OBJECTIVE. We sought to describe the radiographic and imaging features of cherubism.

CONCLUSION. Cherubism is a rare osseous disorder of children and adolescents. Although the radiologic characteristics of cherubism are not pathognomonic, the diagnosis is strongly suggested by bilateral relatively symmetric jaw involvement that is limited to the maxilla and mandible. Imaging typically shows expansile remodeling of the involved bones, thinning of the cortices, and multilocular radiolucencies with a coarse trabecular pattern.

Cherubism is a benign disease of childhood characterized by osseous involvement limited specifically to the mandible and maxilla. It was first described in 1933 by Jones [1] as “familial multilocular cystic disease of the jaws,” but the term “cherubism” was later coined to describe the rounded facial appearance resulting from jaw hypertrophy that was reminiscent of cherubs depicted throughout Renaissance art (Fig. 1A).

The condition was initially characterized as familial, but both hereditary and sporadic cases have since been described.

Bilateral mandibular involvement is a distinguishing feature; only one case report in the literature describes unilateral involvement, in an adolescent [2]. Children typically present as early as 2–3 years old with nontender enlargement of the jaw. The lesions characteristically continue a pattern of variable enlargement until puberty, and then they partially or fully regress and show sclerotic involution in adulthood.

Cherubism is similar to fibrous dysplasia radiographically, especially when the latter is confined to the jaw. The similarity in appearance has prompted the suggestion that cherubism may be a familial form of fibrous dysplasia localized to the jaw [3–5]. We present our experience with 10 cases of cherubism and describe its radiographic and imaging features.

Materials and Methods
This study was conducted with the approval of the Mayo Clinic institutional review board, in accordance with the requirements for a retrospective review; informed consent was not required.

Six patients were selected through an archival search of institutional records via a review of computer-generated patient diagnoses. Four additional patients were identified from the archives of the Armed Forces Institute of Pathology. The diagnosis of cherubism was based in all cases on a combination of histopathologic features, skeletal distribution of lesions, and patient age.

The study group consisted of 10 patients, six males and four females, 5–19 years old (mean, 13.5 years). One patient’s age was unknown. Imaging types reviewed included radiography (n = 5), unenhanced CT (n = 5), and unenhanced MRI (n = 1). MR images included spin-echo T1-weighted images and fast spin-echo T2-weighted images with fat suppression. Two patients underwent serial radiography, and one patient underwent both CT and MRI. Three-dimensional CT reconstruction was available in one case. None of the patients who underwent CT or MRI examinations underwent radiography.

The clinical history and imaging characteristics were reviewed for each patient. Clinical review incorporated the documentation of sex and age at the time of imaging; physical findings, specifically dental arrangement; and family history. Radiographic and CT features included assessment for bilaterality; location, in the mandible and maxilla; extent of involvement; margin, between involved and uninvolved bone; ma-
matrix, defined as absent or present; and the presence and extent of expansile remodeling, periosteal reaction, cortical thinning, and trabeculation. When mineralized fibroosseous matrix was identified, it was subjectively characterized as sclerotic or densely sclerotic. In patients for whom serial radiographs had been obtained or multiple imaging techniques were available, each case was initially evaluated independently on the basis of the criteria just mentioned and then in concert for assessment of progression or comparison between techniques. The MR images were analyzed for signal intensity as compared with that of skeletal muscle, fat, and simple fluid; signal homogeneity; lesion size; and lesion location.

Results

All patients presented with progressive enlargement of the jaw or with the complaint of facial swelling. One patient complained of associated facial pain. Eight patients (80%) had associated dental derangement. The re-

Fig. 1— Images of cherubism.
A, Detail of painting of cherubs from Raphael's Sistine Madonna (c. 1513–1514).
B, Photograph shows cherubism in 8-year-old boy. Note swollen cheeks.

Fig. 2— Cherubism in 9-year-old boy.
A, Lateral CT scout scan shows extensive involvement of maxilla and mandible.
B, Coronal CT scan displayed in bone window shows extent of osseous involvement. Note osseous expansile remodeling, cortical thinning, and multilocular contour with coarse trabecular pattern. Maxillary disease resulting in dental derangement is also seen.
C, Additional coronal CT scan obtained through level of posterior orbit shows extensive symmetric maxillary and mandibular involvement.
maining two (20%) had documented earlier dental interventions. Definitive family history was available in only three cases, all of which were positive for cherubism. One patient was in foster care, so family history was brief and incomplete. No family history was available for the remaining six patients.

All cases displayed bilateral mandibular involvement; six patients (60%) showed concurrent maxillary disease (Fig. 2). One patient had an osseous extension from the mandibular body into the condyles. In seven cases (70%), the entire mandible was abnormal. The remaining focal maxillary and mandibular lesions ranged from 2 to 5 cm (mean, 3.3 cm) (Fig. 3). All lesions revealed expansile remodeling of the involved bones and thinning of the adjacent cortical rims. One lesion was entirely radiolucent, and the remaining nine (90%) showed increased opacity on radiography. CT results were compatible with a fibroosseous matrix (Fig. 4). The matrix showed varying degrees of increased attenuation and was deemed densely sclerotic in two cases (20%). Seven cases (70%) showed expansile osseous remodeling with a multilocular appearance and a coarse trabecular pattern. None of the osseous lesions showed adjacent periosteal reaction or associated soft-tissue mass.

CT clearly depicted the bilateral osseous involvement and expansile remodeling. CT also accurately delineated the extent of involvement and was especially useful in characterizing the osseous matrix. MRI established the lesions to be homogeneously isointense to skeletal muscle on T1-weighted imaging and heterogeneously isointense to skeletal muscle on fat-suppressed spin-echo T2-weighted imaging (Fig. 5).

Discussion

Cherubism has been described as a subtype of fibrous dysplasia, specifically a hereditary craniofacial fibrous dysplasia [3, 4], because of the radiographic similarities between the conditions. Recent genetic analysis, however, has shown them to be separate entities. The genetic basis for cherubism was identified in 1999, when the gene responsible for it was mapped to chromosome 4p16.3 [5, 6]. Ueki et al. [7] found a series of point mutations resulting in amino acid substitutions in the SH-3 binding protein SH3BP2 on chromosome 4p16.3. Of the four subtypes of fibrous dysplasia, three (monostotic, polyostotic, and McCune-Albright syndrome) are known to be related to mutations in the guanine nucleotide-binding protein gene located on chromosome 20q. The fourth (craniofacial) subtype has not been localized to this chromosome [8]. After analyzing results from a family with craniofacial fibrous dysplasia, Mangion et al. [8] determined that cherubism resulted from different mutations and was therefore a distinct entity at the molecular level.

Radiographic images of cherubism in our study revealed a characteristic pattern of expansile remodeling of the bone in all patients, mildly sclerotic matrix in 60%, and internal trabeculation in 70%. No lesions displayed associated periosteal reaction. CT clearly depicted the local extent of lesions limited to the maxilla and mandible, a finding that is often difficult to document on radiography because of the anatomic complexity of the facial bones. Interestingly, all the lesions depicted on CT contained mildly sclerotic matrix with expansile remodeling of the bone and cortical thinning.

Our results are in agreement with those described in the literature [4]. CT results for one case also provided clear evidence of lesion extension and involvement in the mandibular condyle. Sparing of the mandibular condyles has been described as a pathognomonic feature of cherubism [9], but Bianchi et al. [4] found this not to be invariably the case and described a patient with condylar involvement that was seen on CT.

On MR images, cherubic lesions were homogeneously isointense to skeletal muscle on T1-weighted imaging and heterogeneously hypointense to skeletal muscle on fast spin-echo T2-weighted images with fat suppression. These appearances are nonspecific, but they have not been previously described. MRI provides an anatomic outline that allows accurate determination of lesion location and extent.

Imaging Characteristics of Cherubism

Fig. 3.—Cherubism in 5-year-old girl. Radiograph shows expansile remodeling of mandible with characteristic trabeculated appearance and vague matrix at angle of mandible.

Fig. 4.—Cherubism in 16-year-old girl with massive mandibular enlargement and difficulty swallowing. A, Three-dimensional surface-rendering coronal oblique CT scan shows extensive osseous remodeling. B, Coronal CT scan reveals variable appearance of matrix, ranging from radiolucent to densely sclerotic. Note expansile remodeling of bone and trabeculation.
Radiographic differential diagnosis for cherubism includes craniofacial fibrous dysplasia, brown tumor of hyperparathyroidism, Jaffe-Campanacci syndrome, and familial gigantiform cementoma. Although cherubism and craniofacial fibrous dysplasia of individual lesions show radiologic similarities, they may be distinguished clinically and histologically. Features more specific for the diagnosis of cherubism include bilateral mandibular involvement, limitation to the maxilla and mandible, and involution at the time of puberty [8, 10]. In contrast, patients with fibrous dysplasia typically do not present with swollen cheeks, upward turning of the eyes, or dental derangement. All the probands in our series had bilateral mandibular involvement, and more than half (60%) had concurrent maxillary disease. Histologically, patients with cherubism typically have a prominent number of multinucleated giant cells, which are rarely seen in fibrous dysplasia. Brown tumor and Jaffe-Campanacci syndrome are readily distinguished on clinical grounds and are easily eliminated from the differential diagnosis.

Familial gigantiform cementoma is a rare osseous disorder characterized by the production of cementum in the lesions. Mandibular and maxillary involvement are often present. Finical et al. [11] reviewed a series of cases in a single family and described lesions extending into the orbits and nasal septum, locations that exclude the diagnosis of cherubism. Also, gigantiform cementoma lesions are located primarily in the maxilla and are enlarged in a focal rather than diffuse manner. Histologically, cementomas contain cementum and lack multinucleated giant cells.

Study limitations include the fact that this review was retrospective. Our sample was small, and CT and MR images were not available in all cases. Also, we did not perform genetic evaluation on the surgical specimens in our sample.

Although the radiologic and histologic characteristics of cherubism are not pathognomonic, the overall morphologic features are characteristic and consistent among cases; these features therefore allow an accurate prospective diagnosis in the appropriate clinical setting.

References

1. Jones WA. Familial multilocular cysts of the jaws. Am J Cancer 1933;17:946–950