Aglossia-adactyia syndrome

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Summary. Aglossia-adactyia is described in two male patients, aged 31 and 21 years old. Including a previous reported case (Nevin, Dodge, and Kernohan, 1970) there are three patients with this syndrome in Northern Ireland. The aetiology is unknown but in spite of the extreme variability of the clinical manifestation, a dominant mutant gene cannot be ruled out.

Congenital absence of the tongue (aglossia), first described in the eighteenth century by de Jussieu (1718/1719), is an unusual and rare condition. Kettner (1907) was the first to report the association of aglossia and severe anomalies of the hands and feet; however, his patient also had glossopatine ankylosis. The first true case of aglossia-adactyia was described by Rosenthal (1932), in a three-year-old girl with micrognathia, a cleft of the lower lip, absence of the lower incisors, and a tongue which consisted only of a small median rudiment. She also had anomalies of both hands and of the right foot. Gorlin and Pindborg (1964) and Spivack and Bennett (1968) reviewed the published cases of aglossia-adactyia. Since then several new cases, making a total of 16 (Table I), have been described (Kelln, Bennett, and Klingberg, 1968; Temtamy and McKusick, 1969; Hoggins, 1969/1970; Harwin and Lorinsky, 1970; Nevin et al, 1970; Bernard et al, 1971; Cohen, Pantke, andSiris, 1971; Grislain et al, 1971; Hall, 1971). This paper describes aglossia-adactyia in two adults.

Case reports

Case 1. The patient, a 31-year-old male, born 5 January 1942, was admitted to hospital with a left epistaxis. Examination showed an abnormally shaped tongue, severe congenital anomalies of the hands and lower limbs, and mild hypertension.

He is the third born of normal unrelated parents. The father was aged 28 years, and the mother 25 years at the birth of the patient. The mother's pregnancy and

Received 7 June 1974.

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Fig. 1. Case 1, showing small tongue with a poorly defined tip.
TABLE I
AGLOSSIA-ADACTYLIA SYNDROME

<table>
<thead>
<tr>
<th>Reference</th>
<th>Aglossia or Hypoglossia</th>
<th>Micrognathia</th>
<th>Cleft Palate</th>
<th>Anomalies of Limbs</th>
<th>Other Anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosenthal (1932)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Median notch lower lip; abnormal teeth</td>
</tr>
<tr>
<td>Sinclair and McKay (1945)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Incomplete median upper hare lip</td>
</tr>
<tr>
<td>Pulford et al (1956)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Bony fusion of jaw; abnormal teeth</td>
</tr>
<tr>
<td>Shear (1956)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Labial adhesions; carilaginous fusion of jaw</td>
</tr>
<tr>
<td>Dekaban (1959)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Cartilaginous fusion of jaw</td>
</tr>
<tr>
<td>Pettersson (1961)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Abnormal teeth; lack of teeth</td>
</tr>
<tr>
<td>Kelin et al (1964)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Bony fusion of jaws; labial adhesions</td>
</tr>
<tr>
<td>Temtamy and McKusick (1969)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Chest deformity; mental retardation</td>
</tr>
<tr>
<td>Hoggins (1969/1970)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Cartilaginous fusion of jaw</td>
</tr>
<tr>
<td>Nevin et al (1970)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Median cleft lower lip; pectus excavatum; mental retardation</td>
</tr>
<tr>
<td>Harwin and Lorinsky (1970)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Bony fusion of jaw; abnormal teeth</td>
</tr>
<tr>
<td>Bernard et al (1971)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Abnormal teeth; lack of teeth</td>
</tr>
<tr>
<td>Cohen et al (1971)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Bony fusion of jaws; labial adhesions</td>
</tr>
<tr>
<td>Grislain et al (1971)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Cartilaginous fusion of jaw</td>
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<tr>
<td>Grislain et al (1971)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Abnormal teeth; lack of teeth</td>
</tr>
<tr>
<td>Hall (1971)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Abnormal teeth; lack of teeth</td>
</tr>
</tbody>
</table>

There were severe hand anomalies (Fig. 2); the thumb and fifth fingers were hypoplastic and the second, third, and fourth fingers especially on the left, were rudimentary. Radiographs (Fig. 3) showed absence of middle and distal phalanges of the second and third fingers and of the distal phalanx of the fourth finger. The middle phalanx of the fifth finger was markedly hypoplastic. The metacarpal and carpal bones were normal.

In the lower limbs the anomalies were below the knee —right hemimelia and syndactyly of the left second to fifth toes. Radiographs of the left foot showed fusion of the phalanges of the great toe and absence of middle phalanges of the second to fifth toes. The toe and fingernails were thickened and pitted (Fig. 2); a change observed only in the last six months.

Dermatoglyphics were abnormal. The dermal ridges

Fig. 2. Case 1. The dorsal aspects of the hands with severe digital anomalies.

Fig. 3. Case 1. Radiographs of the hands.
on the fourth fingers were 'off the edge' and arches and loops were present on the other fingers. The palmar abcd triradii were absent and the axial triradii (t) were distally placed. A vestige pattern was present in T/1 areas and carpal and ulnar loops in the left and right hypothenar areas, respectively.

Other clinical features were related to the cardiovascular system; an ejection systolic murmur in left parasternal area, blood pressure 18.6/13.3 kPa (140/100 mm Hg) and a grade IV retinopathy of fundi.

Investigations. These showed: haemoglobin 14.6 g/dl; total white cell count $8.0 \times 10^9$/l with a normal differential count; blood urea 5.5 mmol/l (33 mg/100 ml), total plasma proteins 78 g/l with normal electrophoresis, serum calcium and phosphorus were 2.5 and 0.7 mmol/l (10.4 and 2.6 mg/100 ml), respectively and urinary and plasma catecholamines 0.56 \mu mol/24 h (103 \mu g/24 h) and 0.7 \mu g/l, respectively. All these findings were unremarkable. Karyotype was of a normal male (46,XY). Fungus examination of nail clippings was negative. The ECG revealed ischaemic heart disease with T-wave flattening and inversion in leads II, III, aVF, and leads V3 to V6. An intravenous pyelogram and radiographs of the chest, skull, and mandible were normal.

Case 2. The patient, a 21-year-old male, born 22 February 1952, complained of loss of scalp hair. Examination also revealed an abnormally shaped tongue, and congenital anomalies of the hands and feet. He was the first born of a sibship of two. The parents were unrelated; the father was 36 years and the mother 30 years at the birth of the patient. Parents and a sister were normal. There were no orofacial or skeletal defects in the relatives. The patient had had a congenital bilateral paralysis of the external rectus muscle which had been corrected surgically.

The tongue was small and abnormally shaped with no defined tip, an irregular edge and no definitive junction with the floor of the mouth (Fig. 4). He was unable to protrude or touch his lips. Due to the absence of the tongue in the anterior part of the mouth the lower incisors were retroclined.

There were severe hand anomalies (Fig. 5); the thumb and fifth fingers were hypoplastic and the second, third, and fourth fingers, especially on the left, were rudimentary. On the radiographs (Fig. 6) the left second and third metacarpals were slightly smaller than normal. There were no phalanges of the index and middle fingers. A tapering proximal phalanx was present for the thumb, fourth and fifth digits but only in the latter there was a second phalanx, although this was small and abnormal. On the right, the metacarpals were of normal length, but the second metacarpal was slightly tapered distally. There were two short phalanges in the thumb; only one phalanx was present in the third and fourth fingers. There was no middle phalanx of the fourth and
only a small middle phalanx of the fifth finger. The terminal phalanx of the fourth finger was small. All the carpal bones were present, but there was fusion between the trapezoid and trapezium in each wrist and between the hamate and capitate in the left.

The toes were markedly deformed. Radiographs of the feet showed fusion of the right cuneiform bones. The first right metatarsal had a broad base and was tapered; the phalanges were rudimentary. The heads of the other metatarsal bones were hypoplastic with deformed rudimentary phalanges. On the left, the first, fourth, and fifth metatarsal bones were short. The phalanges of the toes were well formed. There was a varus deformity of the first metatarsal.

Dermatoglyphs showed arches on all fingers. The axial triradii \((t)\) were normally situated and the palmar triradii \((abcd)\) were normal. There was a bilateral simian crease.

Investigations. Karyotype was of a normal male \((46,XY)\). Radiograph of the skull was normal. WR, VDRL, and RPCFT were negative.

Comment

The term aglossia-adactylyia is misleading. Aglossia indicates total absence of the tongue which is rarely the case. Although a few cases have had an 'almost' total absence of the tongue (Rosenthal, 1932; Fulford, Ardan, and Kemp, 1956; Nevin et al, 1970; Cohen et al, 1971), hypoglossia is the usual finding. In the present cases the characteristic limb anomalies prompted a close examination of the tongue, which in both patients was small.

The limb anomalies are also extremely variable. Any limb may be involved and variability of the limb anomalies may be observed in the same individual as well as in different patients. In general, the anomalies of the upper limbs tend to be distal to the humerus; those of the lower limb distal to the femur. Hemimelia of the upper limbs and minor anomalies of the feet have been reported in the same patient (Gorlin and Pindborg, 1964; Cohen et al, 1971). Hemimelia of all four limbs was noted by Temtamy and McKusick (1969) while involvement of both left limbs with normal right limbs was reported by Nevin et al (1970). One patient had only syndactyly of the fingers with normal lower limbs (Fulford et al, 1956); while others had varying degrees of finger, hand, and foot anomalies (Rosenthal, 1932; Sinclair and McKay, 1945; Hall, 1971).

Although intelligence is usually normal in aglossia-adactylyia, Cohen et al (1971) have described a patient with mental retardation. In addition to the typical oral manifestations some patients have also had bony or cartilaginous fusion of the jaws (Pettersson, 1961; Temtamy and McKusick, 1969; Hoggins, 1969/1970; Bernard et al, 1971). One of our patients (case 1) had nail dysplasia, a change which had been present for only 6 months and was consistent with a traumatic aetiology. This patient, the oldest reported case of aglossia-adactylyia, although only aged 31 years had electrocardiographic evidence of ischaemic heart disease. In addition to the typical features of aglossia-adactylyia, our second patient (case 2) had congenital bilateral abducens paralysis, a finding which has never been previously observed in this syndrome. However, four patients with glossopalatine ankylosis had cranial nerve lesions; two with unilateral seventh nerve paralysis (Cosack, 1953), one with a bilateral seventh nerve paralysis (Spivack and Bennett, 1968), and one with an unilateral seventh and sixth nerve paralysis (Jurgenussen, 1948). The aetiology of the cranial nerve lesion is unknown.

Glossopalatine ankylosis has features somewhat similar to aglossia-adactylyia; there is usually micrognathia, hypoglossia or aglossia, cleft palate, and hypoplastic anomalies of one or more extremities but the presence of intraoral bands distinguishes it from aglossia-adactylyia. Spivack and Bennett (1968) who reviewed five cases of aglossia-adactylyia and 12 cases of glossopalatine ankylosis have suggested that these two syndromes may be related.

Several theories have been proposed to account for aglossia-adactylyia. Intrauterine environmental factors may be important (Gorlin and Pindborg, 1964). Torpin (1968) suggested that membranous strands produced by the rupture of the amnion in early pregnancy constrict or amputate limbs and may also produce oral anomalies due to the ingestion of amniotic strands which interfere with oral development. In one report the patient's mother had had oral and intramuscular Tigan and oral Bendicistine during the fourth to eighth weeks of gestation. Animal experiments and human observations with
these drugs failed to demonstrate an increase in the incidence of deformities (Hall, 1971).

A genetic basis for this syndrome is possible. A chromosomal basis is unlikely. Normal karyotypes have been recorded in at least six recent cases (Temtamy and McKusick, 1969; Nevin et al., 1970; Bernard et al., 1971; Grislain et al., 1971; Hall, 1971). Both the present cases had normal male chromosome constitutions. Autosomal recessive inheritance also appears unlikely as affected sibs and consanguinity has not been recorded in any family. Some authors have proposed autosomal dominant inheritance. Temtamy and McKusick (1969), found that in the families of seven patients with aglossia-adactylia or glosso-palatine ankylosis, some relatives had orofacial anomalies. In no instance were limb anomalies observed in a relative. These authors suggested that aglossia-adactylia were due to an autosomal dominant gene with extreme variability and reduced penetrance. As most cases are sporadic the condition may be due to a dominant mutant gene. The extreme variability of the syndrome indicates that aglossia-adactylia may be only one of an aetiological heterogeneous group.

The occurrence of three patients with aglossia-adactylia in the small community of Northern Ireland (population 1 550 000) indicates that this disorder is commoner than formerly realized. We suggest that the tongue should be closely examined in patients with limb anomalies. If aglossia or hypoglossia is present, than a detailed family history and examination of relatives should be undertaken and a thorough search made for possible genetic and/or intrauterine factors.

REFERENCES
Kettner, Dr. (1907). Kongenialitäten Zungendefekt. Deutsche Medizinische Wochenschriften, 33, 932.