Departamento de Genética, Instituto de Ciências Naturais
Cadeira de Histologia, Faculdade de Odontologia
Universidade Federal do Rio Grande do Sul, Pôrto Alegre (Brasil)

Cherubism in a Brazilian Kindred

F. M. Salzano, H. Ebling

Jones (1933) was the first to apply the name cherubism to a rare facial deformity in children. This name was suggested because in the classic facial appearance of affected persons the lower half of the face is diffusely enlarged, showing similarities to that of the angelic cherub popularized in Renaissance art. This condition is characterized by a proliferation of fibrous tissues within the jaws; the mandibular rami and adjoining retromolar areas are the usual sites of lesions, but the remainder of the mandible, with the exception of the condyles, may be also affected, with or without maxillary involvement. The roentgenographic appearance is variable and related to the histologic appearance; the more fibrous tumors exhibit well-defined multilocular areas of roentgenolucency and the more calcified tumors appear to be sclerotic or present a ground-glass appearance. The characteristic histologic appearance is that of proliferating fibrous tissue showing multi-nucleated giant cells.

As was emphasized by Anderson and McClendon (1962) the genetic aspects of cherubism have received little attention so far. These authors reviewed all the literature on this subject and concluded that the disease is probably conditioned by an autosomal dominant gene 100% penetrant in males and 50-70% penetrant in females. They stressed the need for more detailed family studies, involving both affected and unaffected relatives of patients. Therefore when the diagnosis of cherubism was made in two brothers of a Caucasian family living in Pôrto Alegre by one of us (H. E.) we decided to investigate this kindred in detail. The present report summarizes the observations which have been made.

Description of the family

Fig. 1 shows the family's pedigree. The information obtained involves seven generations in a total of 75 individuals. 23 of these were examined by the authors as follows: *a*) clinical examinations only: 13; *b*) clinical examinations and X-rays: 7; *c*) clinical, radiographic and histologic examinations: 3. In addition the report of a deceased person as being affected (IV-13) was verified to be probably correct through the inspection of an old photograph.

With regard to the affected persons the informations obtained are as follows

Ricevuto il 23. XII. 1965

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press

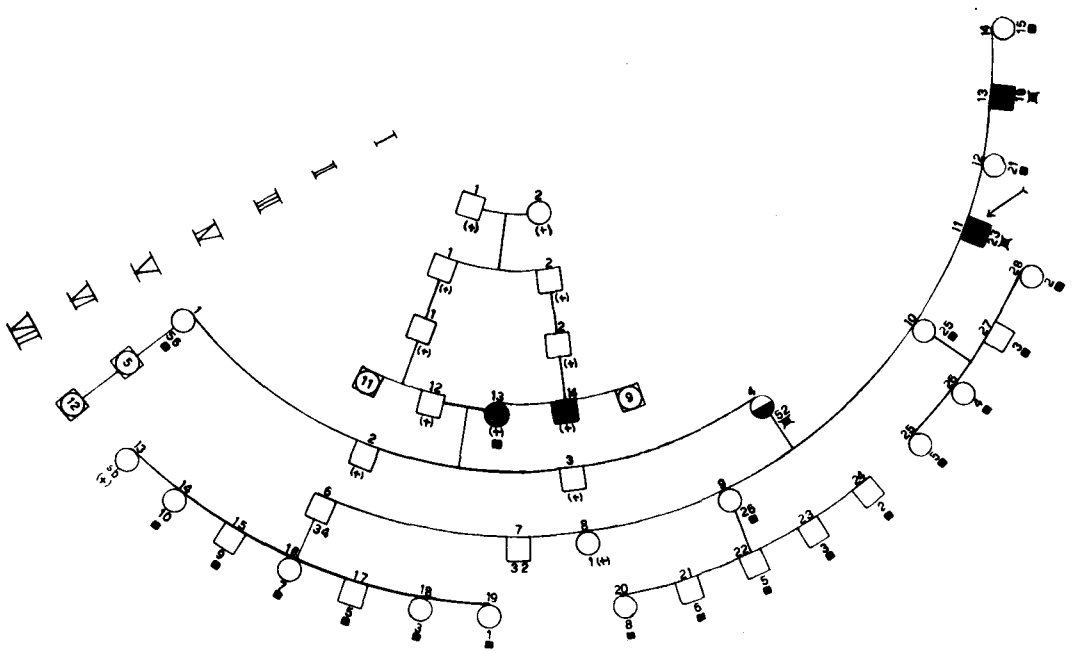

Fig. 1. Pedigree of the studied family. Open circles and squares indicate normal individuals; completely full circles and squares: affected persons; the half-filled circle represents a woman with an atypical form of the disease. The small squares under the circles and squares indicate individuals from whom clinical and X-rays or reliable information were obtained. The small squares with a cross show the individuals from whom clinical, X-ray and histologic determinations were obtained. The letters sb indicate one stillbirth

(Roman numerals refer to the generation, while the arabic refer to the situation of the individual in this generation):

IV-13 - L. C., deceased some years ago, female, white, married, housewife. V-4 reported that she was affected. This information was documented by a photograph, which shows that she presented an unilateral mandibular swelling like her sister and grandchildren, but on the right side.

V-4 - M. J. C., 52 years, female, white, married, housewife. On physical examination she presented a unilateral mandibular swelling on the left side. The histological examination of a biopsy taken from this region showed evidences of a chronic abscess with a thick fibrous layer. In one region osseus tissue with resorption zones could be seen. The X-ray examinations did not disclose a picture characteristic of cherubism.

VI-11 - J. F. L. C., 23 years, male, white, unmarried, garage mechanic.

Anamnesis. Mandibular swelling since childhood (6-7 years). Never felt any pain. Always enjoyed good health.

Physical examination. The first examinations, performed when he was a boy, showed bilateral involvement of the mandible. However the affection showed a regression

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press

with age on the right side. The left side of his mandible showed at the time of the last examination a swelling, more accentuated in the paramedian region (Fig. 2). Palpable and mobile ganglia in the carotid region were also detected. The skin in the region was generally normal but there were differences of pigmentation and exfoliation in the extremity of the nose and in the left ear lobe. Anterior teeth mobile

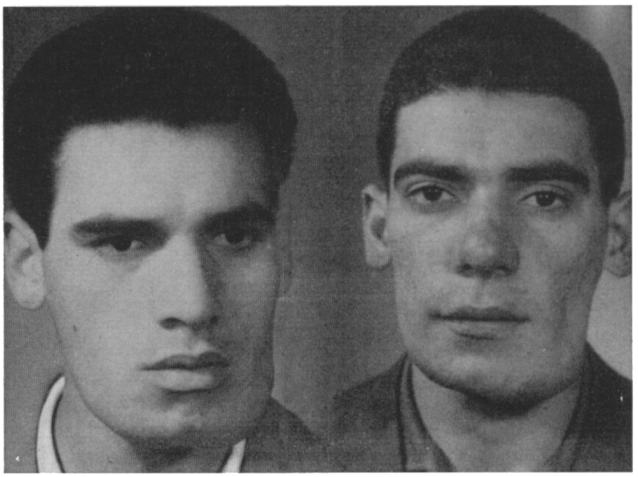

Fig. 2. The two affected brothers

and with tartar. In the posterior region there were only roots. The process could be delimited by palpation as being between the mandible's angle and the premolar region. The inner osseous tissue seemed not to be affected.

X-ray examinations showed an extensive pathologic process involving all mandible including the ascending ramus (Fig. 3).

Surgical cosmetic operation. After a long incision from the mandibular angle until the median line a divulsion of the tissue was performed: the periosteum showed to be much thickened and vascularized. The osseous tissue presented a normal aspect, with a thin layer in the paramedian region. An osteotomy was performed in the most enlarged region. The loculi were filled with perfectly delimitated brownish pathologic tissue showing several darker nodules in its inner part. The pathologic tissue was easily removed by curettage, the loculi remaining well differentiated.

Histopathologic examination. The main findings can be summarized as follows (see Fig. 4): *a*) Observation of zones in which the connective tissue showed hemorrhagic regions of different ages, with focal distribution, many giant cells and many nuclei; *b*) Zones where the connective tissue presented a fibrous aspect, with few vessels, absence of giant cells and at intervals nest-like spiral fibers; *c*) Zones where to the aspect described in *a* there was a superposition of a very large number of calcified spheres similar to calcospherites but larger and less stainable with hematoxylin. Except in one region, no osseous trabeculae were seen; and those observed could

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press

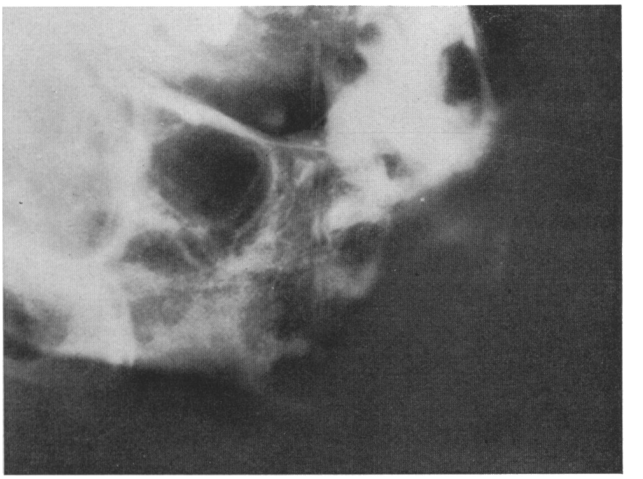

Fig. 3. Radiograph taken from VI-11 before the cosmetic operation. Notice the large cavities and the differences in bone density

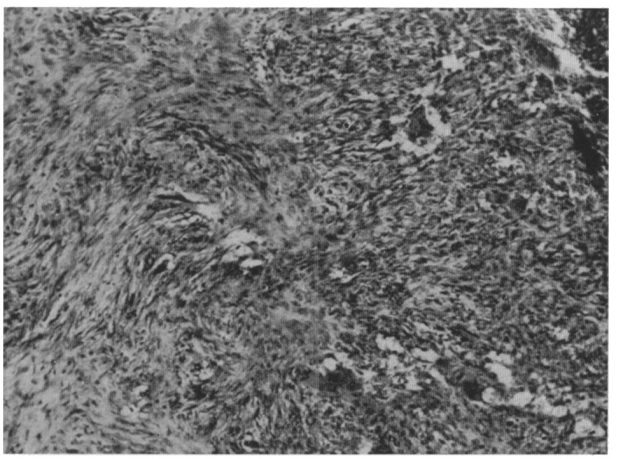

Fig. 4. Histopathologic examination of material from VI-11's mandible. Notice the proliferating fibrous tissue and giant cells. *Method*: hematoxylin-eosin. Enlargement: 100 ×

be considered as being due to a compensation process needed to strenghten the less resistent mandible.

VI-13 - J. C. L. C., 18 years, male, white, unmarried, shop clerk.

Anamnesis. The mandible swelling appeared like in his brother between 6 and 7 years of age. Like VI-11, he never felt any pain and always enjoyed good health.

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press

Physical examination. The pathological process was very similar in the two brothers and affected the same region (cf. Fig. 2). A ganglionar swelling was seen near the left ear lobe, but no other ganglionar reactions were observed. Normal skin and muscles. Temporomandibular articulation normal. In the oral cavity, the lower left side elements 4, 6 and 7 were missing; elements 5 and 8 at the lower left were slanted in the distal-lingual direction (especially element 5). The following teeth were in bad condition: superior right: 4-5; superior left: 5-6; lower right: 7, 6 and 4. Maxillary atresia. Dental articulation normal within the specified limitations. Mucosae with normal aspect and good coloration. No fistulae could be seen in the left mandibular region.

Histopathologic examination. The material consisted of a radicular apex with two included nodules, fragments of normal osseous tissues, zones of surgical hemorrhages and in one region connective tissue with nest-like spiral fibers. Giant cells were also seen.

The physical examinations and X-rays performed in the unaffected members of the family yielded uniformly normal results.

Discussion

The histopathologic picture seen in the two brothers (VI-11 and - 13) was not identical, but this was not unexpected since, as was emphasized by McClendon, Anderson and Cornelius (1962), the microscopic appearance of the tissue is not pathognomic unless correlated with the history and with clinical and roentgenographic findings. Even more atypical were the results of the histological examination of a biopsy taken from their mother (V-4). However the similarity of their clinical symptoms and the fact that IV-13 (mother of V-4 and grandmother of VI-11 and - 13) was also probably affected by the same disease points to a common etiology. The affection in this family is probably conditioned by an autosomal dominant gene with variable expressivity. This and the fact that the histological and radiographical picture in V-4 was atypical agrees well with the conclusions of Anderson and McClendon (1962) that cherubism is probably due to an autosomal dominant gene with reduced penetrance in females (cfr. also Marino, Meguira and Zavala, 1964 and Shuler and Silverman, 1965 for additional studies in Latin American families).

Summary

A description is made of a Brazilian family of white ancestry in which five individuals presented the fibrous dysplasia of the jaws known as cherubism. The information obtained involves seven generations in a total of 75 individuals. 23 of these were examined by the authors and a report about a deceased person was confirmed by photograph. The affection in this family is probably conditioned by an autosomal dominant gene with variable expressivity.

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press

Acknowledgments

Thanks are due to Mr. Antonio C. Campagna who contacted the family and helped in many ways in the first stages of this investigation. Mr. Girley V. Simões also helped in the field studies. This work has been supported in part by the Rockefeller Foundation, Conselho Nacional de Pesquisas, Conselho de Pesquisas of the University of Rio Grande do Sul and PHS research grant RG-08238 from the Division of General Medical Sciences, Public Health Service, U.S.A.

Bibliography

Anderson D. E., McClendon J. L. (1962). Cherubism-hereditary fibrous dysplasia of the jaws. I. Genetic considerations. *Oral Surg.*, **15:** (Suppl. 2): 5-16.

Jones W. A. (1933). Familial multilocular cystic disease of the jaws. *Amer. J. Cancer*, **17:** 946-950.

Marino E. *et al.* (1964). Displasia fibrosa familiar de los maxilares: Querubinismo. *Prensa Med. Argent.*, **51:** 819-823.

McClendon J. L. *et al.* (1962). Cherubism-hereditary fibrous dysplasia of the jaws. II. Pathologic considerations. *Oral Surg.* **15:** (Suppl. 2): 17-42.

Shuler R. K., Silverman F. N. (1965). Dysplasie fibreuse familiale des machoires ou « chérubinisme » dans une famille Haïtienne. *Ann. Radiol.*, **8:** 45-52.

RIASSUNTO

Gli autori descrivono una famiglia brasiliana Bianca, nella quale 5 individui presentavano una displasia fibrosa della mandibola, nota con il nome di cherubismo. Le informazioni ottenute riguardano sette generazioni, per un totale di 75 individui. 23 sono stati esaminati dagli autori ed il reperto riguardante un individuo defunto è stato confermato per mezzo di una fotografia. La malattia in questa famiglia è probabilmente condizionata da un gene autosomico dominante ad espressività variabile.

RÉSUMÉ

Description d'une famille brésilienne Blanche dans laquelle cinq individus présentaient une dysplasie fibreuse des mandibules connue sous la dénomination de chérubisme. Les informations obtenues comprennent sept générations et un total de 75 individus. 23 ont été examinés par les auteurs et le diagnostic d'une personne décédée fut confirmée par une photographie. L'affection en cette famille est probablement conditionnée par un gène autosomique dominant avec expressivité variable.

ZUSAMMENFASSUNG

Verfasser untersuchten eine brasilianische Sippe weisser Rasse, bei der 5 Personen an Dysplasia fibrosa des Unterkiefers, auch Cherubismus genannt, litten. Die Erhebungen erfassten sieben Generationen mit insgesamt 75 Personen. Davon wurden 23 von Verf. selbst untersucht und der Befund eines Verstorbenen durch Photographie bestätigt. Das Leiden ist in dieser Sippe wahrscheinlich durch ein dominantes autosomes Gen wechselnder Expressivität bedingt.

https://doi.org/10.1017/S112096230001341X Published online by Cambridge University Press