

# Syndrome of the month

*Journal of Medical Genetics* 1988, 25, 200–203

## Sclerosteosis

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Sclerosteosis is a severe autosomal recessive disorder in which progressive bone overgrowth leads to gigantism, cranial nerve entrapment, and raised intracranial pressure. About 60 affected persons have been documented, the vast majority in the Afrikaner population of South Africa. In addition, sporadic cases or affected sibs have been reported from the USA, Switzerland, Japan, and Brazil.

Sclerosteosis was first recognised as a distinct entity in 1958 when Truswell<sup>1</sup> described two unrelated South African girls with “osteopetrosis with syndactyly; a morphological variant of Albers-Schönberg disease”. Subsequently Hansen<sup>2</sup> in 1967 used the term ‘sklerosteose’, which in its anglicised form ‘sclerosteosis’ has gained general acceptance. The manifestations in 25 affected Afrikaners were reviewed by Beighton *et al*<sup>3</sup> in 1976 and a further 17 patients were reported by Beighton and Hamersma.<sup>4</sup>

### Clinical features (figs 1 to 3)

Mandibular prognathism and frontal prominence become evident by the age of five years. These deformities progress and in adulthood the face is severely distorted, with dental malocclusion, proptosis, and relative mid-facial hypoplasia. Affected children are tall for their age and adults with the condition may have gigantism. The majority have partial or total syndactyly, usually of the second and third fingers, with deviation of the terminal phalanges and hypoplasia of the nails of the corresponding digits. The bones are resistant to trauma and fractures are infrequent.

Transient palsy of the seventh cranial nerve occurs during infancy and bilateral facial paralysis is usually permanent by adulthood. Progressive bony encroachment upon the middle ear cavities and auditory nerve canals often causes deafness in mid-

childhood. Compression of the optic nerves is an infrequent late complication.

Overgrowth of the calvarium leads to progressive diminution of the capacity of the cranial cavity with raising of intracranial pressure. Severe headache due to this mechanism often develops in early adulthood and several patients have died suddenly from impaction of the medulla oblongata in the foramen magnum.

### Radiographical features (figs 4 to 6)

Sclerosteosis is progressive; cranial sclerosis may be evident in infancy and the changes are usually well established by the age of five years.<sup>5</sup> In adulthood



FIG 1 Asymmetrical overgrowth of the mandible and proptosis are evident. This young woman has bilateral facial palsy and deafness.



FIG 2 Many affected persons have gigantism. This man, who shows the characteristic facial distortion, is well over 2 m in height.

the calvarium is widened and uniformly sclerotic. The base becomes very dense and the cranial nerve foramina may be obliterated. The sinuses remain patent and the sella turcica may be expanded. The mandible is dense and massive, with asymmetrical distortion and dental malocclusion. In the spine, the vertebral end plates and pedicles are sclerotic but

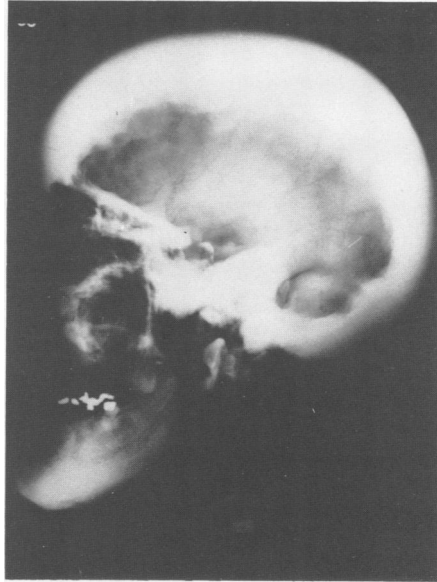
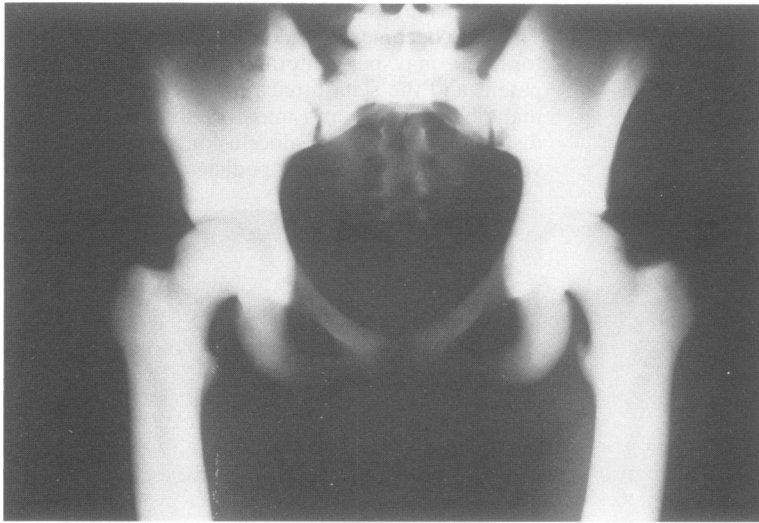


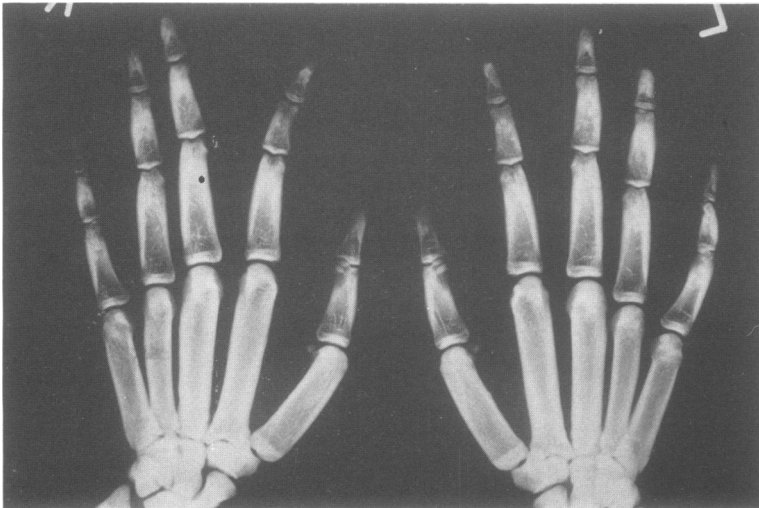
FIG 4 Lateral skull radiograph showing massive calvarial hyperostosis with sclerosis of the base.



FIG 3 A brother and sister with mandibular expansion and facial palsy. Partial soft tissue syndactyly of the second and third digits and radial deviation of the terminal phalanges of these fingers is evident.



**FIG 5** *The pelvis is sclerotic but the bony contours are undisturbed. The femoral cortices are dense and expanded and the modelling of these bones is disturbed.*



**FIG 6** *AP radiograph of the hands. The tubular bones are undermodelled and their cortices are sclerotic.*

the outlines of the bodies are not disturbed. The clavicles and ribs are widened and dense and the scapulae and pelvis are sclerotic but not expanded.

The long bones are massive, with cortical hyperostosis and moderate alteration of their external contours. All the tubular bones, including those of the extremities, are involved in this process. Irregular cortical thickening is a mild but variable feature and is apparently age related. Syndactyly, which is most often present in the second and third fingers, ranges from complete bony union to

minimal skin webbing. Radial deviation of the terminal phalanges may be radiologically evident. The toes are not syndactylous.

#### **Differential diagnosis**

Sclerosteosis must be differentiated from the osteopetroses and other sclerosing bone dysplasias. In this context the severity of the condition and the presence of syndactyly are the most important diagnostic discriminants. In view of the high

TABLE Distinguishing features of sclerosteosis and van Buchem disease.

	Sclerosteosis	van Buchem disease
Reported cases	60	15
Age of clinical presentation	Early childhood	Puberty
Prognosis	Potentially lethal	Comparatively benign
Habitus	Gigantism	Normal stature
Facies	Gross distortion	Prominent mandible
Teeth	Irregular, with malocclusion	Normal
Torus palatinus	Sometimes present	Absent
Cranial nerve palsy	Very common	Inconsistent
Intracranial pressure	Raised	Normal
Syndactyly	Frequent	Absent
Nail hypoplasia	Frequent	Absent
Cranial hyperostosis	Gross	Moderate
Distortion of tubular bones of hands and feet	Marked	Mild

prevalence of sclerosteosis in the Afrikaner population of South Africa, the condition should be suspected in any member of this community who presents with syndactyly or facial palsy.

Sclerosteosis is very similar to the autosomal recessive form of endosteal hyperostosis (van Buchem disease) and as many of the Afrikaners of South Africa had their origins in Holland, where van Buchem's patients were studied, it seems possible that there might be some fundamental link between these disorders.<sup>6</sup> They are both inherited as autosomal recessives and the clinical and radiographical manifestations are similar. No absolute diagnostic marker has yet been recognised, and changes such as periosteal excrescences or raised levels of serum alkaline phosphatase are unhelpful, as they may occur in both conditions (table).

### Management

Prophylactic craniectomy in early adulthood is necessary in most affected persons. Decompression of the seventh and eighth cranial nerves gives inconsistent results. An external hearing aid may be beneficial. Syndactyly requires cosmetic repair.

Orthodontic measures are indicated for dental malalignment.

### Genetics

Analysis of pedigree data confirms that sclerosteosis is an autosomal recessive condition. The gene frequency in the Afrikaner people is estimated at 0.0035, with 10 000 clinically normal heterozygotes in this population. Heterozygote detection may be possible on the basis of recognition of minor changes which are apparent on skull radiographs.<sup>7</sup>

Prenatal diagnosis has not yet been achieved, but it might be possible to recognise syndactyly in a potentially affected fetus by means of fetoscopic techniques.

I am grateful to Gillian Shapley for typing the manuscript. Material in this review appeared in *Sclerosing bone dysplasias* and in my monograph *Inherited disorders of the skeleton* and I am grateful to the publishers, Springer Verlag and Churchill Livingstone, for their permission for these to be reproduced. My research into this disorder has been supported by grants from the Medical Research Council of South Africa, the Mauerberger Foundation, the Harry Crossley Foundation, and the University of Cape Town Staff Research Fund.

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