Palmoplantar keratoderma, nail dystrophy, and hereditary motor and sensory neuropathy: an autosomal dominant trait

J L TOLMIE*, D E WILCOX*, R McWILLIAM†, A ASSINDI†, AND J B P STEPHENSON†

From *the Duncan Guthrie Institute of Medical Genetics, and †Fraser of Allander Unit of Paediatric Neurology, The Royal Hospital for Sick Children, Glasgow G3 8SJ.

SUMMARY Autosomal dominant inheritance of a syndrome comprising palmoplantar keratoderma, nail dystrophy, and hereditary motor and sensory neuropathy (HMSN) was observed in three generations of one family. Nail dystrophy affected the toe and fingernails; it was present at birth or developed during early childhood. Palmoplantar keratoderma became apparent in later childhood. Each subject with nail dystrophy and keratoderma also had clinical or electrophysiological evidence of axonal neuropathy.

Extensive genetic heterogeneity is present in the hereditary motor and sensory neuropathies (HMSN) and palmoplantar keratodermas (PPK). They occur as dominant, recessive, or sex linked traits, and also with other abnormalities in a variety of rare inherited syndromes.1 2 We report a Scottish family in which an autosomal dominant syndrome of nail dystrophy, HMSN, and PPK is segregating.

Case reports

The proband (V.1, fig 1) first walked at the age of 17 months. Her gait was unusual and lower limb spasticity was thought to be present. Plantar fas-

FIG 1 Family pedigree. A horizontal bar above the symbol denotes subjects clinically assessed by the authors. It was not possible to ascertain who was affected in the first generation.
Palmoplantar keratoderma, nail dystrophy, and hereditary motor and sensory neuropathy

Palmoplantar keratoderma, nail dystrophy, and hereditary motor and sensory neuropathy were performed at the age of four years. By the age of eight years talipes equinovarus was present. Bilateral Steindler procedures were unsuccessful in lengthening the arches of her feet. Nail dystrophy and PPK were noted at three years and 10 years respectively. Examination at the age of 15 years showed clinically normal sensory function, absent knee jerks, retained ankle jerks, and extensor plantar responses, but no spasticity was detected. The sensory nerve action potential (SAP) was undetectable in the sural nerve. The motor nerve conduction velocity (MNCV) could not be estimated because the common peroneal nerve was not able to be stimulated at an acceptable amplitude level. Muscle biopsies were obtained from both feet and histochemical examination showed many fibres in large areas to be of a single fibre type, implying extensive reinnervation after partial denervation.

II.2, III.3, and III.4 were reported to have had keratoderma and nail dystrophy. II.2 and III.3 were remembered as having suffered cramping muscular pains in their calves at night. None of these persons was thought to have had signs of motor disability during life.

III.2 was examined at the age of 56 years. She developed dry, thickened skin on her palms and soles with horizontal cracks on the outer third of the palmar creases at around 12 years of age. Her nails were thickened with pitting and vertical ridging which was less severe than in her son, IV.2. Her gait was normal and there was no muscle wasting, but she had mild pes cavus deformity and reduced ankle jerks. Sensory testing was normal, ankle jerks were diminished, and plantar responses were flexor. The SAP was absent in the median, ulnar, and sural nerves; MNCVs were 41 and 44 m/sec in the common peroneal and ulnar nerves.

IV.2 attended hospital during childhood because of intoeing which corrected spontaneously. Palmoplantar keratoderma and nail dystrophy were noted in early childhood. At the age of 40 years he has mild pes cavus, keratoderma with circular callosities on his soles and palms, and severely dystrophic nails with painful, longitudinal cracks (fig 2). His knee

![Nail dystrophy and keratoderma affecting subject IV.2.](http://jmg.bmj.com/)

Fig 2: Nail dystrophy and keratoderma affecting subject IV.2.
nerve was 45 m/sec. A muscle biopsy at the time of open reduction of her hip was normal in appearance.

**Other Investigations**

Normal Giemsa banded karyotypes were obtained from peripheral blood lymphocytes of subjects IV.2 and V.1. Flow karyotypes were also normal from IV.2, his healthy spouse, and their affected daughter. Two clinically unaffected adults, IV.1 and IV.3, had nerve conduction studies performed which gave normal results. Unaffected children were not subjected to electrophysiological tests.

**Discussion**

The syndrome exhibits variable expression. At the age of 60 years II.2 had no symptoms attributable to her neuropathy but moderately severe pes cavus was present in her son and nephew. Walking was not significantly impaired in these persons. Nail dystrophy was documented at birth in V.8, while the youngest age at which keratoderma was noted was six years. The nail dystrophy was most severe in IV.2 (fig 2) where its clinical appearance and quality suggested lichen planus. However, a nail biopsy, including matrix tissue, was not considered justified to investigate this. The keratoderma comprised punctate lesions on abnormal surrounding skin. It is worth noting that punctate keratoderma and nail dystrophy without HMSN is a recognised autosomal dominant trait.

The marginal slowing of MNCV with absence of SAP in asymptomatic and symptomatic affected subjects, the neuropathic EMG in IV.4, and the muscle biopsy findings in V.1 strongly suggest an underlying axonal neuropathy. The clinical evidence
of pyramidal tract dysfunction in cases V-1 and IV-2 was interesting as it suggests the syndrome of peroneal muscular dystrophy with pyramidal signs, a distinct autosomal dominant trait not known to be associated with dermatological abnormalities.

A similar autosomal dominant condition to the one reported here was present in an Italian family with palmoplantar keratoderma and Charcot-Marie-Tooth disease. The clinical and electrophysiological findings were thought to indicate an axonal neuropathy. However, nail dystrophy was not noted in that report whereas it was a constant finding among the affected subjects we examined. We therefore believe that these conditions are distinct.

Two families have been described in which keratoderma and spastic paraplegia were inherited together. The first comprised four brothers with mental retardation, spastic paraplegia, pes cavus, striate keratoderma of the palms, and diffuse hyperkeratosis of the soles. The normally intelligent mother of these men had abnormal nails, hyperkeratosis of the soles, and slight clawing of the toes; sex linked inheritance was thought likely. Nerve conduction studies were not reported.

In the second family, autosomal dominant inheritance of a distinctive keratoderma with spastic paraplegia occurred. Extensor plantar responses and increased reflexes were present and focal hyperkeratotic papulonodules were present on the palms and soles. Nail dystrophy was not noted in any persons; thus we feel that on available evidence this condition is distinct from the one we report.

We thank Professor Rona MacKie of the Department of Dermatology, the University of Glasgow, and Dr Andrew Weir of the Institute of Neurological Sciences, Glasgow, for advice; and Dr David Doyle of The Institute of Neurological Sciences, for interpreting the muscle biopsies.

References


Correspondence and requests for reprints to Dr J L Tolmie, Duncan Guthrie Institute of Medical Genetics, Yorkhill, Glasgow G3 8SJ.
Palmoplantar keratoderma, nail dystrophy, and hereditary motor and sensory neuropathy: an autosomal dominant trait.

J L Tolmie, D E Wilcox, R McWilliam, A Assindi and J B Stephenson

doi: 10.1136/jmg.25.11.754

Updated information and services can be found at:
http://jmg.bmj.com/content/25/11/754

These include:

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/