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Peripheral Neuropathy: An Unrecognized Feature of Hereditary Vitreoretinal Degeneration?

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Autosomal-dominant inherited vitreoretinal degeneration (VRD), first described by Wagner [1] in 1938, is characterized by myopia, cataract and degenerative changes of the vitreous and the retina. Later, Jansen [2] observed two families with additional reti-noschisis and retinal detachment. Systemic manifestations associated with VRD including marfanoid habitus, premature degenerative arthropathy, facial clefting and sensorineural deafness were described by Stickler and co-workers [3, 4]. Maumenee [5] separated VRD into group I consisting of Wagner’s and Janson’s disease and group II, VRD with systemic anomalies such as Stickler’s syndrome.

We report here on three members of a family with hereditary VRD associated with peripheral neuropathy. A 39-year-old woman complained of progressive visual loss in her right eye over a 3-month period. Her corrected visual acuity was 20/400 in the right and 20/50 in the left eye. The ophthalmologic findings have been reported in detail [6]. Medical history was unremarkable in all available members of the family over three generations, except for patient R.M. In addition to her visual problems, she reported nocturnal tingling sensations in both feet and an unsteady gait during darkness. She had clinodactyly of both 5th fingers, thin terminal phalanges and asymmetry of the ears, but there was no joint laxity, arachnodactyly, hyperelastic skin or cleft palate. Neurologic examination revealed a distal hyp- and dysesthesia of a ‘stocking glove’ distribution, which was mild at the upper and more pronounced at the lower extremities. She had difficulties to identify different toe positions and the vibration sense was diminished in the lower extremities. There was unsteadiness of standing and gait with closed eyes. The muscle reflexes were weak but could be symmetrically elicited and the Babinski’s sign was negative. Her son also had a ‘stocking glove’ hypesthesia of the upper and lower extremities. The daughter had bilateral distal hypestheia of the lower extremities only. Laboratory investigations including ESR, red and white blood cell count, electrophoresis, immunoelectrophoresis, urea, electrolytes, liver function tests, blood sugar, cryoglobulins, lipids, apolipoproteins, vitamins B₆ and B₁₂, folic acid, thyroid hormones, porphyrines, antinuclear antibodies, rheuma factors, serological screening for *Borrelia burgdorferii* antibodies and virus titers, plasma phytanic acid and heavy metals (Hg, Pb, Cd in 24-hour urine samples and plasma) were all within the normal range. Chromosome analysis (Q and G banding) of the mother and both children revealed normal karyotypes. X-ray scans were taken of the skull, vertebral column, pelvis, hands, knees, ankles and feet of the mother and showed bilateral hallux valgus, an additional carpal ossicle and mild degenerative changes of the sacroiliacal and hip joints. MR scans of the brain were normal in the mother and both children. Electrophysiologic tests consisted of motor and sensory nerve conduction velocity (ENG) and needle electromyography (EMG) of at least four muscles. Patient R.M. had diminished nerve conduction velocity (38 m/s) of the sural nerve (normal range 48–65 m/s) and EMG yielded polyphase motor unit action potentials (MUAPs) in both extensor hallucis longus muscles (fig. 1). ENG of

Fig. 1. Needle electromyogram of the left extensor hallucis muscle in patient R.M. shows a polyphasic MUAP.

the son revealed a diminished amplitude (5 uV, normal values >10uV) and a normal velocity over the peroneal nerve. EMG showed polyphase MUAPs in the anterior tibial muscles.

Patients who suffer from hereditary VRD rarely come to the attention of neurologists because the disease was previously thought to spare the nervous system. An association of VRD with systemic connective tissue abnormalities has been reported [3], but our patients had no indication of Marfan’s syndrome, Ehler’s Danlos syndrome, Pierre Robin sequence or related diseases. Recently, molecular genetic evaluation in Stickler pedigrees revealed a mutation in the procollagen gene [7]. The mutation causes a truncation of the procollagen II a-chains which may lead to a disturbed organisation of the a-chains to triple helical collagen molecules. These facts could explain a destabilisation and liquefaction of the vitreous gel in hereditary VRD and the presence of type II collagen in hyaline cartilage [8] and neuroretinal tissues [9] could explain the skeletal, vitreal and retinal changes in Stickler’s syndrome. A translocation t5;17 (q15;q23) was described to seggregate with Stickler’s disease [10]. In our family, no chromosomal abnormalities were present. It is still unclear whether the disease starts with a primary regression of the vitreous or if neuroretinal dystrophic changes precede the vitreal abnormalities. The presence of peripheral neuropathy in our VRD pedigree is of interest as it puts further weight on the assumption that VRD may not only be associated with connective tissue changes but also with ectodermal abnormalities. The neurologic symptoms and electrophysiologic findings in our family were least prominent in the daughter and more severe in the mother, as were the ocular findings. This would be compatible with a slowly progressing genetic neuropathy. Although our patients refused CSF examination and nerve biopsy, the observation suggests that peripheral ner-

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vous system involvement might be a previously unrecognized feature of hereditary **VRD** with systemic involvement. A common etiology cannot be proven based upon the observation of a single family, but the observation should encourage systematic neurological investigations in patients with hereditary **VRD**.

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