The radiology of sclerosteosis

By P. Beighton, M.D., Ph.D., F.R.C.P.
Department of Human Genetics, Medical School, University of Cape Town, South Africa

B. J. Cremin, F.R.A.C.R., F.R.C.R.
Department of Radiology, Groote Schuur Hospital, Cape Town, South Africa

and H. Hamersma, M.B., Ch.B., M.D.
University of Pretoria, South Africa

(Received March 1976)

ABSTRACT

Sclerosteosis is an unusual disorder in which increased skeletal density is associated with abnormalities of bony modelling. The condition is progressive and complications arise due to cranial nerve involvement. Death from raised intracranial pressure occurs in early adulthood.

In order to define the range and extent of the bony abnormalities, the radiographic features of 18 affected individuals have been analysed. The recognition of characteristic changes permits diagnostic precision.

Increased skeletal density and abnormalities of bony modelling are features of a number of uncommon genetic disorders. These conditions have often been grouped together as "osteopetrosis", "Albers-Schönberg disease", or "marble bones". However, in recent years a number of entities with consistent and characteristic clinical and radiographic stigmata have been separated from this general category.

Sclerosteosis is a disorder of this type which has attained the status of a distinct entity. In order to define the radiographic features of this condition, which is virtually confined to the Afrikaner population of Southern Africa (Beighton et al., 1976) we have studied 18 affected individuals. The radiographic findings are presented and discussed in this paper.

CLASSIFICATION

Understanding of the "osteopetrosis" group of disorders has been greatly facilitated by the classification proposed by Gorlin et al. (1969), following their critical review of the literature concerning these conditions.

1. Osteosclerosis
   In these conditions increased radiological density of bone is the predominant feature. Abnormalities of bony modelling, if present, are of minor degree. The autosomal dominant and autosomal recessive forms of true osteopetrosis, together with pycnodysostosis, are the most important disorders in this group.

2. Craniofuscular dysplasias
   Abnormal modelling of the skeleton is the major feature of this group of disorders, while increased radiological bony density is of lesser degree. Involvement of the cranium may lead to nerve compression and complications include facial palsy and deafness. Pyle's disease, the autosomal dominant and recessive types of craniometaphyseal dysplasia, and rarities such as craniodiaphyseal dysplasia and frontometaphyseal dysplasia fall into this category.

3. Craniofuscular hyperostoses
   Overgrowth of the cranium and tubular bones predominate, while increased radiological density is less marked. Sclerosteosis, the subject of this presentation, features in this group together with van Buchem's disease, osteoectasia and Engelmann's disease.

4. Miscellaneous
   Disorders which do not fall into any of the three previous categories, but which have sometimes been considered as forms of osteopetrosis include melorheostosis, osteopoikilosis and osteopathia striatum.

PATIENTS STUDIED

During the course of a nation-wide survey of skeletal dysplasias in South Africa, 21 patients with sclerosteosis were examined. These individuals, who were members of 15 separate kindreds, were all of Afrikaner stock. The pattern of transmission of the condition in these families was consistent with autosomal recessive inheritance.

Radiographic studies were undertaken in 18 of these patients, nine males and nine females, their ages ranging from nine months to 56 years. The description of their radiographic features forms the subject of this paper.

CLINICAL FEATURES

Individuals with sclerosteosis are unusually tall, adult males generally exceeding 198 cms. in height, while females may attain 183 cms.

Overgrowth of the cranium leads to distortion of the facies, the brow and lower jaw becoming massive. Facial palsies consequent upon cranial nerve compression contribute to the abnormal appearance.
The radiology of sclerosteosis

and the affected individual's problems are compounded by the development of deafness and involvement of the optic nerve (Fig. 1). Death in early adulthood is the usual consequence of progressive rise in intracranial pressure (Beighton et al., 1976).

Syndactyly of the 2nd and 3rd fingers is a prominent feature. This abnormality is variable in degree, ranging from cutaneous webbing to complete bony fusion (Fig. 2). The digits are mis-shapen, with radial deviation of the terminal phalanges, and the nails may be dysplastic.

**RADILOGICAL FEATURES**

The outstanding radiographic changes in the affected individuals were massive increase in the size and density of certain components of the skeleton, the skull and tubular bones being predominantly involved.

The manifestations were age-related. The skull radiographs of three unequivocally affected children aged nine months, three and a half and five years were ostensibly normal, and their hand radiographs revealed no bony changes other than syndactyly. However, definite thickening of the skull and distortion of the phalanges were present in a seven-year-old girl. All the children examined had a normal epiphyseal age development.

In older individuals the bony density and abnormal modelling became increasingly evident throughout childhood and early adult life before apparently becoming static by the end of the third decade.

**Skull**

The major feature was a dense thickening of the calvarium with complete obliteration of the diploic space (Fig. 3). The increase in bone density and width commenced from the inner table of the cranial vault and progressed so that the internal diameter of the cranium was reduced by adulthood. The frontal sinuses were enlarged, the vascular markings were prominent and the occipital venous sinuses were often well outlined. The bones of the base of the skull were particularly dense and narrowing of the exit foramina was confirmed by tomography in three patients. The sella turcica was enlarged and rounded in six of the 12 adults.

---

*Fig. 1.* The characteristic facies in sclerosteosis—a 45-year old male with mandibular hyperplasia, facial palsy and proptosis.

*Fig. 2.* Sclerosteosis in a 33-year-old female. Soft tissue syndactyly of the 2nd and 3rd fingers has been surgically corrected.
The body of the mandible was massively enlarged in the adults, with resultant prognathism. The jaws were usually edentulous or deficient in teeth and the density of the bone was such that it was not possible to recognise the lamina dura.

**Thorax**

The clavicles were generally enlarged, the thickening and widening being most marked medially. The ribs were widened with increased density so that the inner texture of the bones was not readily visible (Fig. 4).

**Vertebrae**

Changes in the vertebrae were confined to their posterior aspects, notably the pedicles and laminae of the lumbar and sacral vertebrae (Fig. 5). The vertebral bodies showed no increase in density. The only degenerative changes noted in the intervertebral disc spaces were present in a 35-year-old male.

**Pelvis**

Increase in density predominantly involved the lower portions of the iliac bones and the ischial and pubic rami. Bony outlines were generally normal although relative hypoplasia of the iliac wings was a consistent feature (Fig. 6.).

**Tubular Bones**

These bones were massive, with marked cortical thickening and some degree of disturbance of modelling (Fig. 7). The thickening of the cortex generally extended along the whole length of the shafts. However, in the femora the cortical thickening was confined to the upper two thirds, while the lower third had an abnormal configuration, the metaphyseal region being widened, with lack of normal diaphyseal constriction (Fig. 8).

The hand changes were an outstanding feature of the condition (Figs. 9 and 10). Every patient had some degree of syndactyly and the tubular bones of the hands were enlarged, dense and distorted with radial deviation of the terminal phalanges. In the only patient in whom the feet were X-rayed, the metatarsals and phalanges showed similar features.
The radiology of sclerosteosis

FIG. 5. Lumbar spine—lateral radiograph. The vertebral bodies are relatively normal, increased bony density being of significant degree only in the pedicles.

FIG. 6. Pelvis—antero-posterior radiograph. Density is increased particularly in the lower portions of the iliac bones and in the ischial and pubic rami. The iliac wings are relatively hypoplastic.

FIG. 7. Humerus—antero-posterior radiograph. The cortex is thickened and bony modelling is disturbed.

FIG. 8. Knees—antero-posterior radiograph. Modelling defects are particularly evident in the lower ends of the femora, where the metaphyseal region is widened.
FIG. 9. Hands—antero-posterior radiograph. Changes in the bones of the hands are a prominent feature of sclerosteosis. The shafts of the metacarpals and phalanges are distorted, with increased cortical thickening.

FIG. 10. Hand—antero-posterior radiograph. Syndactyly of the 2nd and 3rd fingers is variable in degree. This patient has marked soft tissue union and phalangeal malformation.

DISCUSSION

Although sclerosteosis is a rarity, there is no doubt that it is a separate and distinct entity. In the past, a few case reports appeared under the loose designation “osteopetrosis”. Truswell (1958) first recognized that the condition was a unique disorder, to which Hansen (1967) later applied the designation “sclerosteosis”. Although by no means a true description of this condition, the appellation of “sclerosteosis” has now gained popular acceptance.

Other than the Afrikaner patients, the only other case reports have concerned a kindred in New York (Kelley and Lawlah, 1946) and a girl in Japan (Sigiura, 1975).

Sclerosteosis is a potentially lethal disorder, and early death is preceded by distressing complications. For this reason, diagnostic precision is of paramount importance, as this will permit accurate prognostication and rational genetic counselling. At the present time therapy is limited to surgical decompression of entrapped cranial nerves, craniotomy to relieve raised intracranial pressure, cosmetic surgery to the face and hands, and the provision of a hearing aid.

The radiological features of sclerosteosis bear some resemblance to those of virtually all the disorders mentioned in the classification section. However, the syndactyly and severe distortion of the phalanges serves to distinguish sclerosteosis from these conditions. Furthermore, sclerosteosis is the only disorder in this group in which excessive height occurs. The facial changes and tall stature gives sclerosteosis a superficial resemblance to acromegaly. Nevertheless, even in patients with enlargement of the sella, radiographic distinction is an easy matter, as cranial hyperostosis and modelling defects of the long bones are not features of acromegaly. In this context, it may be relevant that extensive investigations in two of our patients with sclerosteosis have revealed no endocrine abnormality.

In our experience, the only condition which could be confused with sclerosteosis is van Buchem’s disease (hyperostosis corticalis generalisata). One of the authors (H.H.) visited Holland to examine affected individuals and concluded that the disorders differ in that patients with van Buchem’s disease are of normal stature, have less distortion of the face and have little involvement of the hands. This contention is supported by the case descriptions of eight patients published by van Buchem (1971), none of the individuals having syndactyly or other significant digital involvement.

As sclerosteosis is transmitted as an autosomal recessive, an affected individual must inherit an abnormal gene from each of his parents in order to develop the disorder. These “carrier” parents are themselves clinically normal. On a basis of the prevalence of sclerosteosis in South Africa, it can be calculated that at least one in 140 individuals of Afrikaner stock is a heterozygote or carrier of the gene.

This population prevalence is of practical significance for the radiologist, as it is possible that the carrier might be detected by the recognition of
minor degrees of widening and loss of trabeculation of the calvarium (Beighton and Hamersma, 1974). This problem is presently under investigation, as a reliable technique for determination of carrier status would have far reaching implications for eventual control of the disorder.

ACKNOWLEDGMENTS

We are grateful to Sister Lecia Durr for assistance with the family studies, to Mrs. R. S. Henderson for preparing the illustrations and to Mrs. Gretu Beighton for typing the manuscript.

Our thanks are due to Professor A. S. Truswell, Dr. G. K. Klintworth and many other colleagues for their kindness in facilitating access to affected individuals.

The investigation was supported by grants from the South African Medical Research Council, the University of Cape Town Staff Research Fund and the Hettie de Beer Fund.

REFERENCES


Book review

The upper brain stem in the human: its nuclear configuration and vascular supply. By B. Schlesinger, pp. 266, illustrated, 1976 (West Germany, Springer-Verlag) $159.90.

This book describes the anatomy of the upper brain stem in great detail. It is based on painstaking anatomical dissections performed by the author and on his study of collections of myelin stained specimens.

The author first describes in considerable detail his method of making and analysing oblique sections of the brain stem in a way which allows him to reconstitute a three dimensional matrix which depicts the precise spacial relationships of the structures in the sections. In this way he has established the form, position and variation of nuclei, fibretracts and of the fine vascularization. In 36 specimens the vessels were injected in various ways and then studied by radiography and by anatomical sectioning. There is an excellent discussion on the variations in vascular anatomy, which confirms that the usually described pattern is an idealized conception and that the exception to this pattern is the rule. Finally, there is a short chapter on the syndromes associated with specific vessel occlusions.

Unfortunately, some of the nomenclature varies from that generally accepted by neuroradiologists, although the latter is usually referred to in discussion. The book is beautifully illustrated with photographs of dissections, radiographs of specimens and excellent diagrams. A great deal of the minute anatomy is of much greater interest to neurosurgeons and neuroanatomists than to neuroradiologists, but the chapters on variation of the larger vessels are of neuroradiological interest and will be useful for reference.

B. E. Kendall.