in hypoparathyroidism, described here. Drowsy and ataxic gaitability. Poppedal reflexes, previously noted in this patient, were also present. The skin of the patient was unremarkable.

In the past year, the patient had had three episodes of acute confusion or psychosis in familial hemiplegic migraine. *Acta Neurol Scand* 1982;65:369–75.


**Muscle histology of hypocalcaemic myopathy in hypoparathyroidism**

Sir: In addition to having the typical signs of idiopathic hypoparathyroidism, the patient described here showed features of hypocalcaemic myopathy, rarely reported previously in this condition.1–6

A 65 year old woman was admitted to hospital with complaints of intermittent carpopedal spasm (tetany) and easy fatigability. She had noted carpopedal spasm 20 years before. Five years before admission, she had had operations for bilateral cataracts. For the past year, she had had three drowsy attacks associated with vomiting and cold sweating, each of which lasted for 5 to 10 minutes. There was no past history or family history of neuromuscular disease.

On physical examination, the patient was normal in stature and appearance. She had varicose veins and ecchymoses on both legs. The skin was dry and not infected. Neurological examination revealed hoarseness, mild dysphagia and moderate weakness predominantly affecting the proximal limb muscles. Muscle stretch reflexes were diminished with hypotonicity. There was no sensory disturbance or incoordination. The WAIS score revealed a verbal IQ of 86. A typical carpal spasm appeared 30 seconds after a blood pressure cuff was inflated. The Chvostek sign was present on both sides.

On laboratory investigations, serum calcium was low (5.0 mg/dl) and phosphorous 7.0 mg/dl. Unfortunately serum myoglobin level was not measured. The parathyroid hormone (PTH) concentration, 0.18 ng/ml, was less than normal. Reaction to exogenous PTH (Ellsworth-Howard test) was positive. Serum vitamin D3 level was 12 ng/ml (normal 14–42). The level of serum creatine kinase (CK) was high (756 IU/l, normal < 110) with mild elevation of lactic dehydrogenase and aldolase activity. The MB isozyme of CK was 5% and MM 95%. Electrocardiography showed a prolonged QTc of 0.58 second. Echocardiographic examination revealed cardiomyopathy and a pericardial effusion of 350 ml. Computed tomography revealed bilateral symmetrical calcification of the basal ganglia and the dentate nuclei. Electroencephalography showed slowing of background activity without localising features. An electromyographic finding was an increase in polyphasic long-duration potentials in the distal part of the leg, but was normal in the proximal muscles. Motor nerve conduction velocities were normal.

The muscle biopsy specimen was taken from the quadriceps femoris muscle. Light-microscopical examination revealed variety in fibre size without fibre necrosis, vacuole or inflammatory cell infiltration. Routine ATPase reaction showed type 2 fibre atrophy (fig a). Electron microscopical examination showed perinuclear accumulation of mitochondria and focal myofibrillar degeneration. A few muscle fibres had concentric laminated bodies. In addition to these examinations, immunohistochemical localisation of myoglobin was studied. The formalin-fixed paraffin-embedded 3-μm-thick sections were stained using anti-myoglobin rabbit serum (1:200, DAKO, Denmark) by PAP method of Sternberger.7 In our patient, negative immunoreaction for myoglobin was observed in some muscle fibres, many of which correspond to atrophic type 2 fibres, positive reaction, on the contrary, was observed in the remaining fibres (fig b). In control patients with amyotrophic lateral sclerosis, almost all fibres, including atrophic type 2 fibres, were immunostained for myoglobin, though the intensity was varied. Normal muscle fibres of necropsied patients without neuromuscular diseases were also immunostained.

After administration of calcium and 1α-hydroxyvitamin D3, serum level of calcium and CK returned to normal values.

Tetany, muscle weakness, easy fatigability, pericardial effusion and other symptoms and signs disappeared within 4 weeks.

The calcium ion plays many important roles in neuromuscular function. In hypocalcaemic patients, increased excitability of neuromuscular junction results in the well-known manifestation of tetany, mainly affecting the distal muscles. However, there are several manifestations: proximal muscle weakness, easy fatigability and elevated muscle-associated enzymes, and designated them as hypocalcaemic myopathy related to direct effect of hypocalcaemia on muscle fibres. Fram et al., however, pointed out that the elevated serum enzyme levels could be related to the tetany. In our patient, tetany appeared only two or three times a day, lasting for a few seconds, and serum CK activity did not fluctuate after the tetany of three minutes duration was induced by forearm ischaemia, suggesting that the tetany could be minimally related to the high CK activity.

![Figure](http://jnnp.bmj.com/10.1136/jnnp.50.6.817)
The morphological studies of muscle biopsy specimens have shown normal or non-specific changes in the reported cases. We studied immunohistochemical localisation of myoglobin in biopsied muscles. Myoglobin, a small molecule (17,000 daltons), is a soluble protein and is found abundantly in cardiac and skeletal muscles. Serum myoglobin increases with muscle cell damage, and it is a more sensitive indicator than CK activity. Sidney et al have shown using an indirect immunofluorescent technique that myoglobin disappears from cardiac muscle fibres and appears only in the interstitial spaces after 30 minutes of ligation of a coronary artery. Interestingly, immunohistochemical study of our case revealed that some muscle fibres, mainly small atrophic fibres, were negative for myoglobin stain in contrast with positive stain of the remaining fibres. This suggests that hypocalcaemia may lead to myoglobin leakage from skeletal muscles. With respect to the experimental data of Streffer et al., who demonstrated the leakage of cellular enzymes in calcium-free media, Kruse et al suggested that hypocalcaemia may lead to reversible alterations in enzyme contents of skeletal muscles without structural changes. Finally, our findings indicate that hypocalcaemic myopathy is a distinct clinical entity.

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References

Diagnosis of juvenile-adult form of neuroaxonal dystrophy by electron microscopy of rectum and skin biopsy

Sir: Generalised neuroaxonal dystrophy (NAD) was originally described as the pathological hallmark of an infantile neurologic disorder which is characterised by delayed motor and speech development and combinations of dystonia, hypotonia or rigidity and spasticity, optic nerve involvement, and dementia. The disease is often familial. It terminates fatally toward the end of the first decade of life.1-4 It became obvious that late-onset forms of neuroaxonal dystrophy exist, which begin in late childhood or adolescence and present with a more or less protracted course.5,6

Whether these diseases are truly different nosologic entities from the disorder first described by Hallervorden and Spatz in 1927 and bearing their names, is still a matter of debate.8 By neuropathological definition, Hallervorden-Spatz-syndrome is a localised form of neuroaxonal dystrophy with predilection of the disease process for the pallidum and substantia nigra, in which pathological pigmen is accumulated. Though abnormal pigmentation is a pathognomonic feature of Hallervorden-Spatz-syndrome, it has occasionally been observed also in other infantile forms of generalised neuroaxonal dystrophy.8

If the diagnosis is suspected during life, it should be ascertained by biopsy. In infantile and late-infantile forms of neuroaxonal dystrophy, brain biopsy,4,10,11,12 may be replaced by biopsy of tissue other than CNS, including peripheral nerve and motor end plates,13-16 rectum,17,18 skin and conjunctiva,19,20 and dental pulp.21 Much less information is available about late-onset cases. A cortical brain biopsy established the diagnosis in a sporadic case of a young adult with neuroaxonal dystrophy.22 We report a patient with juvenile-adult neuroaxonal dystrophy, in whom electron microscopy of rectal and skin biopsies verified the diagnosis.

A 32 year old Caucasian woman had an unremarkable family history. She first developed signs of the disease at age 14 years, when she began to articulate poorly. At that time her school performance was still high, but deteriorated, so that she graduated from high school with low marks. She did less well in gymnastics and was reported to be "clumsy". At 23, her handwriting became poor, and first dystonic and athetoid postures were observed. She was examined in this medical centre at age 31. Previous efforts had failed to provide a diagnosis. Her physical examination was normal. On neurological examination she had a severe dystonic and athetoid gait disorder but was still able to walk unaided. Her speech was barely intelligible due to disturbed articulation and prosody. Athetoid movements were absent at rest and when she was not tense but with fingers especially of the right hand remained in a dystonic posture. Examination of the cranial nerves revealed abolished vertical and slowed horizontal optokinetic responses. Muscle stretch reflexes were normoactive on both sides. Both plantar responses were flexor. Muscle tone of the limbs was slightly decreased. Sensation was undisturbed. There were no obvious cerebellar signs.

On psychological testing, memory impairment and dull affect were observed. Her performance IQ of 96 compared with the premorbid IQ of 136. There were signs of an organic syndrome on Benton visual retention and Raven SPM tests. Electroencephalography was normal. Computed tomography and magnetic resonance imaging showed a width of the third ventricle at the upper limit of normal but were otherwise unremarkable. There were no signs of peripheral nerve involvement as determined by electrodagnosis and EMG. Visual and auditory evoked potentials were revealed delayed latencies, and somatosensory evoked potentials a slight reduction in amplitude of the early component.