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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 retinoschisis 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 $B_6$ and $B_{12}$, 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 the son revealed a diminished amplitude (5 μV, normal values >10 μV) and a normal velocity over the peroneal nerve. EMG showed polyphase MUAPs in the anterior tibial muscles.

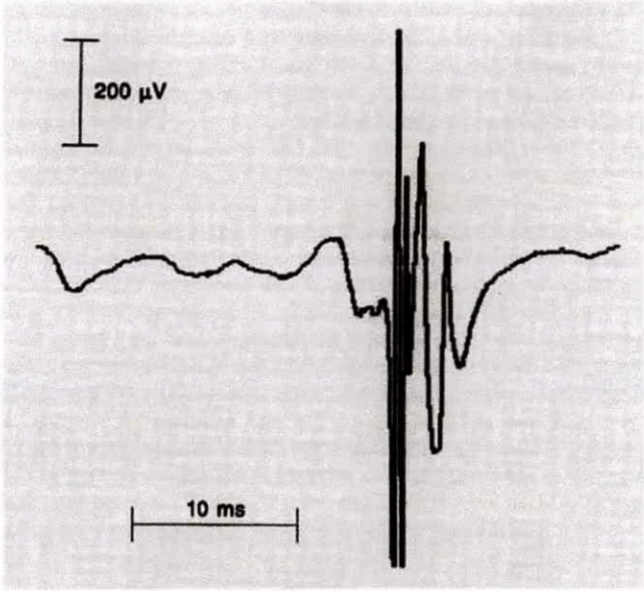


**Fig. 1.** Needle electromyogram of the left extensor hallucis muscle in patient R.M. shows a polyphasic MUAP.

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 α-chains which may lead to a disturbed organisation of the α-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-

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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## The Alien Grasp Reflex


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Following brain damage a number of primitive reflexes emerge including a group of prehensile movements, the most common being the grasp reflex [1, 2]. We report a case in which a profound grasp reflex, of which the patient was consciously aware, formed the main presenting complaint.

A 56-year-old right-handed female presented with a 2-month history of functional impairment of the left hand. Her main complaint was of being 'unable to let go of things'. This was most apparent as an inability to release grip with her left hand on objects such as door handles. Attempting to pull the hand away merely increased grip strength such that she would have to prize her fingers off the handle with the other hand. In other situations such as tying up rubbish bags, the left hand would tenaciously grip the bag and prevent release until the fingers were forcibly opened by the other hand. She had a flat affect with an expressionless face and a left-sided facial weakness. Limb tone was increased on the left with lead-pipe rigidity, pyramidal weakness, brisk reflexes, an extensor plantar and a 4–6 Hz resting tremor. Bilateral grasp reflexes were present, the left being profound. Even with an examiner resting two static fingers in the grasping hand, the patient was unable to relax her grip and release the fingers to command. Attempting to withdraw the fingers from the patient's hand increased the grasp intensity. There were bilateral palmomental and foot grasp reflexes. Assessment on general intellectual ability (WAIS-R) and a range of focal cognitive tests revealed a verbal IQ of 82 and performance IQ 80, reflecting a mild degree of general intellectual deterioration. Language, visual perceptual and memory skills were normal. Generation of words on fluency tests was adequate but she gave concrete interpretations to common proverbs. Her responses on a test of cognitive estimation were below normal limits. She had considerable difficulty with a Stroop task. Thus, the most notable feature of her neuropsychological assessment was her impaired performance on tests of frontal lobe executive function. A CT brain scan was obtained (fig. 1) and a diagnostic aspiration biopsy was performed. Histology of the lesion was that of an anaplastic oligodendroglioma. After surgery she received a radical course of radiotherapy receiving 60 cGy in 30 fractions over 6 weeks. Following treatment her affect noticeably improved. Her tremor ceased but mild residual left-sided pyramidal weakness persisted. Although the primitive reflexes persisted, the left grasp was much less marked. Postoperatively the character of the grasp reflex had changed in that she was able to release the grip of her left hand voluntarily, exhibiting characteristics of a classical grasp reflex.

The presence of a grasp reflex, in full consciousness, indicates cerebral disease with damage characteristically occurring in either

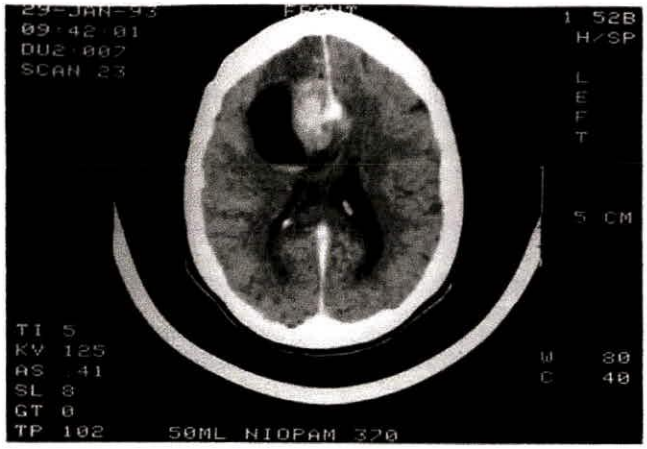


**Fig. 1.** Contrast-enhanced CT brain scan. There is a large ill-defined enhancing noncalcified cavitating mass lesion in the right frontal lobe, with enhancement of the medial border. Midline shift with spread of the mass across the falx and into the left region is seen.

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# Report on the Symposium "Neurology and Public Health in Europe", organized by the WHO and the EFNS, Marseille, 15 September 1995

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The symposium "Neurology and Public Health in Europe" was organized by the Unit of Neuroscience, Division of Mental Health, of the WHO (Acting Chief Dr L. Prilipko) and by the EFNS, Task Force on European Cooperation (Chairman Professor Dr F. Gerstenbrand). The purpose of the meeting was to gather further information on the organization of the medical speciality of neurology within each European public health system, including patient care, therapeutic and diagnostic possibilities for neurological diseases, organizational structures of neurological hospitals and neurological departments, postgraduate medical education for specialists, and the fee system. The symposium was held within the framework of the global initiative of the WHO "Neurology and Public Health", which aims at drawing the attention of the general public and all those involved in health care to the great importance of neurological diseases. The initiative will be carried out in several phases. The first phase concentrates on the development of a knowledge base on the current situation in the different European countries. So far, 11 workshops have taken place, one of them within the framework of the EFNS Congress in Berlin (December 1993) on neurological management in German-speaking and East European countries.

All European ministries of health were informed about the organization of the symposium in Marseille. The Swedish ministry sent a delegate. Several European ministries asked for a final report.

Professor Dr F. Gerstenbrand reported on the increasing neurological tasks in health care and stressed that, thanks to modern neurodiagnostic techniques and results in basic research, ranging from neurobiochemistry to genetics, neurology has new possibilities for the treatment of neurological disorders. Whereas, in former times neurology was mainly concerned with the medical management of chronic diseases, it has developed into one of the most important medical specialities, with possibilities for rehabilitation and restoration even after very severe illnesses. Some 15–20% of all patients suffer from a primary neurological disease, a further 20% present neurological complications due to their basic disease. The institutions for medical management of neurological patients have to be widely extended; this is true for acute management as well as for neurorehabilitation.

The papers presented at the symposium showed that there is a considerable difference in the medical management of neurological patients due to the differing organization of the public health system in the various European countries. Dr Godwin-Austin reported that in the English system patient management is normally overseen by the general practitioner and in the hospital by the general physician. The neurological patient can be referred by the general practitioner or the general physician to the neurological consultant; the referring physician is responsible for therapy and follow-up treatment. A continuous monitoring by the consultant neurologist is possible.

The report of Professor Binder on neurological management in Austria showed that in the Austrian system the neurological specialist and the neurological departments are responsible for the neurological patient during the acute stage, follow-up treatment in the hospital, as well as during outpatient after-treatment. If necessary, cooperation with other medical specialities as well as the general practitioner is possible. The neurological management in central European countries such as Slovenia and the Slovak Republic is very similar.

In several European countries neurology shares the responsibility for the neurological patient with neighbouring specialities such as neurosurgery and internal medicine, and the consultant system plays a minor role. So far, in most of the European countries a considerable number of neurological patients have been treated at non-neurological departments or at departments without adequate facilities or experience. This concerns, in particular, patients after a stroke, the most frequent neurological

illness with a very high death rate. It is well known that stroke patients who are not treated at specialized departments have longer hospitalization periods and poorer treatment results. Also for other neurological illnesses, especially brain injury and spinal cord injury, the question of who should be responsible for treatment has not been satisfactorily answered.

Speakers from Italy, Slovenia, Slovakia and Croatia reported on the neurological service and the existing neurological institutions in their countries. A paper by Dr Kirbas, Turkey, was at hand and excerpts from it were read. In the general discussion Professor Vereshchagin spoke about neurology in Russia, and Docent Kalvach about the neurological service in the Czech Republic. Further discussion remarks were made by Dr Olsson, the Swedish delegate, Dr Aarli from Norway, Professor Davaki, the Greek delegate and Dr Kruja, the delegate from Albania.

It was stressed that the establishment of a European database is necessary and should be achieved in co-operation between EFNS and WHO.

Several national delegates reported on the post-graduate education system for specialists in neurology. There are remarkable differences due to the different goals of post-graduate education, either training for the work of a consultant or for the position of the head of a neurological department or clinic with direct responsibility for the patient during acute and follow-up phases. The number of neurological practitioners varies widely between the different European countries: approximately 200 in Great Britain, 600 in Austria, 2000 in Italy, and 10,000 in Russia. In relation to the population, the number of neurologists is especially high in Slovakia.

The duration of post-graduate education and the curriculum differ widely. In the EU-countries, a final examination is required after a minimum of 4 years training in neurology and additional training in internal medicine and other specialities related to neurology, with a total of 6 years.

Neurological hospitals or neurological departments at general hospitals exist in most European countries. The number of available neurological beds, however, does not meet the demand. Considerable improvements are needed in the field of neurorehabilitation. In most cases, neurorehabilitation is carried out in combination with rehabilitation for other diseases. There are only very few centres for neurorehabilitation, especially for patients after brain injury. Several European countries, e.g. Austria and Turkey, have graduated plans for the enlargement and improvement of neurological departments and other neurological services, but their implementation depends on the economic conditions. In Turkey, the first of three phases, i.e. the creation of independent neurological departments, has already been started.

Professor Federico of Italy reported on neurological projects sponsored by the EU. The possibility of submitting project proposals was discussed and it was pointed out that the EFNS organizes workshops providing information about application procedures chaired by Professor Amaducci of Florence, chairman of the EFNS Committee on European Affairs.

Professor Gerstenbrand presented the activities planned by the EFNS with a view to extending and improving neurological services in Europe. He reported on the newly established Task Force for European Co-operation of the EFNS, of which he was appointed chairman. The primary requirement is the establishment of a database of existing neurological services in the different European countries, including departments for acute treatment, follow-up and neurorehabilitation as well as research centres and their fields of interest with possibilities for co-ordination and consultation between neurological departments and research centres. It was stressed that close co-operation between related specialities, above all with neurosurgery, but also with internal medicine, is necessary. Furthermore, there is an urgent demand for specialized neurological units, e.g. for neurointensive care, which should be available at each major neurological department.

It is the joint intention of the EFNS and WHO to co-operate with other European institutions for the purpose of standardization and harmonization of post-graduate training and continuing medical education systems in all European countries. Furthermore, the EFNS wants to co-operate with European and non-European neurological institutions in arranging post-graduate education opportunities in subfields of neurology.

In his paper concerning WHO activities in the field of neuroscience, Dr Prilipko placed particular emphasis on the already existing advancement programme in the field of psychiatry and the current efforts in order to strengthen the WHO activities in the area of neurology. The Unit of Neuroscience of the WHO is developing programmes for international projects for the global registration of neurological diseases. The WHO Unit of Neuroscience is interested in a close co-operation with the EFNS regarding the enlargement and improvement of neurological services; future joint activities are planned.

It was decided to elaborate and publish a joint report on the proceedings of the symposium. The abstracts of the reports and discussion remarks will be used to prepare a joint report which will be sent to the ministries of health in the different European countries.

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