiltrative, borders. Smooth or lobulated surfaces and peripheral resorption of normal bone are demonstrated by these lesions.

SYNONYMS

The extensive literature on this subject loosely employs the term "osteoma" to cover a wide variety of osseous lesions, some of which are clearly nonneoplastic but are of traumatic origin. Included in these categories are old osteochondromas with eburnated cartilaginous caps, traumatic and inflammatory bony protuberances, examples of hyperostosis frontalis interna, and monostotic fibrous dysplasia involving the skull, as well as hyperostotic lesions of the calvarium.

HISTORICAL ASPECTS

There are clear-cut examples of osteomas from ancient times. A fine example of an ivory osteoma has been demonstrated on the right side of an Egyptian skull of Roman vintage. Seventeen skull osteomas found in Neolithic Anglo-Saxon graves have been described by Brothwell.[4] Thirteen examples of skull "button osteomas" have been encountered in Indians of the Pecos Pueblo.[13] A pre-Columbian skull found in Ancon, Peru, shows an osteoma occurring in the left orbit. The often discussed "exostosis" of the femur of the *Pithecanthropus erectus* most likely represents a post-traumatic periosteal myositis ossificans.[9]

INCIDENCE

Since many osteomas are asymptomatic, their true prevalence is not known. In 1941, Teed collected 321 cases from the

pertinent literature between 1886 and 1939 involving the frontal sinuses.[35] Childrey noted 15 cases among 3510 (0.42 per cent) largely asymptomatic patients with paranasal sinus roentgenograms. Data from Finland[34] and West Germany[31] vary from 0.1 to 1 per cent of the patients examined in larger otolaryngology clinics.

The most frequent involvement of the frontal sinus among the paranasal sinuses has been confirmed by other, larger studies as well.

SIGNS AND SYMPTOMS

Most osteomas present as a painless, slowly enlarging, hard lump noticed by the patient for at least two years. The lesion's bulk and pressure produce headaches, facial asymmetry, and difficulty in nasal breathing. Patients with large osteomas of the orbit may present with ophthalmic complaints, such as exophthalmos, blindness, or even pneumoencephalos in association with a frontoethmoidal localization. In a review of 21 patients treated in Oxford, England, the cranial vault lesions were asymptomatic and were removed for cosmesis only. Among the 14 nasal sinus tumors, the left frontal sinus presentation (10 instances) was most common, with symptoms of frontal headaches, bulging of the eyes, recurrent sinusitis, and visual alterations.[6]

Some of these lesions cause severe debilitating symptoms, as in the patient reported by Hudolin et al. who had a large frontal sinus osteoma that extended into the cranial fossa and caused mental deterioration, headaches, incontinence, epileptic seizures, and habitual alcoholism.[14] Large osteomas of the mandible may cause bizarre defects in vision and balance by their close proximity to the carotid sinus and internal carotid artery.[19]

LOCATION, AGE, AND SEX DISTRIBUTION

Lautenbach from the University Dental Clinic in Bonn, Germany, reports 36 cases equally distributed in the maxilla and the mandible. A 3:1 female to male ratio was noted. Ages varied from 16 to 74 years, with the sixth decade of life having the most lesions. Histologic examination of the 36 lesions revealed 22 compact, 8 mixed spongy and compact, and 6 spongy types.[16]

The presence of multiple osteomas should arouse the suspicion of an associated Gardner's syndrome, although cases have been reported in which multiple osteomas occurred in the absence of this syndrome complex.[19]

HISTOGENESIS

There is considerable doubt and controversy about the exact derivation of this lesion. Lichtenstein regards osteomas, like osteoid osteomas, as a special type of benign osteoblastoma, i.e., related benign tumor entities of osteoblastic derivation.[18] Aegerter and Kirkpatrick describe these lesions as hamartomas of the periosteum; they believe that the lesion is always formed by intramembranous ossification

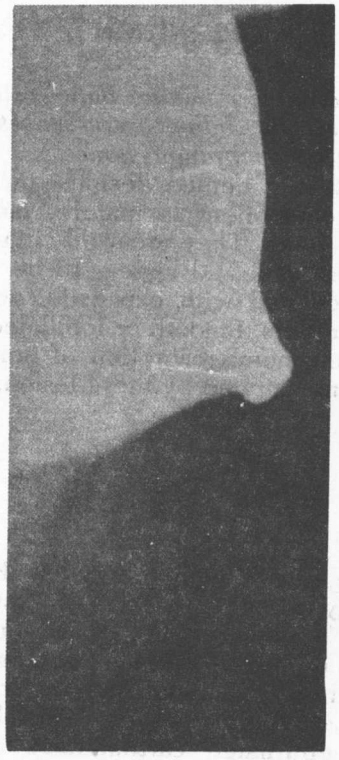

Figure 1–1. Osteoma of the occipital bone in a 34-year-old man. No history of trauma.

that represents only a simple exaggeration of a normal physiologic process.[1] Similarly, Vinogradova considers osteomas to be developmental anomalies of bone but not true tumors.[37] According to Jaffe, this lesion may represent the terminal, ossified stage of a fibrous dysplasia.[15] Smith and Zavaleta[33] and Reed and Hagy[28] believe that ossifying fibromas may differentiate into more mature osteomas.

Some of the skull lesions classified as osteomas may in fact be a reaction to a low grade inflammatory process with subsequent progressive osseous reparative reaction (Fig. 1–1). Based on study of three sequential biopsies, a case of Garré's sclerosing osteomyelitis was diagnosed in its final form clinically, radiographically, and microscopically as an osteoma.[28]

Animal Studies

Long-term multigeneration studies in CF-1 mice regularly found the incidence of spontaneous osteomas to be approximately 10 per cent, the skull being involved in about 90 per cent of this minimally inbred strain, over a period of six consecutive generations.[7a]

Osteomas in mice may also be induced by injection of the RFB osteoma virus of CF-1 mice. These periosteally located exostoses occur two to three months following the injection of the murine virus into the newborn. A rapid growth spurt can be observed in these osteomas for a few weeks, as many as 36 have been seen in a single rodent, after which the lesions increase only slowly in size.[10] This osteoma-producing virus (RFB) is distinct from the osteosarcoma virus (FBJ).

HISTOLOGIC STUDIES

Compact or Ivory Osteoma

Compact or ivory osteoma (ivory exostosis) consists of dense, compact, mature lamellar bone (Fig. 1–2). The periphery of these lesions shows interanastomosing trabeculae of mature cancellous bone. The periosteal surface of the compact osteoma exhibits layers of lamellar bone without attempt at remodeling. In the deeper portions of this lesion, a coarse mosaic pattern of the lamellar bone is present. No attempt at haversian system formation is made, and only occasionally can one encounter marrow spaces (Fig. 1–3). It seems that the original haversian systems of the central portion of the lesions became obliterated and the osteocytes degenerated.

Trabecular or Spongy Osteoma

The trabecular or spongy osteoma may be central (endosteal) or peripheral (subperiosteal) in its location. Histologically, they reveal a chiefly cancellous, trabecular

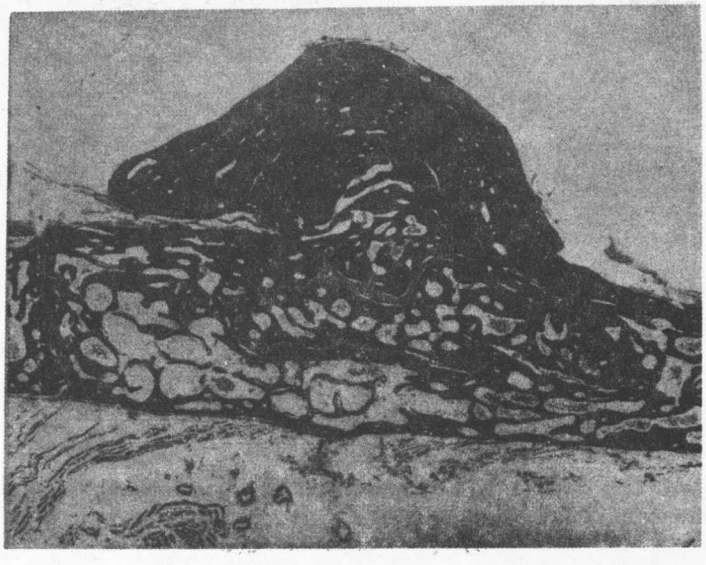

Figure 1–2. Compact, or ivory, osteoma (also known as ivory exostosis) represents a protuberance on the surface of a membrane type of bone without evidence of a cartilage cap. (Hematoxylin-eosin stain. Magnification ×4.)

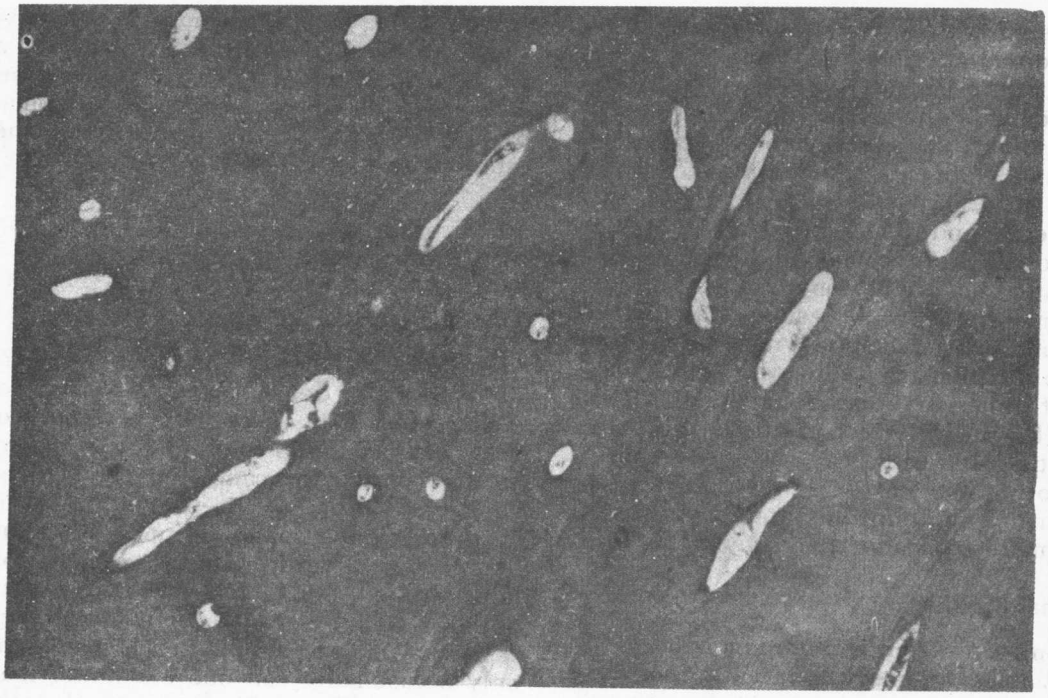

Figure 1–3. Ivory osteoma showing densely compact mature lamellar bone without marrow spaces. (Hematoxylin-eosin stain. Magnification × 50.)

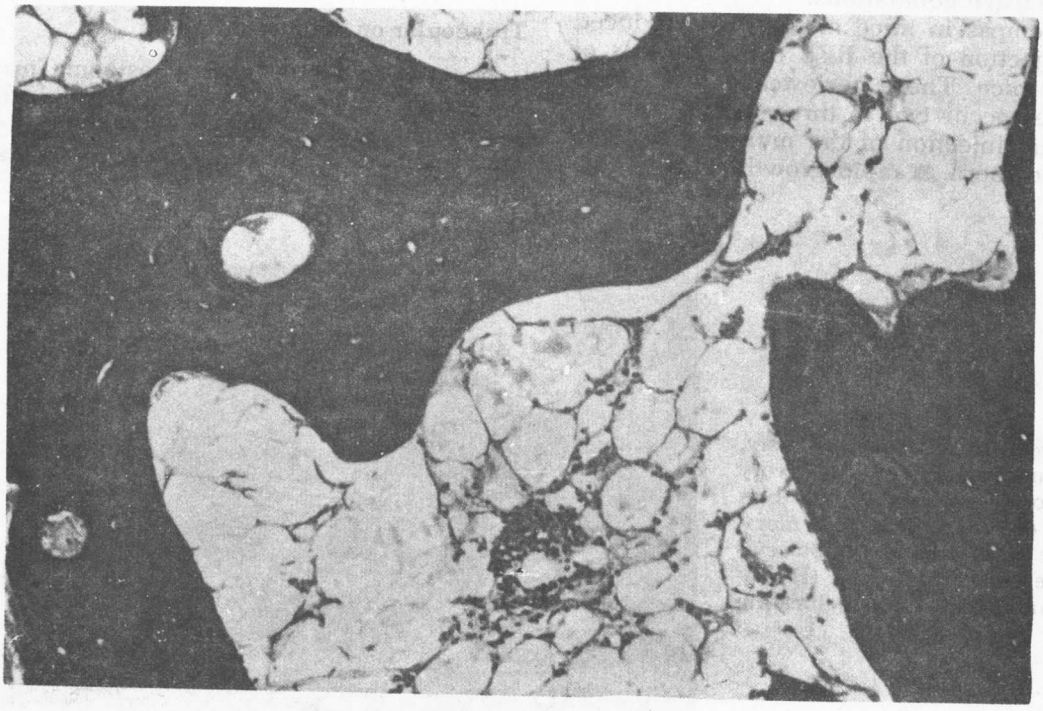

Figure 1–4.. Trabecular osteoma with cancellous bony architecture and fatty marrow. (Hematoxylin-eosin stain. Magnification × 50.)

architecture with peripheral cortical bony margin (Fig. 1–4). The trabeculae are thin with fatty marrow present in the intertrabecular spaces. Radiographically, the subperiosteal, or peripheral, osteoma presents as a dense radiopaque lesion protruding from the surface of the bone. The central, or endosteal, type appears as a well-delineated sclerotic mass with clear outlines and smooth borders. No destruction of adjacent bone is noted.

The so-called cancellous osteoma of the long bones referred to in earlier literature is now considered to be an osteochondroma (osteocartilaginous exostosis) in which the cartilaginous cap is eburnated and replaced by fibrous tissue following the cessation of skeletal maturation. Occasionally, osteoma diagnosed as such may represent the final complete ossification of an osteochondroma.

TREATMENT

Treatment consists of surgical excision if the lesion is symptomatic and painful. Large lesions should also be removed for diagnostic purposes, and complete removal yields curative recurrence-free results. Otherwise, no treatment is necessary.

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GARDNER'S SYNDROME

Gardner's syndrome consists of the tetrad of abnormal growths: intestinal polyposis involving the small and large bowel, osteomas, fibromas of the soft tissues, and sebaceous cysts of the skin. This was described in a single Utah family group during the period 1950 to 1953.[14, 15, 27] Although it was Gardner and his coworkers who, in the 1950's, first postulated a mendelian dominant role of predictable inheritance of a single defective gene for the tetrad of physical characteristics of this syndrome, there were several cases with similar attributes reported as early as 1912.[3, 10] These studies firmly established the various associated traits as a definite genetic entity and demonstrated that this syndrome is inherited as an autosomal mendelian dominant disorder with the pleiotropic effects of a single mutant gene, as well as additional heterogeneity in hereditary polyposis.[26] Several separate, but

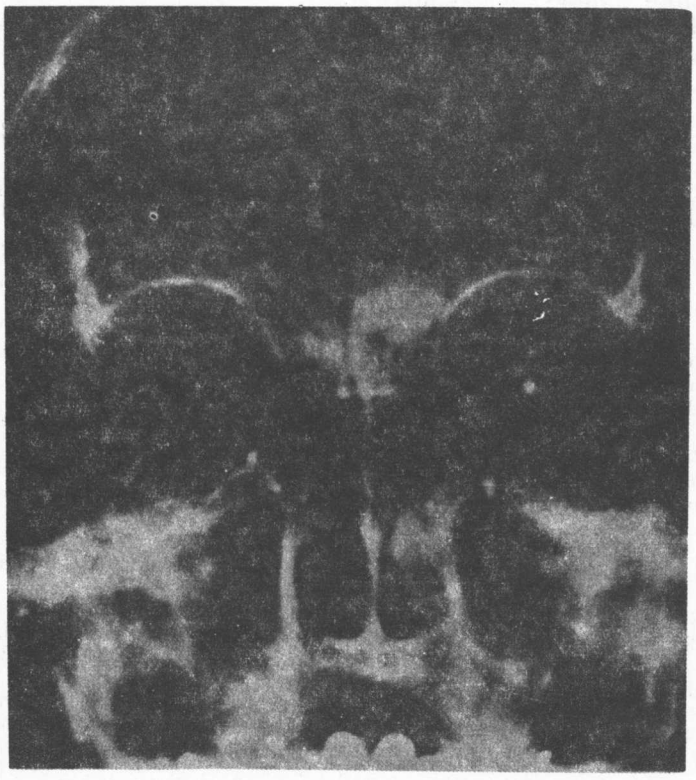

Figure 1–5. Bilateral frontal sinus osteomas in a 62-year-old woman with Gardner's syndrome.

closely linked, defective genes may also account for this syndrome. Fibrosarcoma, dental abnormalities characterized by supernumerary and unerupted teeth, and carcinoma of the ampulla of Vater, as well as thyroid carcinoma, have since been described in association with this syndrome.[2, 12, 13, 16]

Less than 10 per cent of all patients exhibit the complete tetrad of skin and soft tissue lesions with bone tumors and intestinal polyps. About 45 per cent of the patients at risk display some or all aspects of the symptoms. In a survey of 280 patients with this syndrome, 40 (14 per cent) showed bone abnormalities.[5, 35] The multiple and solitary osteomas so characteristic of this disease appear most frequently in the frontal bone (Fig. 1–5). The mandible, maxilla, sphenoid, ethmoid, zygoma, and temporal bones, in descending order of frequency, are involved. Other bones of the appendicular skeleton, usually femur or fibula, can also be affected. It is important to remember that the bony tumors usually precede the other manifestations and continue to develop regardless of any other lesion. In addition to the osteomas, localized cortical thickening of long and short tubular bones, reminiscent of Leri's melorheostosis, are also present with abnormal tubulation.[28, 29] In none of the cases reported in the literature could a malignant transformation in the benign bony lesions be established. A case of osteogenic sarcoma occurring in a 15-year-old girl, a member of a family with Gardner's syndrome,[5, 35] and an instance of chondrosarcoma of the hyoid bone also associated with this syndrome have been reported.[17] A familial sarcoma of bone arising in the tibia of the mother and in the femur of her 13-year-old son has been described in a polyposis coli family.[19] The clinical significance of the progressive (size and number) intestinal polyps lies in the fact that practically all patients with untreated colonic polyposis will indeed develop carcinoma. Since some of the cancers are multiple in the colon or rectum and are detected only in advanced stages, the crude survival rate is about 27 per cent.

Danes has done extensive genetic studies on Gardner's syndrome and found that when only the classic clinical methods of study are employed, this syndrome is rarely diagnosed before the age of 30 years, which is generally too late for useful genetic counselling.[6, 7, 8] Using skin fibroblast markers in tissue cultures of affected individuals and certain family members, 11 to 31 per cent heteroploidy was noted; in contradistinction, fibroblasts obtained from skin biopsies of those with familial polyposis showed only up to 1 per cent heteroploidy. Since this marker is present in individuals at risk before the syndrome is clinically diagnosable, an earlier detection of the affliction is feasible, making effective genetic counselling a stronger reality. The lack of fibroblast markers in patients with familial polyposis strengthens the thesis that Gardner's syndrome is a truly separate and distinct entity.[6, 7, 8]

Bone Abnormalities in Gardner's Syndrome

There are various bony proliferations (osteomatosis) varying from slight, localized, occasionally wavy thickening to large protuberant masses. In their analysis of the roentgenologic features of the bony abnormalities, Chang and his associates found that the character of these lesions depended on the location and the type of bone.[5]

Osteomas of the skull are of two major types: (1) Those that arise from the inner or outer tables are protuberant, frequently have a broad base, and present as a lump. These lesions are best detected in somewhat underexposed tangential roentgenograms. (2) Those that appear next to the paranasal sinuses are without corresponding lumps on the facial surface. Special tomographic views are often necessary to appreciate these lesions.

The most characteristic bone lesion appears to be a protuberant, dense, lobulated osteoma involving the cortex of the mandibular angle. Central enostoses, irregularly eburnated lesions next to teeth also showing other dental abnormalities, were often noted.

Whenever an examining physician or dentist discovers any bony or soft tissue stigmata of a presumed Gardner's syndrome, he is obligated to refer the patient for proctosigmoidoscopy and roentgenographic barium enema to exclude the asymptomatic presence of familial intestinal polyposis. It is also suggested that other members of the family be examined.

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2

OSSIFYING FIBROMA

DEFINITION

Ossifying fibroma is a gradually expansile, well-marginated, often asymptomatic, central fibro-osseous lesion most commonly found in jawbones that may, owing to its large size, cause pain, swelling, or paresthesia. If left untreated, the tumor may reach enormous proportions and have a grotesque appearance (Fig. 2–1).

SYNONYMS

1. Cementoossifying fibroma.[23, 49]
2. Benign fibro-osseous lesion of periodontal ligament origin.[24, 59]
3. Fibro-osseous lesion of bone.
4. Osteofibroma.[33]
5. Fibro-osteoma.[14]
6. Ossifying fibroma (fibrous dysplasia).[17]
7. Fibrous osteoma.[37]
8. Benign nonodontogenic tumor of jaw.[60]

Fibro-osseous lesions of the mandible and maxilla are one of the more confusing and controversial groups of lesions faced by a diagnostician. There are endless numbers of synonyms, and, in the absence of clear-cut distinctions between the various entities, the terminology is hopelessly confusing and nebulous. It is difficult to establish whether the lesions in question are truly neoplastic or simply developmental anomalies or reactive processes.

HISTORICAL ASPECTS

Ossifying fibrous tumors of the jaw and the maxilla were reported as early as 1865 in British literature. Menzel[33] from Vienna seems to have been the first in 1872 to describe the first case of ossifying fibroma as osteofibroma (Fig. 2–1). Montgomery[34] popularized the term "ossifying fibroma," Figi[14] designated the lesion "fibrous osteoma," and Furedi[16] named it "fibro-osteoma."

INCIDENCE

Since several authorities accept various divergent lesions as fibro-osteoma, ossifying fibroma, and fibrous dysplasia, the incidence and predominant location data are widely variable and not very useful. For instance, about 90 per cent of the ossifying fibromas reported by Waldron occurred in the mandible and almost exclusively in women.[57] Others, however, maintain that this lesion is most common in the maxil-

I. Ein Fall von Osteofibrom des Unterkiefers,
operirt und mitgetheilt
von
Dr. Arthur Hennsel,
Assistenzarzt an der chirurgischen Klinik des Professor Billroth in Wien.

Figure 2–1. Ossifying fibroma of the jaw with a 25 year history of slowly increasing size in a 35-year-old Hungarian woman.

la,[17] with no significant sexual predilection.[23, 24]

LOCATION, AGE AND SEX DISTRIBUTION

Except for the juvenile variety, the lesion seems to occur after the second decade of life, mostly in the third and fourth decades. It predominantly affects women and arises close to the roots of the teeth or the periapical aspects of the jaws. The antrum and the molar area of the mandible are the favored sites, although occurrences in other locations in the craniofacial bones have also been reported.[7, 29]

Ossifying fibromas have been reported in extragnathic long bones.[20, 26, 31a] In the 14 cases encountered, all but two occurred in the tibia. One lesion involved the humerus and another arose in the femur (Fig. 2–2). The clinical differential diagnosis may include bone cyst, fibrous dysplasia, nonossifying fibroma, fibromyxoma, or even adamantinoma. Although it is more common to see solitary lesions, multiple ossifying fibromas may occur, especially in Negroes.[25, 41] According to Markel, ossifying fibroma and adamantinoma of long bones are somehow related.[31a]

VARIOUS TYPES

In contrast to ossifying fibroma, *fibro-osteoma* is defined as a more solid, well-circumscribed tumor most commonly involving the maxilla and the paranasal sinuses.[41] Many authors interchange the terms "ossifying fibroma" and "fibro-osteoma," depending on whether the fibrous or the bony tissue component predominates in the lesion. Others believe fibro-osteoma to be larger in size, often producing clinical swelling.[24] On radiographic examination, these lesions appear to be radiopaque with a ground-glass appearance. They frequently involve several teeth but are not closely associated with the periodontal membrane. Hamner et al. feel that fibro-osteoma is microscopically separable from ossifying fibroma, the former lesion showing larger trabeculae of lamellar bone with artifactual space surrounding them. The fibroblastic stroma is more myxoid, less collagenized, with adequate blood supply.[23] Some believe that fibrous osteomas can mature into osteomas on the one hand or into ossifying fibromas on the other.[15, 40, 50] Those in favor of this histologic separation cite the clinical features of fibrous osteomas that occur in older patients and have a lower recurrence rate than ossifying fibromas.

In 1946, Billing and Ringertz[2] distinguished four distinct developmental stages in the maturation process of fibro-osteoma: (1) Least differentiated, "osteoid fibroma," a soft fibroma-like tumor, (2) moderately mature; (3) mature, so-called osteomas; and (4) the most differentiated, "eburnifying fibromas," which most commonly occur in the ethmoid bone or the adjacent portion of the frontal bones.

Lesions originally diagnosed as ossifying fibroma may become quiescent, and micro-