NEUROFIBROMATOUS MACROGLOSSIA

By T. BIRD and G. O. CLARK* (Dundee)

MACROGLOSSIA due to neurofibroma is an uncommon condition. First described by Abbott and Shattock in 1903, it was discussed in more detail by Spencer and Cade in 1931, and again in 1952, with a review of the literature, by Ayres, Delaney and Blacker. Despite its rarity, the condition presents a clear clinical picture easily distinguishable from macroglossia due to the relatively commoner abnormalities, such as haemangioma, lymphangioma, or muscular hypertrophy.

CASE 1

The patient, a healthy, well-nourished girl of 9 years, was referred to hospital because of a painless, one-sided swelling of the tongue. Enlargement of the right side of the tongue was first noted by her mother when the child was 6 weeks old, at which time an operation for "tongue-tie" had been performed. The swelling had remained static in relative size, enlarging only with the rest of the tongue. There was no disability, and both eating and speaking were normal.

Examination of the mouth showed marked enlargement of the right side of the tongue, with roughness and granularity of the mucosa due to hypertrophy of the papillae. Posteriorly, the swelling ended sharply at the line of the circumvallate papillae, and medially it was bounded by the midline, except at the tip, where it spread, fanwise, to the left side (Fig. 1). It was firm, non-compressible and was not tender. The right submandibular salivary gland was enlarged, its duct was red and thickened and its opening patulous; despite this appearance of inflammation the gland was painless and freely mobile. This latter enlargement had been present, according to the mother, for about two years, and varied in size from time to time.

The left side of the tongue and mouth were normal, and no other swellings were found in the neck.

Physical examination revealed a slight degree of arachnodactyly, a few small café-au-lait spots near the left elbow, but no subcutaneous nodules of any kind. There was a loud systolic murmur in the third left intercostal space.

Radiographs of skull, skeleton, chest and right submandibular region showed bilateral cervical ribs and two fissures, thought to be developmental, in the anterior part of the mandible, but no other abnormality.

There is no family history of neurofibromatosis, and the patient's three siblings are all well.

A wedge was taken from the lingual swelling for microscopical examination. Bleeding was normal in amount and easily controlled by catgut suture.

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Pathological Report

A small wedge of tissue, 1 by 0·5 by 0·5 cms., fixed in formol-corrosive solution, and showing on section a white whorled surface. Paraffin sections were stained by haematoxylin and eosin, van Gieson, Gomori's trichrome, lissamine tartrazine, Loyez' stain for myelin, periodic acid Schiff, and Southgate's mucicarmine.

Microscopically, there are numerous convoluted fasciculi of hypertrophied nerve bundles which extend superficially to the epithelium and penetrate deeply into the muscle of the tongue. These fasciculi are composed of a vacuolated oedematous collagenous stroma, of moderate cellularity, surrounded by a lamellar sheath with the appearance of perineurium (Figs. 3 and 4). The stroma is only faintly eosinophilic and mucin cannot be demonstrated. Myelinated nerve fibres are present in many of the larger trunks (Fig. 5), and an occasional ganglion cell is seen among the proliferating Schwann cells (Fig. 6). There are no Verocay bodies or palisading of nuclei to suggest neurilemmoma. The tumour is not encapsulated, and although the enlarged nerve trunks penetrate deeply, the surrounding connective tissue and skeletal muscle show no changes apart from compression. The overlying epithelium appears normal. Necrosis is not seen and there is no evidence of malignancy.

Diagnosis: Plexiform Neuroma (Neurofibroma) of tongue.

CASE 2

The patient, a healthy boy of 3 years, was referred from his school clinic because of a painless one-sided swelling of the tongue. Enlargement of the left side of his tongue was first noted by the mother shortly after his birth, and no increase in size had since been seen. Although his speech was rather indistinct this was not considered to be due, in any significant degree, to the lingual swelling.

Examination of the mouth showed moderate enlargement of the left side of his tongue (Fig. 2), the overlying epithelium showing hypertrophy of the filiform papillae. The swelling extended to involve the right side, both at the tip and posteriorly near the foramen caecum, where it was bounded by the circumvallate papillae.

The submandibular salivary glands and the floor of the mouth were not involved. There were no swellings in the neck and complete examination revealed no evidence of cutaneous neurofibromatosis or any other abnormality. Radiographic examination of the skeleton was normal.

It was noted, however, that the boy's mother had several cutaneous nodules on the face, and further examination showed similar nodules in the skin of the chest, abdomen and back and scattered café-au-lait spots. These had been present for about 5 years, having first been noticed shortly after the birth of her first child. The patient's 2 siblings are normal and there is no further history of neurofibromatosis in the family.

A wedge was taken from the boy's tongue for microscopical examination, bleeding being easily controlled. The opportunity was also taken to remove a disfiguring nodule from the mother's chin.

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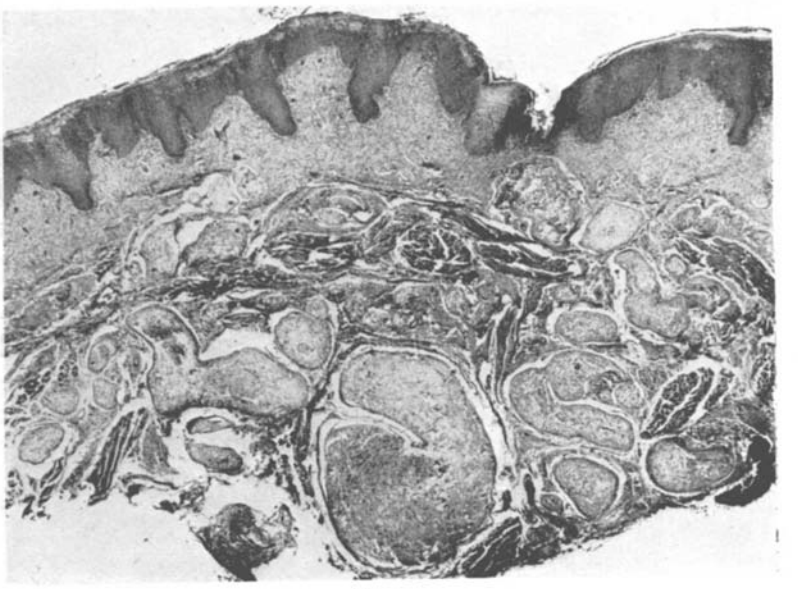


FIG. 3.
Case 1. To show general structure of lesion. H. and E. ×18.

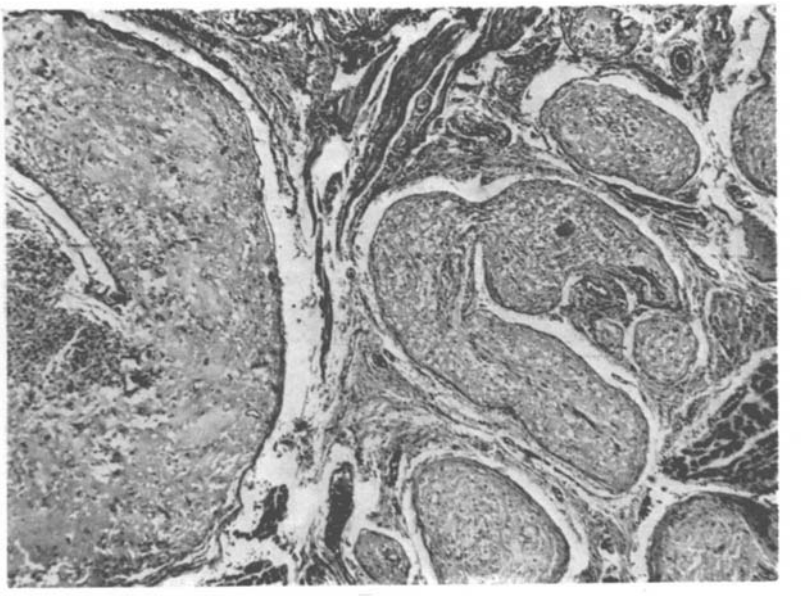


FIG. 4.
Case 1. Higher power view of Fig. 1. H. and E. ×64.

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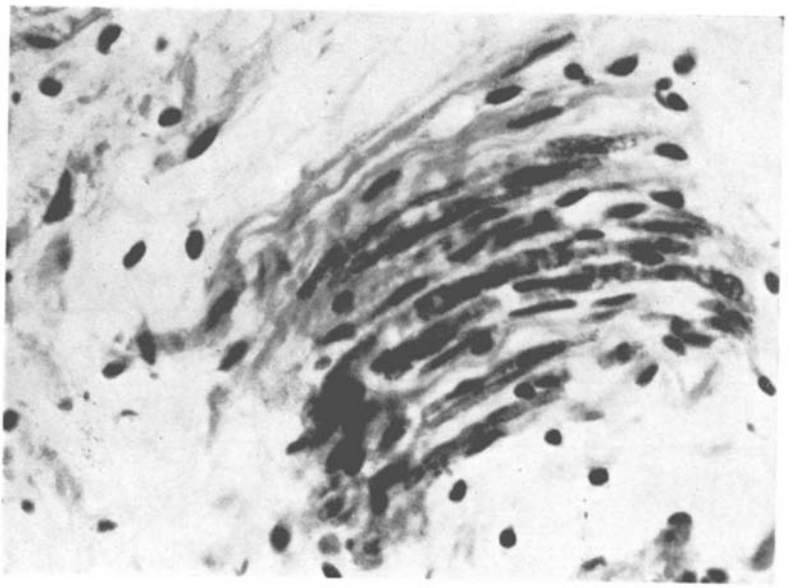


FIG. 5.
Case 1. Myelinated nerve fibres. Loyez ×360.

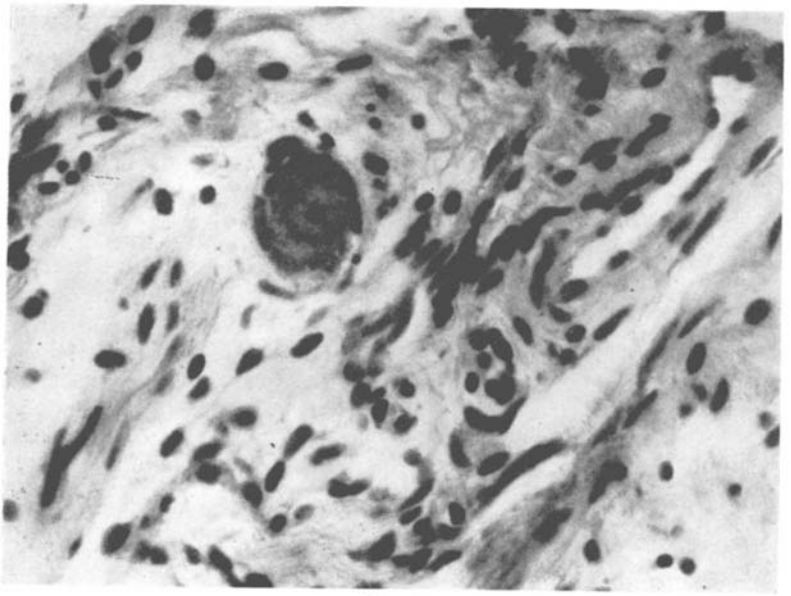


FIG. 6.
Case 1. Ganglion cell in enlarged nerve bundle. H. and E. ×400.

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Pathological report (*a*) *Tongue* (*b*) *Nodule from mother's chin.*

(*a*) A small wedge of tissue 1 by 0·5 by 0·5 cms. fixed in 10 per cent. formol saline, showing on section many small worm-like structures beneath a thickened epithelium. Paraffin sections were stained as in Case 1, while frozen sections were stained for nerve fibres by Bielschowsky's method.

Microscopically the appearances are essentially the same as in the first case, but the enlarged nerves are much less cellular, and contain fewer myelinated nerve fibres, lying in a more vacuolated, oedematous stroma (Fig. 7). Again,

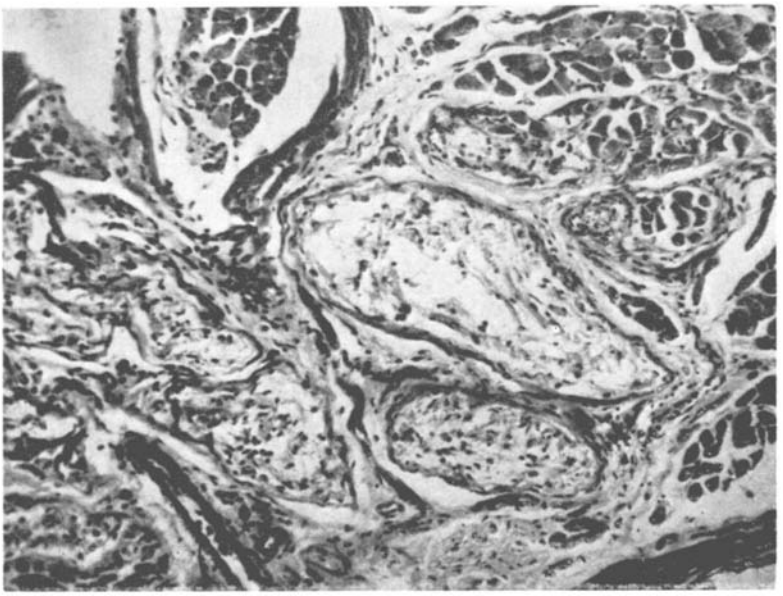


FIG. 7.
Case 2. Showing similar appearances to Case 1. Gomori Trichrome ×120.

occasional ganglion cells are seen in some of the enlarged trunks. The overlying epithelium is irregularly thickened and shows marked hyperkeratosis.

(*b*) A spherical skin-covered nodule 1 cm. in diameter. Microscopically a rather fibrous, poorly cellular tumour, with the appearance of a solid neurofibroma.

Discussion

The literature has been reviewed as recently as 1952 by Ayres *et al.*, who collected 11 cases and added another of their own. They fail to mention, however, Billington's case (1903) of neurofibroma of the right lingual nerve, present from the age of 5 years. Incomplete surgical removal was carried out twice; later the patient developed subcutaneous nodules and died aged 38, with neurofibromatous swellings on the spinal cord, lumbar and sacral nerve plexuses. Although this case is incompletely

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described, it would appear to be similar to the condition now being discussed, and, if acceptable, would make, with our cases, a total of 15 cases now reported.

All of the cases described have shown a macroglossia (often associated with hypertrophy of the lingual papillae) which is usually sharply defined and strictly unilateral. In contrast to this, the macroglossia due to angioma or muscular hypertrophy is usually diffuse, often larger, and not sharply confined to one side. The lesion is generally noticed at birth, a few in later infancy, and one (Spencer and Shattock, 1908) at the age of 22. There is a tendency for the enlargement to spread to the floor of the mouth, to involve the homolateral submandibular salivary gland, and even to extend widely into the neck, thus making complete excision impossible (Abbot and Shattock, 1903, Spencer and Shattock, 1908).

Of associated lesions subcutaneous neurofibromatosis, café-au-lait spots, or both, have occurred most commonly—in seven cases. In the absence of obvious neurofibromatosis, the observer may well be hesitant to accept a pale brown spot as important, and indeed we regard the spots in our case as of very doubtful significance. Concomitance of the macroglossia with congenital defects has been noted only twice; in our first case there is mild arachnodactyly, bilateral cervical ribs and a cardiac murmur of doubtful aetiology.

In all cases, the histological appearance has been that of non-encapsulated plexiform neuroma, consisting of hypertrophied tortuous nerve trunks containing myelinated axon cylinders, in an oedematous stroma, often with proliferation of Schwann cells. None of the cases have resembled the equally uncommon neurilemmoma of the tongue, which usually presents as a well-encapsulated tumour (Stout 1949, St. Clair Robertson 1952), and which, on histological examination shows regimentation of fibres, palisading of nuclei, tendency to cystic degeneration and absence of nerve fibres.

Spencer and Shattock (1908) demonstrated by dissection of their case that the nerves involved were the lingual, glossopharyngeal and hypoglossal. In our cases the nerve involved is almost certainly the lingual. In favour of this supposition is the sharp localization of the swelling to one side of the tongue, except at the tip, in both cases, and at the foramen caecum in case 2, sites where it has been shown (Hovelacque, 1927) that there is, in fact, a spread of the normal lingual nerves across the midline. It may also be noted that the lingual nerve gives some fibres to the submandibular salivary gland. The abrupt termination of the swelling posteriorly at the sulcus terminalis again favours the lingual nerve as the site of origin.

Stout (1949) states that neurofibromata containing ganglion cells are exceedingly rare, but ganglion cells in enlarged nerve trunks have been demonstrated in both our cases, and have been reported in two of the

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previous cases. Abbott and Shattock (1903) believe that ganglion cells are found only if the glossopharyngeal nerve is involved, but it is now known that they may occur within nerve bundles in the normal mammalian tongue (Gairns and Garven, 1952). This probably accounts for the relative frequency of ganglion cells in neurofibroma of the tongue.

Although 12 of the 13 cases previously reported have been treated by excision, complete removal is usually impossible, and recurrence is frequent (Ayres *et al.*, 1952). There would seem to be a possibility of malignant change, especially after repeated operations, but unfortunately few cases have been followed for more than a year or two. In addition, other neurofibromatous areas may occur in the nerves proximal to the superficial lesion (Abbott and Shattock, 1903) and Stout (1949) notes that plexiform neuroma may progress centripetally along a peripheral nerve to reach the central nervous system, usually the spinal cord, and cause death thereby, although the tissue may show no evidence of malignant change.

It is felt that any attempt at excision is contra-indicated in our cases. There is at present no interference with function, and excision in the reported cases has been extremely difficult or impossible owing to involvement of the tissues of the floor of the mouth—almost certainly present in the first of our cases. Excision would appear to be feasible in the second case, but in the absence of symptoms we prefer to wait and observe.

As we have now seen two cases during the past four months, it is felt that neurofibromatous macroglossia is perhaps not of such great rarity as the small number of reported cases would indicate. The condition of the tongue in the second case was not so striking, and we feel that the diagnosis might well have been overlooked if the first case had not already been seen.

Summary

Two cases are described of macroglossia due to plexiform neuroma (neurofibroma), and attention is drawn to the clinical picture of firm, unilateral enlargement of the tongue, noticed usually at birth or in infancy, and sometimes associated with generalized neurofibromatosis and café-au-lait spots.

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