Syndrome of the month

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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 described two unrelated South African girls with “osteopetrosis with syndactyly; a morphological variant of Albers-Schönberg disease”. Subsequently Hansen 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 in 1976 and a further 17 patients were reported by Beighton and Hamersma.

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. In adulthood

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

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

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

**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
Sclerosteosis

**TABLE**  Distinguishing features of sclerosteosis and van Buchem disease.

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

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.7 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.

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**References**


**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.

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