Amyloid associated muscle pseudohypertrophy: amelioration of motor dysfunction with plasmapheresis and dimethyl sulphoxide

Deposition of AL-amyloid in the skeletal muscle with the clinical picture of muscle pseudohypertrophy has rarely been described. Common clinical findings include macroglossia, dysphagia, dysarthria, and skeletal muscle enlargement and induration. This diagnosis carries an extremely poor prognosis; the patients die of respiratory failure despite vigorous chemotherapy for the underlying myeloma. We describe a patient with amyloid associated muscle pseudohypertrophy who responded to treatment with plasmapheresis and dimethyl sulphoxide (DMSO).

A 65 year old man was in good health until the age of 61 when he noted swelling and clumsiness of the fingers. At the age of 63, he developed swelling with ankylosis of his four limbs (figure A; table). The patient then lost the ability to open his mouth and chew. He was next seen 18 months later with progressive muscle enlargement and stiffness (figure B). On examination, he seemed very muscular and athletic. The muscles were diffusely firm with a wooden consistency. The superficial veins in all limbs were engorged. There was pronounced macroglossia with a hard rubbery consistency, and he had difficulty swallowing solid foods. Resistance to passive movements was noted in all limbs with a decreased range of motion (table). Muscle strength was slightly reduced and tendon reflexes were decreased. The patient walked slowly with a stooped posture and with few associated movements.

Serum IgA was increased to 475 mg/dl, and immunoelectrophoresis showed monoclonal IgA in serum and free monoclonal κ chains in urine. Bone marrow examination showed 30% plasma cells. A bone scan showed an increased uptake of 99mTc-methylene diphosphonate in the shoulder and pelvic joints, indicating amyloid deposition. Pulmonary function tests showed a restrictive defect (table). Serum creatine kinase was normal. Nerve conduction studies showed bilateral carpal tunnel syndrome. Tissue pressure of the quadriceps femoris in the supine position measured by a needle manometer method rose to 78 mm Hg, whereas that of three healthy controls was (mean SD) 10 (3) mm Hg.

A left quadriceps femoris muscle biopsy showed a pronounced variation in fibre size with type 2 fibre atrophy, and mild neurogenic changes. In addition, there was accumulation of material staining with Congo red in the blood vessel walls and, to a lesser extent, in the perimysium. On immunoperoxidase staining for heavy chains-κ, α, and μ, and light chains-κ and λ (1:2000, Dakopatts, Copenhagen, Denmark), only the λ light chain was positive in a distribution closely matching that of the material staining with Congo red. On electron microscopy, deposits of typical amyloid filaments were found in close contact with, or superimposed on, amorphous material.

The patient was treated weekly with plasmapheresis and daily rectal instillation of 10 ml DMSO. After two plasma exchanges, neuromuscular function apparently improved (table). The treatment was

Effects of plasmapheresis and dimethyl sulfoxide on motor, respiratory, and renal functions

<table>
<thead>
<tr>
<th>Range of motion (%)</th>
<th>shoulder</th>
<th>Fingertip</th>
<th>Hip</th>
<th>kneecap</th>
<th>ankle</th>
<th>GP (kg)</th>
<th>VC (%)</th>
<th>PaO, (mm Hg)</th>
<th>CCr (ml/min)</th>
</tr>
</thead>
</table>

Table showing the range of motion for the shoulder, Fingertip, Hip, kneecap, and ankle, along with grip power (GP), vital capacity (VC), oxygen tension (PaO,), and creatinine clearance (CCr). The table compares the data before and after treatment with and without DMSO.

*Posterior view of patient. (A) 1st admission at the age of 63. (B) 2nd admission 18 months later at the age of 65. (C) Six months after treatment with plasmapheresis and DMSO.
followed by administration of prednisolone (50 mg/day) and melphalan (6 mg for 10 days) each month with monthly intravenous injections of cyclophosphamide (300 mg). Thereafter, the patient showed gradual improvement in motor, respiratory, and renal functions (fig. C, table). Four months after treatment, the tissue pressure of the quadriceps femoris in the supine position fell to 47 mm Hg. Serum IgA concentrations were consistently less than 200 mg/dl. There were no serious side effects of DMSO and an unpleasant breath odour was the patient’s main concern. Nine months after treatment, we noted a levelling off or a slight decline in some variables. Six months after treatment, the patient aspirated his secretions and died.

AL-amyloidosis results from conversion by proteolysis of monoclonal light chains into insoluble amyloid fibrils which can be recognised by Congo red staining. Light chain deposition disease is another pathological state associated with plasma cell dyscrasia.1 In our patient with IgA lambda monoclonal protein, the skeletal muscle pseudohypertrophy, simultaneous deposition of AL-amyloid and LIGHT chain light chains were shown by amyloid staining, immunohistochemistry, and electron microscopy. In general, muscle dysfunction in amyloid associated muscle pseudohypertrophy remain unclear. Most attention to date has been directed toward the weakness.1 A possible factor causing motor impairment in our patient was a decreased range of motion, predominantly affecting proximal joints. Involvement of shoulder joints showing shoulder pad sign1 is pathognomonic of amyloidosis.1 A factor hampering mobility is increased muscle tissue pressure reflected as wooden firmness. Increased muscle pressure is not produced by amyloid infiltration alone but may be related to deposition of cholesterol,4 4-sulfuric acid and silicon in muscles,4 tense muscle fascia secondary to amyloid deposition, or impaired tissue perfusion by amyloid angiopathy. The pressure is further increased by the activity to the point that it interferes with muscle blood flow.

The goal of treatment in amyloidosis is to prevent further deposition of amyloid and to promote its resolution. In our patient, plasmapheresis and DMSO treatment resulted in an appreciable level of improvement in motor, respiratory, and renal functions. The ability of DMSO to make amyloid fibrils soluble for digestion has been demonstrated.4 Amyloid/light chain-derived materials dislodged from various organs are likely to impair renal function. Therefore, to remove these breakdown products and the precursor mononuclear immunoglobulins, plasmapheresis was combined with DMSO. Because of the grave prognosis and disabling symptoms of amyloid associated muscle pseudohypertrophy, a trial of plasmapheresis and DMSO may be warranted even though the improvement may be moderate and of limited duration.

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Opossums, a rare complication of cocaine misuse

Opossums is a rare eye movement disorder, mostly seen in postviral encephalopathy or occult neuroblastoma in children, or as a paraneoplastic phenomenon in adults. It rarely occurs after giving drugs or toxins. A single report of the opsoclonus-myoclonus syndrome in association with cocaine use has been described in this journal.2 We present a patient with opossums, myoclonus, and ataxia.2

A 29 year old man was admitted to hospital with vertigo, nausea, and vomiting. He was unable to stand and walk, because his legs were shaking. The first symptoms had occurred two weeks after taking street cocaine, with paroxysmal vertigo which became continuous the next day, then progressive shaking of the legs, and finally of the whole body. The patient did not complain of headache. There was no weight loss, fever, or recent infectious disease. There was a medical history of migraine and hyerventilation. He admitted heroin misuse until eight years ago and incidental cocaine misuse in recent years. The patient took 10 mg diazepam daily because of nervousness but no other drugs. Since the appearance of nausea he used 6–5 mg thiethylperazine a day.

General examination showed no abnormalities. Neurological examination showed normal consciousness and there was no evidence of nuchal rigidity. The optic fundi could not be examined because of intermittent involuntary eye movements. The pupil reactions were normal, as were the visual fields. There were continuously intermittent conjugated nystagmus beats in all directions, often finishing with a circumscription movement. The abnormal eye movements increased under the influence of stress. The patient had a trembling voice and slight myoclonic jerks of his head and neck. He was unable to stand and walk because of vertigo and ataxia. When sitting he showed a dissequilibrium. There was no other neurological deficit.

Blood and CSF examination were normal except for a slightly raised CSF protein (0.72 g/l). Viral serologies were negative. Electrocardiography, chest radiography, brain CT and MRI, EEG, and brainstem auditory evoked potentials were normal. Electro-oculography at fixation in different directions showed concentric eye movements with a short rotation at the end of the movement. With the eyes closed there were coarse eye movements in all directions with a frequency of 8 Hz. The abnormal eye movements were in superposition of normal eye movements.

During his stay in the disebiquilibrum gradually improved. The opossums changed to Furtney syndrome. In the few weeks oculomotor examination showed only sporadic horizontal ocular myoclonus in vertical movements. Follow up months after his admission to the hospital yield no ocular myoclonus or ataxia and the patient stated that he felt perfectly well.

In our patient opossums was very likely associated with taking cocaine. After extensive diagnostic evaluation no other cause could be found. The disorder appeared after incidental misuse of cocaine and was self limiting. One other such patient was described.

Various neurological complications of cocaine are known. Neurovascular disorders, either haemorrhagic or ischaemic, can occur after taking the drug.2 Seizures and migraine are other neurological complications. Interestingly, increases in brain serotonin by inhibition of its uptake is an effect of cocaine. Maybe our patient, who had migraine, was more sensitive to this effect of cocaine, as segmental dysfunctions or seizures have been reported in patients with migraine. The lack of any anatomical substrate supports this. On the other hand, a direct toxic effect of cocaine or on omnipresent substan- cies cannot be ruled out.

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Further evidence of increased risk of mortality from Parkinson’s disease

It is often considered that since the introduction of levodopa treatment, there has been little difference in mortality from Parkinson’s disease compared with the general population.1 However, to date, only three studies have investigated the mortality in a group of patients with Parkinson’s disease compared with a matched control group. Rajput et al, in their review of case notes, found a mortality for patients with Parkinson’s disease 1-6 times that of controls,2 and the community based prospective case-control survey of Ebmeier et al in Aberdeen found a 2-35-fold higher death rate.1 In a recent issue of this journal, Ben-Shlomo and Marmot published the results of a long term community based prospective study showing a 2-6-fold increased risk of mortality for Parkinson’s disease.1 We report the results of a population based survey of subjects aged 65 and over that provides further evidence of increased mortality due to Parkinson’s disease.

The population studied was a representa- tive, randomly selected sample of 2792 subjects, aged 65 and over, living at home in Gironde, France (PAQUID study), com- posed of 1122 men (40-2%) and 1670
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