Familial Jaw Cysts in Charcot-Marie-Tooth Disease*

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Charcot-Marie-Tooth disease is a relatively benign inherited neurological disorder (Bell, 1935). Clearly affected subjects have slowly progressive weakness and atrophy of certain distal muscle groups; within an affected family others who carry the gene may show only minor or insignificant clinical abnormalities, such as pes cavus, slight weakness of foot dorsi-flexion, or absence of the Achilles tendon reflex. Both the obvious and the minimally symptomatic carriers of the gene have a low peripheral nerve conduction velocity (Dyck, Lambert, and Mulder, 1963), and the ease of confirming the diagnosis by objective electrophysiological measurement of nerve conduction velocity has enabled several investigators to compile and report large pedigrees (Dyck *et al.*, 1963; Myrianthopoulos *et al.*, 1964).

Recurrent, multiple jaw cysts are known to occur in family clusters (Thoma and Blumenthal, 1946). They are also a prominent clinical feature of the naevoid basal cell syndrome, in which multiple basal cell carcinomas occur in patients with a variety of skeletal and connective tissue abnormalities, including a distinctive lamellar calcification of the falx cerebri (Pollard and New, 1964). The naevoid basal cell syndrome is transmitted in a Mendelian autosomal dominant pattern (Anderson *et al.*, 1967).

We report here a family in which jaw cysts and early lamellar calcification of the falx are associated with Charcot-Marie-Tooth disease.

Subjects and Methods

The family studied contains 29 living members who are over 18 years of age and at risk to carry the gene. Of these, 24 were examined by us and 23 had measurements of peripheral nerve conduction velocities by established clinical electrodiagnostic methods. Skull x-rays of 16 subjects and jaw x-rays of 11 were reviewed by us. The pedigree is shown in the Fig.

Results

Of the 29 living family members studied, 16 were found to have evidence of Charcot-Marie-Tooth disease on clinical and electrodiagnostic grounds. III.5 had definite evidence of the syndrome when he was examined by us before he died, and III.6, who died before this family study was begun, had, on the report of physicians and family members, the physical gait and grip difficulties. We considered V.4 a probable case at age 21, because he showed slight weakness in dorsi-flexing his feet and had nerve conduction velocities in the leg at or just below the lower limit of normal. Heavy lamellar calcification of the falx was visible on skull x-rays of 4 affected subjects: III.6, IV.9, IV.8, and V.3. In the propositus, V.3, the calcification was easily seen in an x-ray taken when she was 12 years old. Though faint falx calcification was found in several other carriers of various ages, only one other carrier, IV.16, showed, at age 45, moderately heavy lamellar calcification of the falx. No such lamellar calcification was seen in the x-ray of family members unaffected by Charcot-Marie-Tooth disease.

The propositus, V.3, had her first of eight operations for symptomatic jaw cysts when she was 8 years old. Her father, IV.8, had an operation for a large multilocular cyst of the mandible at age 45; her uncle, IV.9, had a small cyst of the mandible noted on x-ray at age 48; her aunt, IV.10, had three cysts removed from the mandible and maxilla; and her grandmother, III.6, was operated for three distinct cysts in the mandible at age 62. The cysts were all characterized pathologically as dentigerous. No other jaw cysts were found in the remainder of the family, either by history or on a survey of jaw x-rays. The x-ray appearance of both the falx calcification and the jaw cysts is indistinguishable from that seen in subjects affected with the naevoid basal cell syndrome.

Discussion

Diverse non-neurological abnormalities occur in patients with any one of many hereditary

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FIG. Pedigree of the family.

neurological syndromes (Bell, 1935), but the association of Charcot-Marie-Tooth disease, multiple jaw cysts, and early lamellar calcification of the falx cerebri has not been reported previously. The association of these clinical findings could be fortuitous in the family reported here, or could be a consequence of the pleomorphic effects of a single gene segregating in this family. While a plaque or button-like calcification of the falx is seen in as many as 7% of the general population (Dyke, 1930), the type of lamellar calcification observed in our patients is rare (Anderson *et al.*, 1967). The appearance of heavy calcification at 12 years of age, as in the proband, is also remarkable. Falx calcification occurs with unusually high frequency in the naevoid basal cell syndrome (Pollard and New, 1964), in other hereditary disorders in which there is an abnormal response to parathyroid hormone, and occasionally in Gardner's syndrome.

Almost all familial cases of jaw cysts have been described as occurring in conjunction with manifestations of the naevoid basal cell syndrome. In families which exhibit the naevoid basal cell syndrome, the jaw cysts are reported often to precede the naevi by several or many years (Anderson *et al.*, 1967). There is no way of knowing at the present time whether epidermal signs of the naevoid basal cell syndrome will appear at some time in the future in members of the family described here.

In each family in which mildly affected carriers of the Charcot-Marie-Tooth gene were sought through

careful clinical examinations and measurements of peripheral nerve conduction velocity, the inheritance was found to be autosomal dominant (Dyck *et al.*, 1963; Myrianthopoulos *et al.*, 1964). The same clinical and electrodiagnostic criteria have not been used in constructing those pedigrees cited as examples of autosomal recessive, X-linked dominant, or X-linked recessive inheritance (Pratt, 1967). If V.4 has the disease, as we think he does, the present family demonstrates autosomal dominant inheritance. If he is not affected, then the pedigree contains no instances of male-male transmission and is compatible with either autosomal dominant or X-linked dominant inheritance.

Summary

Multiple recurrent jaw cysts and lamellar calcification of the falx cerebri have been found in several affected members of a large kindred with Charcot-Marie-Tooth disease.

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