Peripheral nerve involvement in Batten-Spielmeyer-Vogt's disease¹

BIRGIT BLATT LYON

From the Department of Clinical Neurophysiology,
Copenhagen County Hospital at Gentofte, Denmark

SYNOPSIS Electromyography and sensory and motor nerve conduction were studied in 23 patients with Batten-Spielmeyer-Vogt's disease ('juvenile amaurotic idiocy', cerebral ceroidlipofuscinosis). A slight to moderate slowing of the sensory conduction velocity was found in the median as well as in the sural nerve, more pronounced in the distal than in the proximal segments. The findings are interpreted as evidence of impaired transmission of the peripheral nerves in Batten-Spielmeyer-Vogt's disease.

Electrophysiological studies of patients with Batten-Spielmeyer-Vogt's disease have mainly and justly concentrated on the central nervous system and the eyes, and have accordingly been studies of the electroencephalogram, the evoked cortical responses, or the electroretinogram. Pathological and biochemical investigations have, however, demonstrated signs of more generalized pathological features (Carpenter *et al.*, 1972; Joosten *et al.*, 1973; Rapola and

Haltia, 1973). This study was undertaken to evaluate the functional involvement of peripheral nerves and muscle in this disease.

METHODS

PATIENTS The patients examined were all the known living patients with Batten-Spielmeyer-Vogt's disease in Denmark. There were 23 patients in all, belonging to 16 families with a total of 45 children. The diagnosis was established by the clinical signs accompanied by a decrease or lack of electroretinogram and the presence of an increased amount of vacuolized lymphocytes in the blood. At the time of the electro-

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FIG. 1 Clinical findings in 23 patients with Batten-Spielmeyer-Vogt's disease at the time of electrophysiological examination for peripheral nerve involvement.

physiological examination for peripheral nerve involvement their age range was 5 to 19 years (average 13 years). The clinical findings are summarized in Fig. 1.

TECHNIQUE A three channel electromyograph with photographic recording from a cathode-ray oscilloscope was used (DISA type 14 A 30). Electromyography was performed with concentric needle electrodes 0.65 mm in diameter with an inner platinum core of 0.07 mm² surface, in the anterior tibial muscle. The following electromyographic parameters were determined: (1) the pattern during maximal voluntary effort (when the patient's mental status did not permit cooperation for voluntary maximal contraction, the anterior tibial muscle was brought to contraction by plantar pin-prick stimulation); (2) the occurrence of spontaneous activity of short duration outside the endplate zone; (3) the mean duration of 20 or more different motor unit potentials produced by weak voluntary effort; and (4) the incidence of polyphasic potentials.

Motor nerve conduction velocity was determined in the deep peroneal nerve, and orthodromic sensory nerve conduction velocity was determined in distal and proximal segments of the lateral popliteal or sural nerve, and in the distal segments of the median nerve (from digit 1 and 3 to wrist). A rectangular electrical impulse of 0.2 ms duration was delivered from a stimulator with a double screened output transformer. The sensory stimulus was applied via surface electrodes (on the fingers) or Teflon-coated stainless steel needle electrodes with a 3 mm bared tip placed near the nerve according to the principles described by Buchthal and Rosenfalck (1966) and Behse and Buchthal (1971). The needle electrodes served as pick-up electrodes for the sensory potentials as well: in the sural nerve at the level of the lateral malleolus, the sura and the popliteal fossa; in the lateral popliteal nerve at the capitulum fibulae; and in the median nerve at wrist. For sensory latency determination the stimulus was maximal or supramaximal. The current required for maximal stimulation varied with the site of stimulation and

FIG. 2 Sensory and motor nerve conduction velocity in different segments of the median, sural, and deep peroneal nerves in 23 patients with Batten-Spielmeyer-Vogt's disease. ○: patient < 15 years. ●: patient > 15 years. A–E: sensory conduction velocities. A: from digit 1 to wrist (17 patients), B: from digit 3 to wrist (17 patients), C: from dorsum pedis to malleolus lateralis (17 patients), D: from malleolus lateralis to sura (21 patients), E: from sura to fossa poplitea (21 patients). F: motor conduction velocity from capitulum fibulae to ankle (23 patients). The unbroken line indicates the mean and the hatched area the range of velocities (± 2 SD) obtained from normal nerves in subjects 5 (left)–20 (right) years old, without signs and symptoms of neuromuscular disease (median nerve: Buchthal et al. (1974); sural and deep peroneal nerve: Behse and Buchthal (1971)).

FIG. 3 Amplitude of sensory action potentials in the median and sural nerves related to age of patients with Batten-Spielmeyer-Vogt's disease. Mean and variation of normal controls indicated as in Fig. 2. The amplitude (log scale) is indicated along the μV -axis. A: stimulus digit 1, recording at wrist. B: stimulus digit 3, recording at wrist. C: stimulus dorsum pedis, recording at malleolus lateralis. D: stimulus malleolus lateralis, recording at sura.

the type of stimulating electrodes. The current was monitored and registered separately on one channel of the electromyograph. The sensory potentials were recorded via an input transformer and an amplifier with a short blocking time, a lower limiting frequency of 20 Hz and an upper limiting frequency of 3 100 Hz. The stimulus artefact was compensated by a pulse of the same shape and of opposite sign, inserted in series with the recording electrodes (Andersen and Buchthal, 1970). The sensory potentials were recorded on single sweeps and with photographic superposition of 20 responses. The sensory latency was measured to the first positive peak of the sensory action potential. When the responses were smaller than 2 μV electronic averaging of 128–256 responses was used (DISA Digital Averager 14 G 01).

The surface temperature of the extremity under examination was kept constant at 35–37°C by use of a thermocoupled infrared heater.

RESULTS

NERVE CONDUCTION VELOCITY *Sensory nerve conduction velocity* (CV_s) was studied in the sural nerve (21 patients), lateral popliteal nerve (two patients), and median nerve (17 patients). CV_s was decreased slightly or moderately compared with normal controls matched for age and temperature. The decrease was found in all segments of the nerves, but was most pronounced

in the distal parts (digit 1 and 3 to wrist and dorsum pedis to malleolus lateralis), where the decrease averaged 19% in the upper as well as in the lower extremity, as compared with an average decrease of 5% in the more proximal parts (malleolus lateralis to sura, sura to fossa poplitea) (Fig. 2) and retinaculum superior to capitulum fibulae (not shown). CV_s from digit 1 and 3 to wrist was below the 95% confidence limit of normals in 76% of the patients. The slowing in CV_s generally did not increase with age: CV_s in patients below 15 years of age did not differ from that in patients above 15 years of age in the median nerve or in the distal segments of the sural nerve. However, the CV_s from sura to fossa poplitea was slightly lower in the older patients ($P < 0.001$).

Shape and size of sensory potentials These were rarely abnormal (Fig. 3). The amplitude of the sensory potentials at wrist was below the 95% confidence limit of normal subjects in two of 17 patients only, and the amplitude of the sensory potential at sura when stimulating the sural nerve at malleolus lateralis was decreased below the 95% confidence limit in four of 21 patients.

FIG. 4 Sensory conduction velocity in median nerve related to age in 17 patients with Batten-Spielmeyer-Vogt's disease. Left: digit 1 to wrist. Right: digit 3 to wrist. Mean and range of velocities (± 2 SD) of normal controls indicated as in Fig. 2. The slowing, which averages 19% is not age dependent.

Motor nerve conduction velocity (CV_m) This was studied in the deep peroneal nerve in all patients (Fig. 2F). In four the CV_m was decreased below the 95% confidence limit of normal subjects; these patients were above 15 years old. In two of the four patients the distal motor latency from ankle to m. extensor digitorum brevis was increased, and the motor latency in the posterior tibial nerve from fossa poplitea to the m. gastrocnemius was increased as well. Motor latencies from capitulum fibulae to m. tibialis anterior and m. peroneus longus were within normal range in all patients.

ELECTROMYOGRAPHY The electromyographic findings were mostly normal. During maximal voluntary effort of the anterior tibial muscle there was a pattern of interference or reduced interference in all cases. Spontaneous activity of short duration (fibrillation potentials) was found in one patient only. The mean duration of motor unit potentials, which was determined in 19 patients, was increased in one, but normal in 18. An increased incidence of polyphasic potentials was found in only three of the 19 patients.

DISCUSSION

Studies of peripheral nerves in Batten-Spielmeyer-Vogt's disease are few. Kristensson *et al.* (1967) found pathoanatomical changes in necropsy material, and Joosten *et al.* (1973) found

ultrastructural changes in biopsies of the sural nerve in two cases.

If the results in this study are to provide evidence of impairment of the impulse transmission in peripheral nerves in patients suffering from Batten-Spielmeyer-Vogt's disease, then several other factors which could be responsible for the slowing in conduction velocity must be eliminated. The following factors were considered: majority of the patients (16) were on anticonvulsive treatment with diphenylhydantoin, which in long-term treatment has been suspected of causing a slowing in motor nerve conduction velocity (Chokroverty and Rubino, 1974; Eisen *et al.*, 1974). In the present study the slowing of sensory conduction velocity was, however, present to the same degree in the treated and the non-treated group ($P > 0.2$). The patients were all screened with a negative result for diabetes mellitus. That the slowing found could be explained by nutritional deficiency was unlikely as there was no difference between patients under home-care and institutionalized patients. In the deep peroneal nerve a more pronounced slowing of motor conduction velocity was found in the older and more severe cases, among whom the bedridden patients were found. This slowing might be due to pressure on the nerves in these emaciated patients. It is not likely that pressure accounts for all the abnormal sensory findings since the same degree of slowing in CV_s was found in the median nerve and in the sural

nerve, the latter being rarely exposed to entrapment.

Since Batten-Spielmeyer-Vogt's disease is inherited in an autosomal recessive manner, the aetiological agent is supposed to be present from the very beginning of the patient's life. As the clinical course is a progressing one, it was of interest to compare the degree of slowing in nerve conduction velocity in younger and older individuals. The finding of an evenly distributed slowing throughout the age-classes (Fig. 4) with no increase with age and duration of the disease, speaks against any progressive demyelination or loss of axons. A persistent change in nerve membrane permeability would be in agreement with the findings in this study. A decreased peroxidase activity, as demonstrated by Armstrong *et al.* (1974) might have an impact on membrane permeability.

Clinically, the picture was dominated by cerebretinal signs, which masked the peripheral nerve involvement—for instance, weak or absent tendon jerks were found in only three patients. The nerve conduction study has provided evidence of impairment of transmission in the peripheral nerves and thus disclosed an affliction of these structures.

The patients in this unique group have been under the care of Dr J. Danielsen and his staff at Filadelfia Hospital, Dianalund, and Professor J. Melchior at the Department of Pediatrics, Gentofte Hospital.

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