Cerebral myelopathy due to calcium pyrophosphate dihydrate deposition disease

Calcium pyrophosphate dihydrate deposition disease (CPPD) is characterised clinically by arthritis (pseudogout), radiographically by chondrocalcinosis (heavy punctate and linear radiodensities seen in both hyaline and fibrocortilage), and pathologically by the identification of CPPD crystals in the synovial fluid. In addition to synovial membrane and joint capsule involvement, the disease may also occur in tendons and ligaments.

Cervical myelopathy is a rare complication of CPPD, and has only recently been documented to occur in the anterior cervical spinal canal.

An 85 year old woman, who had for many years had mild arthritis of both wrists, presented with a two year history of intermittent paraesthesiae of her right hand, exacerbated by prolonged sitting. One month before admission she developed neck and right shoulder pain. Two weeks later, she noted progressive upper extremity, followed by lower extremity, paraesthesiae. A week later, when she could no longer walk, she was admitted to hospital. Her weakness and paraesthesiae worsened, and three days before her transfer to New York Hospital, she developed urinary incontinence. Cervical spine MRI without gadolinium-DTPA (figure 1) revealed an extra-axial soft tissue mass at the cervico-medullary junction, causing cord compression and odontoid erosion. CT scan confirmed the presence of calcifications within the mass.

Her examination on admission to hospital showed minimal neck tenderness, spastic quadriaparesis with diffuse atrophy, profound loss of proprioception and vibration, and a C5 level to pinprick. At surgery, there was an extradural mass at the base of the skull, associated with thickened fibrous scar tissue and dura, and with odontoid destruction. An extensive surgical resection of the mass was performed.

Histological examination of the surgical specimen revealed dense fibrous connective tissue and granulation tissue with fibrocartilaginous metaplasia. Within the metaplastic regions were haematoxyphilic deposits of CPPD crystals which were positively birefringent in polarised light (fig 2).

Subsequent radiographs revealed typical chondrocalcinosis of both wrists and knees. No associated metabolic disease was identified; serum calcium, phosphorus, blood sugar, electrolytes, creatinine, magnesium, iron studies, serum protein electrophoresis, liver and thyroid function tests were all within normal limits. Her ultimate neurological recovery included improved strength in all limbs, but proprioception remained unchanged, and she was unable to walk. She died approximately six months later, of aspiration pneumonia. No necropsy examination was obtained.

CPPD crystal deposition disease occurs with a population frequency of 1:1000. The prevalence increases with age, and approaches 45% for patients 85 years of age and older. 66% of patients have chronic arthritic complaints; two thirds of this group will have superimposed intermittent acute episodes. Fifteen per cent of patients are asymptomatic. 2 The disease can be sporadic, or associated with metabolic disease, trauma, or surgical procedures. Associated metabolic conditions include haemochromatosis, hyperparathyroidism, hypophosphatasia, hypomagnesaemia, hypothyroidism, neuropathic joints, and amyloidosis.

1 Various radiographic and clinical findings occur in the spine of patients with CPPD disease. Resnick1 found radiographic abnormalities of the cervical spine in 52 of 57 patients, including disc space loss with adjacent vertebral body sclerosis and osteophytes, apophyseal joint abnormalities, and subluxation. Calcification of the syndesmodyodontoid region has been noted in patients with CPPD disease, but symptoms are generally absent. 4 Calcified intervertebral discs may be present, and are usually asymptomatic; rarely, spinal pain and stiffness mimicking ankylosing spondylitis occur.

Cervical myelopathy as a result of cord compression secondary to CPPD is rare. Only two patients with pathologically documented lesions at the anterior cervico-medullary junction have been previously reported; other patients had lesions at or below the third cervical vertebra, in the posteriorly located ligament flavum. All cases were clinically similar, and none were diagnosed before surgery.
Letters to the Editor

All three patients (including ours) with involvement of the posterior longitudinal ligament and transverse atlas ligament, were women older than 65 years old, most known CPPD disease; two had been symptomatic for more than one year. None had an associated metabolic disease. In our patient, the mass nature of the lesion, its anterior location, and the presence of calcifications on the CT scan led to a pre-operative diagnosis of meningioma. Other diagnostic possibilities included chordoma, schwannoma, or a metastatic lesion, as well as posterior longitudinal ligament ossification, or rheumatoid arthritis.

The exact cause of CPPD crystal deposition is unknown. CPPD crystal formation may result from either elevated levels of calcium, elevated levels of inorganic pyrophosphate, decreased phosphatase activity, changes in connective tissue matrix, or any combination of these factors. Once deposited into cervical ligaments, the crystals may then promote inflammation, cartilagenous metaplasia, and degeneration.

CPPD deposition disease may be considered in an elderly patient presenting with a progressive cervical myelopathy, who has a ligamentous calcified mass in the anterior cervico-medullary junction, and who has radiographic evidence of chondrocalcinosis. Resection and/or decompression may provide beneficial neurological improvement in some patients.1

We thank Dr Russell Patterson for permission to report his patient.

CHRISTINE R WELLS
Department of Neurology, New York Hospital, New York, USA
SUSAN MORGELLO
Department of Pathology (Neuropathology), New York Hospital, New York
EDWARD DICARLO
Department of Pathology, Hospital for Special Surgery, New York, NY, USA


Acid maltase deficiency presenting with a myopathy and exercise induced urinary incontinence in a 68 year old male.

Pompe’s disease, or type II glycosgenosis, was first described in 1932 and was shown to be due to a deficiency of the lysosomal enzyme acid alpha-1,4-glucosidase (acid maltase) in 1963. Usually the disease presents in infancy with hypotonia, respiratory difficulty and cardiac failure. The same enzyme deficiency may present in adults with a myopathy and symptoms can begin as late as the sixth decade.1 Respiratory muscle involvement is common, may be the presenting feature and is said to distinguish acid maltase deficiency from other limb girdle myopathies.2 Recently we have identified a case of adult acid maltase deficiency with an unusual presentation. A 68 year old man first noticed difficulty with walking at the age of 65, no neurological symptoms could be identified before this. He complained of progressive painless, mild leg weakness, difficulty rising from a chair and from lying to sitting. For several months he had experienced urinary incontinence which occurred without warning and despite voiding before exercise, after a minimum of 20 minutes walking and not at any other time. There were no symptoms of prostatism, faecal incontinence, upper limb weakness or breathlessness.

As examination cranial nerves and neck strength were normal. His standing posture was abnormal with an exaggerated lumbar lordosis due to truncal weakness. He could not sit up from lying with the arms folded and had difficulty rising from a low chair. There was mild weakness of shoulder abduction but otherwise the upper limbs were normal. The left quadriceps was wasted and he had a mild distal and moderate proximal leg weakness of an asymmetric distribution, worse on the left. The reflexes were reduced but preserved and sensation normal. The general examination, including the prostate was normal.

Plasma creatinine kinase was raised at 429 U/L (normal 24-161). EMG of the leg muscles including the left rectus femoris showed no definite abnormality. A quadriceps muscle biopsy demonstrated marked vacuolar degenerative changes in the sarcolemma of the muscle fibres with prominent positive staining for acid phosphatase in relation to the vacuoles. Many of the vacuoles contained fine granular material, some of which contained abundant glycogen. On electron microscopy some of the glycogen deposits were membrane bound (lysosomal) [fig]. Muscle glycogen content was increased to 3.38 mg/100 mg wet weight (controls, n = 12, 0.34 ± 0.23). Acid alpha glucosidase activity was reduced in muscle, leukocytes and cultured skin fibroblasts (table). Pulmonary function tests (lying and sitting), ECG, chest radiograph, abdominal ultrasound, IVU and a bone scan were all normal. A videocystometrogram, performed in the supine position at a filling rate of 20 ml/minute, showed gross detrusor instability (maximum subtracted detrusor pressure 70 cm water) with total incontinence occurring at a capacity of 250 ml. There was no bladder neck incompetence or stress incontinence demonstrated on strain and voiding was unobstructed. His urinary incontinence responded well to treatment with an anticholinergic drug.

All forms of glycosgenosis type II are inherited as an autosomal recessive trait. Unlike the infantile variety in which a lack of acid maltase deficiency clinically affects only skeletal muscle, and this disorder may be mistaken for polysomytosis or a genetically determined myopathy of unknown aetiology.3 Most reported cases present between the second and fourth decade with symptoms generally preceding presentation by several years. The oldest previously described case was of an infant whose parents were first cousins.4 In this case this patient had normal respiratory function but an unusual pattern of incontinence, which has not been previously described in this disease. The relationship between the onset of his myopathy and the development of urinary incontinence in this patient were not coincidental. Many patients with detrusor instability remain asymptomatic, probably because they augment urethral closure pressure by increased striatal muscle activity in the sphincter mechanism. We postulate that the inability to withstand increases in detrusor pressure only occurred because of striated pelvic floor muscle fatigue associated with exercise. An alternative explanation is that his detrusor overactivity was due to a neurogenic mechanism. There is some evidence that in the adult form of acid maltase deficiency a respiratory mutant component may contribute to muscle weakness because of involvement of spinal motor neurons.4

Although a high protein, low carbohydrate diet has been proposed for the treatment of this condition, with some evidence of improvement in studies of single cases, our patient’s disability was mild and his age may

Table Acid alpha glucosidase activities (nmol/min per mg protein)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Control* mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>muscle</td>
<td>0.013 ± 0.026 (0.20-0.33) [n = 3]</td>
</tr>
<tr>
<td>leucocytes</td>
<td>0.0005 ± 0.023 (0.14-0.39) [n = 4]</td>
</tr>
<tr>
<td>cultured skin fibroblasts</td>
<td>0.017 ± 1.03 (0.60-1.46) [n = 8]</td>
</tr>
</tbody>
</table>

*Age and sex matched controls (leucocytes), paediatric controls (muscle and fibroblast). There was no difference in leucocyte activities in paediatric and adult controls.
Cervical myelopathy due to calcium pyrophosphate dihydrate deposition disease.

C R Wells, S Morgello and E DiCarlo

_J Neural Neurosurg Psychiatry_ 1991 54: 658-659
doi: 10.1136/jnnp.54.7.658

Updated information and services can be found at:
http://jnnp.bmj.com/content/54/7/658.citation

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/