was responsible for the abnormal movements, as similar CT findings have been reported in other cases of hemidystonia. In the necropsied cases partial destruction of the caudate nucleus and the putamen has been described. Why there is a delay between the occurrence of the hemiplegia and the onset of the abnormal movements, which frequently appear after the weakness has improved, is unknown. It has been proposed that aberrant central nervous system sprouting subsequent to a non-progressive cerebral insult is responsible for this delay. In the present case as well as in previous ones, the chronological progression with the onset of dystonic symptoms after the improvement of the hemiplegia, and subsequent worsening of the movements, would be in keeping with this hypothesis.

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References


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Recapture from bilateral wrist-drop in Whipple’s disease

Sir: The neurological manifestations of Whipple’s disease are varied, and have been described in conjunction with characteristic histological features occurring in the central nervous system. The central element of the CNS involvement comprises dementia, ophthalmoplegia and myoclonus. Hypothalamic disturbance, meningitis and seizures have also been observed. These neurological complications have emerged despite successful treatment of the intestinal component of Whipple’s disease with tetracycline or penicillin. This report details the unusual occurrence of peripheral nervous system involvement in conjunction with the more common systemic and CNS features of Whipple’s disease.

A 59-year-old male engineer presented in June 1985 with lethargy, confusion, weight loss and ophthalmoplegia. He had a 9-year history of arthritis affecting the right knee, and for 12 months he had difficulty remembering details at work. Over this time he had become sexually impotent, and his family described personality change with anxiety, lethargy and frequent aggression. From April 1985 he suffered with intermittent diplopia which progressed to loss of all voluntary eye movements. He became intermittently confused and drowsy during the daytime with indistinct rambling speech. In the 3 months before admission he had also developed steatorrhea, and had lost 7 kg in weight.

On admission he complained of tiredness, and soreness of his eyes. His alcohol intake was minimal, and his only medication was slow-release indomethacin. Examination revealed pallor, mild generalised wasting, finger clinching, clubbed lymphadenopathy and areas of hyperpigmentation on the lower legs and feet. His abdomen was distended and rectal examination revealed pale greasy stools. There was a soft pansystolic murmur at the cardiac apex, and some basal crepitations in the lung-fields. A tense, tender effusion of the right knee joint caused limitation of knee movement. He was orientated in person, but not in time or place, with a poor short-term memory. His intellectual state fluctuated from mild disorientation to confusion, and he had episodes of daytime hypersomnolence and absence. He suffered bilateral conjunctivitis and filamentous keratitis, but there was no iritis. His pupils reacted sluggishly to light, and his visual fields were full to confrontation. The eyes were fixed in forward gaze; no accommodation response to convergence was possible, and pursuit and voluntary eye movements were absent. There were no doll’s eye movements or optokinetic nystagmus. He had an intermittent convergent spasm affecting the left eye, bilateral ptosis and prominent left palatal myoclonus. Mild dysarthria was noted with limitation of tongue and palatal movement. Peripheral tone, power and sensation were initially normal.

Abnormal laboratory findings included hypomicrocytic, hypochromic anaemia (Hb 7.0 g/dl) with low serum iron and TIBC. Serum albumin was also low (30 g/l), and serum electrophoresis showed diffuse elevation of immunoglobulins. ERW (Westergren) was raised to 110 mm/h. Normal findings included syphilis serology, serum thyroxine, TSH and testosteron, vitamins E, B1, and folate, and red cell lead and transketolase.

Malabsorption was confirmed with duodenal faecal fat estimation of 23 g (normal below 5 g) and an undetectable urinary excretion of xylose in 5 hours after a 5 g dose. Gastric scopy revealed severe erosive oesophagitis, and barium studies of the small intestine demonstrated thickened mucosal folds in the distal ileum. Histology of an axillary nodule showed reactive changes only, and there was no evidence of amyloid on rectal biopsy. Liver biopsy, performed at laparoscopy, showed non-specific hepatitis with a PAS-positive Kupffer-like cells in the portal chima. Jejunum Watson capsule biopsy was performed and confirmed Whipple’s disease with numerous PAS-positive macrophages in the lamina propria. Electron microscopy identified rod-shaped organisms within the macrophages. The CSF was acellular with protein of 500 mg/l (normal 250–450) and glucose 3.8 mmol/l, with negative VDRL assay. An EEG showed a generally low voltage recording with little alpha activity in the high and low-voltage slow waves in the temporal regions. CT head scan revealed generalised atrophy with dilatation of the lateral ventricles and widening of sulci. Assessment with the Weschler Adult Intelligence Scale (WAIS) gave a verbal IQ of 123, but a poor performance memory and digit span.

The ophthalmoplegia was not responsive to IV edrophonium, nor to group B vitamins and vitamin E taken during the course of investigations. Before the institution of specific therapy, physical examination revealed progression of muscle wasting with proximal muscle weakness. Daytime hypersomnolence and confusion persisted with intermittent polydipsia and hyperphagia.

Six weeks after presentation, bilateral wrist-drop became apparent with quick abrupt onset of severe weakness occurring in the right and then left forearms. He neither
used crutches, nor misplaced his arms whilst sitting. There was profound weakness to MRC grade 1/5 in left and right wrist and finger extensors. Weakness to grade 4/5 was noted in shoulder abduction, elbow flexion and extension, hip and knee flexion, and knee extension bilaterally. There was no reliable sensory deficit detected. Reflexes were brisk, particularly in the legs, and plantar responses normal. His gait was unsteady, but there was no limb ataxia.

Nerve conduction studies (table) indicated a peripheral neuropathy, with moderate slowing of median, radial and ulnar sensory nerve conduction. The right median motor conduction was also slow. Consistent with bilateral wrist-drop, the dominant abnormality was in the radial nerves where motor stimulation at Erb’s point, axilla and elbow evoked small amplitude potentials (< 500 μV) from the brachioradialis using a concentric needle electrode. Electromyographic sampling from brachioradialis revealed profuse fibrillation potentials and positive sharp waves bilaterally, in contrast to no spontaneous activity in the triceps, abductor pollicis brevis and both first dorsal interossei. No voluntary motor unit potentials were recorded from the right brachioradialis, and very few from the left, whereas an almost complete interference pattern was recorded from the other upper limb muscles. A muscle biopsy taken from the quadriceps showed predominance of type 1 fibres, but no specific abnormality. Sural nerve biopsy (taken after treatment had begun) revealed non-specific perivascular cuffing with polymorphonuclear leucocytes.

Treatment was begun in early August with co-trimoxazole 960 mg three times daily and prednisolone 100 mg on alternate days. Over 6 months the dose of prednisolone was slowly reduced and stopped but that of co-trimoxazole was maintained. Serum and CSF concentrations of sulphamethoxazole and trimethoprim were monitored before and 2 hours after doses; satisfactory simultaneous levels in serum and CSF were found, with 49.6 and 11.6 mg/l for sulphamethoxazole and 5.1 and 1.5 mg/l for trimethoprim respectively at 2 hours. The conjunctivitis responded to methylerolose and tetracycline eye ointment. After 6 months of therapy, the arthritis, facial myoclonus and ptosis had recovered, and full extension of both wrists was possible. There was some recovery in lateral eye movements, but not in vertical gaze. The episodes of daytime hypnornolence and confusion became shorter and less frequent. The ESR fell to 10 mm/h, and daily faecal fat excretion and xylose absorption returned to normal. Further nerve conduction studies performed at this time were normal (table). Electromyography showed no spontaneous activity and almost complete interference pattern in the brachioradialis and forearm extensors, in keeping with the clinical recovery.

The neurological presentation in this case included the features of dementia, ophthalmoplegia and myoclonus which form the central element of nervous system involvement in Whipple’s disease. Hypothalamic disturbance was further suggested clinically. The noted episodes of absence and dissociation have also been observed frequently in cerebral Whipple’s disease, with or without motor seizures, and often without evidence of seizure activity on the EEG. Less than 10% of patients with intestinal Whipple’s disease have neurological symptoms, although pathologically there is no doubt greater involvement. The development of neurological features in untreated Whipple’s disease generally heralds a terminal phase in the illness.

Peripheral nervous system involvement in Whipple’s disease is not well recorded. Peripheral motor neuropathies have not been previously attributed directly to Whipple’s disease, but rather as a late result of malnutrition. In the present case, a low serum albumin was observed but serum folate, B12 and E, and red cell transketolase were normal. Nerve conduction studies were abnormal in a previously reported case of Whipple’s disease with glove and stocking sensory loss and absent ankle jerks, but with no motor deficit. In another case, PAS-positive inclusions in macrophages were seen in mesenteric ganglia, but there have been no other reports of direct involvement of the peripheral nervous system.

Although the dominant weakness in our case was in a radial nerve distribution, there was a slowing of conduction in other upper limb nerves. A mechanical cause for the radial nerve palsies could not be entirely excluded, but this seemed unlikely in the absence of a history or electrophysiological evidence of entrapment. There was full recovery in forearm power (with the left preceding the righy by 2 months) following the institution of prednisolone and co-trimoxazole.

No bacilliform or PAS-positive macrophage inclusions were noted in the quadriceps muscle biopsy, although these have been found previously in a case of myopathy in Whipple’s disease. The sural nerve biopsy also showed no characteristic histological findings of Whipple’s disease. Lumbar puncture infrequently yields PAS-positive macrophages, and clinical meningitis is considered rare. Elevation of protein and cell count is sometimes noted, however, in the CSF.

The CT scan in the present case revealed generalised cerebral atrophy and dilated ventricles, features which have been noted in other cases of Whipple’s disease presenting with confusion, ophthalmoplegia and facial myoclonus.

Our patient improved with a combination of co-trimoxazole and prednisolone. Tetracycline has been widely used in Whipple’s disease, but concern has been raised by reports of progression and relapse of CNS disease following tetracycline.

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<td>During initiation of therapy</td>
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<td>Sensory conduction:</td>
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<tr>
<td>Right radial nerve conduction from:</td>
<td>Velocity</td>
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<tr>
<td>thumb to wrist (orthodromic):</td>
<td>34 m/s, amplitude 10 μV</td>
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<tr>
<td>wrist to hand (antidromic):</td>
<td>35 m/s, amplitude 20 μV</td>
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<td>Right median nerve (F3):</td>
<td>40 m/s, amplitude 15 μV</td>
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<tr>
<td>Right ulnar nerve (F2):</td>
<td>35 m/s, amplitude 10 μV</td>
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<td>Motor conduction:</td>
<td>Small amplitude potentials</td>
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<td>Right radial nerve:</td>
<td>recorded from a concentric needle in brachioradialis.</td>
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<td>Stimulus</td>
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<td>Axilla</td>
<td>6-8</td>
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<td>Elbow</td>
<td>4-8</td>
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<tr>
<td>Right median nerve:</td>
<td>Elbow to wrist:</td>
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<td>velocity—42 m/s</td>
<td>velocity—48 m/s</td>
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therapy. Co-trimoxazole has been used successfully as a sole agent in resolving dementia and intestinal involvement in Whipple's disease, and in conjunction with ampicillin and chloramphenicol in reversing another case of CNS disease. Co-trimoxazole penetrates well the blood-brain barrier, confirmed as in this case by CSF antibiotic assay. The role of steroids with antibiotics is more controversial, but prednisolone may have been responsible for the rapid improvement in right knee effusion, and in mobility, and the swift resolution of left wrist weakness. Prednisolone has been suggested previously as responsible for recovery from meningeal involvement in Whipple's disease. As disordered immunity may play a role in Whipple's disease, the use of steroids is perhaps indicated if neurological damage is threatened. Full recovery from nervous system disease however may be limited by glosis and neuronal loss. Finally, peripheral nervous system involvement should be considered as part of the spectrum of the disease.

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References

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Asymptomatic cardiac arrhythmias in periodic paralysis

SIR: After the original report by Klein ef al. in 1963, several new cases of periodic paralysis associated with cardiac arrhythmias have been described2–7 (see table). In all of the reported cases, alterations of cardiac rhythm were principally characterised by isolated and paired ventricular ectopic beats and bidirectional ventricular tachycardia. The serious and rare arrhythmia may be considered a possible sign of periodic paralysis when found in a young patient. These cases of periodic paralysis with associated arrhythmias have been regarded as exclusively ventricular in origin with poor prognosis. We present what we believe is the first report of a case of periodic paralysis associated with a benign cardiac arrhythmia of atrial origin.

A 16 year old white male with no family history of neuromuscular disease suffered acque episodes of paralysis involving upper and lower limbs, lasting 2–4 days twice a year, since the age of 9 years. During hospitalisation in our Department because of one of these crises at the age of 13, laboratory data, including myoglobin, CK, aldosterone, and thyroid function tests were all normal. Serum and urinary potassium and other electrolytes were measured daily and were consistently normal. A biopsy of the left quadriceps muscle showed no structural alteration and no glycogen accumulation with PAS. Trichromic stain showed a slight increase in interstitial connective tissue and the electron microscopy showed a few fibres...