system respectively. Thus the whole clinical feature of the patient could be diagnosed as pure autonomic failure, which chiefly concerned the cardiovascular system. The main pathological changes were found in the dorsal vagal nuclei and intermediolateral columns, which were considered to be the neuroanatomical system with the predominating involvement of the degenerative process. Along with the existence of eosinophilic bodies in the sympathetic ganglia, these findings are similar to those described in pure autonomic failure.

By contrast with the previously reported cases, this patient showed the absence of neuronal loss or Lewy bodies in the substantia nigra and locus coeruleus. This suggests that pure autonomic failure could be recognised as a clinicopathological entity separated from multiple system atrophy or Parkinson's disease.

Although motor neuron disease does not usually coexist with autonomic failure, our patient exhibited loss of anterior horn cells and pyramidal tract degeneration. In addition, we found symmetric patches of myelin loss in the posterior columns, degeneration in the spinocerebellar tracts, and loss of cells from Clarke's columns. This type of distribution is similar to that reported in familial forms of motor neuron disease. Furthermore, Lewy body-like hyaline inclusions and swollen cord-like axons, which were both noted in our patient, have often been described in these familial cases. Whether a familial form of motor neuron disease constitutes a distinct disease entity or not, our patient shares its characteristics.

The autonomic nervous system may be affected in motor neuron disease, with—for example, a mild degree of neuronal loss in the intermediolateral columns. However, our patient showed the obvious neurodegenerative changes reported in pure autonomic failure as well as those described in a familial form of motor neuron disease. Therefore, this case shows an unusual constellation of pure autonomic failure and motor neuron disease.

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Glutaric aciduria type 1 in adulthood

Glutaric aciduria type 1 (GA-1) is an autosomal recessive disorder caused by deficiency of the mitochondrial enzyme glutaryl CoA dehydrogenase, which oxidises and carboxylates glutaryl CoA, an intermediate step in the metabolism of lysine and tryptophan. The onset of clinical manifestations is usually within the first year of life with an acute encephalopathic illness, often triggered by intercurrent infection. A severe dystonic-dyskinetic syndrome is common in most patients, but others are less severely affected and asymptomatic cases have been described. It is a rare condition with only about 100 cases reported in the medical literature since its original description in 1975.

However, it has been suggested that GA-1 is underdiagnosed and may exist undetected in populations of children and adults labelled as having cerebral palsy. We report a patient with GA-1 in whom the diagnosis was made at the age of 50 years when she was referred for reassessment of chronic neurological disability.

The patient was the product of a full term normal delivery and there were no problems in the neonatal period. Motor development was mildly delayed, and she did not start to walk until the age of 18 months when she was noted to drag her right leg. At the age of 7 years she was admitted to hospital with a "paralytic illness". She remained in hospital for four months and at the time of discharge required callipers to walk. Her manual dexterity was poor and her speech was slurred. These neurological disabilities subsequently remained stable. At the age of 12 a right subthalamic fusion was performed, and eight years later the left femur was strengthened. She was able to complete her education at a normal school and then worked for 10 years in a factory before getting married. She was referred to us at the age of 50 because of increasing difficulty in walking caused by pain in the right ankle. There were no new neurological symptoms and no symptoms of autonomic dysfunction. She was being treated with a non-steroidal anti-inflammatory drug and was on hormone replacement therapy. She had not received any neuroleptic medication. Both her parents were caucasian and had died in their 80s. They had had no neurological illnesses, and there was no consanguinity. The patient has two siblings and three children of her own, all of whom are well with no neurological disorder.

Examination showed a severe dysarthria which made her speech very difficult to comprehend. Psychometric testing, however, showed her performance to be in the average range, within a normal range. The non-verbal part of the WAIS-R was not performed because of limited manual dexterity, but good average scores were achieved on the tests of non-verbal reasoning. There was a left exotropia, but extraocular movements were otherwise normal. There was pronounced lingual dystonia and orofacial dyskinesia. Her right leg was hypoplastic and she used callipers and two sticks to walk. There
was dystonic posturing and clawing of both hands. Power was reduced (grade 4) at the wrists and in the hands, worse on the right. The right leg was flaccid, and there was no movement at the right ankle. Power was reduced (grade 4) proximally in both legs. The right ankle jerk was absent, but all the other tendon reflexes were brisk. The right plantar response was absent, the left exten- sor. There were no cerebellar or sensory signs. General examination was normal.

The following investigations were normal or negative: routine haematology and biochemistry, serum copper and caeruloplasmin, serum and urinary amino acids, syphilis serology, antinuclear factor, lupus anticoagulant, and anticardiolipin antibody. Constituents of CSF were normal including lactate (1-15 mmol/l; normal range: 0-5-1-8 mmol/l), and pyruvate (83 mmol/l; normal range: 40-138 mmol/l). Motor and sensory nerve conduction velocities and amplitudes were within normal limits.

Brain MRI showed large CSF spaces around the anterior portions of both tempo- ral lobes (figure). There was also a mild degree of generalised cortical atrophy and focal areas of signal abnormality in the white matter of both cerebral hemispheres. A trace of glutaric acid was present in the urine, with a small peak of 3-hydroxyglutaric acid. Glutaryl CoA dehydrogenase activity, mea- sured by release of labelled CoA, from [1-14C]glutaryl CoA by cell homogenate, was undetectable in cultured skin fibroblasts (0-0 and 0-0 compared with 12-9, 13-9, 19-6, 20-1, 12-5 and 12-7 pmol/mg protein/min in simultaneous controls) and was <1% of normal in blood lymphocytes (0-06 and 0-02 compared with 11-3 and 10-8 pmol/mg protein/min in a simultaneous control) confirming a diagnosis of GA-1.

The dystonia and dyskinesia with severe dystarthis but relative preservation of cogni- tive function in this patient is typical of GA-1. In addition, the bitemporal enlargement of CSF spaces on MRI, although occasion- ally reported in other conditions, is strongly suggestive of GA-1. No other cause was identified for this patient’s neurological dis- order.

Most patients with GA-1 present in the first year of life with acute metabolic decompen- sation and encephalopathy. A recent review of reported cases suggests that 97% of those surviving an acute encephalopathic onset are leukoencephalopathies.2 Our patient presented with delayed walking and dragging the right leg. Up to 25% of cases may present insidiously and there is some evidence that the prognosis in this group is better with only 64% being left with severe disability.2 It is rare for new neurological deficits to develop after the age of 3 years, and after this age any residual disability remains static.3 Our patient is unusual in that, after a gradual onset, there was further deterioration in neurological function at the age of 7. The details of that episode are lim- ited, but as the neurological sequelae are typical of GA-1, it seems reasonable to attribute it to GA-1 rather than to implicate a second disease process. From the age of 7 until 50, her neurological state remained stable. The current decline in mobility was thought to be related to degenerative joint disease rather than neurological deteriora- tion.

The proportion of cases diagnosed in infancy that have a maternal history, as is, yet unknown given that GA-1 was first described only 20 years ago. At the age of 50 years, our patient is the oldest documented case with GA-1. Four other clinically affected patients with GA-1, in whom the diagnosis was made after the age of 18 (aged 19, 23, 28, and 37), have been reported.4 It is likely that there are other unrecognised cases of GA-1, born before the condition was first described, who have survived into adulthood.

The diagnosis of GA-1 in clinically sus-pected cases is usually made by demonstrat- ing excretion of 3-hydroxyglutaric acid and 3-hydroxyglutaric acid in urine. Glutaric acid is found in the urine in other metabolic disorders such as multiple acyl-CoA dehy- drogenase deficiency, but the presence of 3- hydroxyglutaric acid makes the diagnosis of GA-1 almost certain, as it has not been found in any other condition.1 However, during periods of neurological stability, which will invariably be the case in adults, excretion may become undetectable. Neuroradiological findings (enlarged fron- totemporal CSF spaces and signal abnor- malities in cerebral white matter and, in severe cases, in the basal ganglia) may also suggest a diagnosis of GA-1, but they are not specific. Similar abnormalities are seen in the basal ganglia in the mitochondrial encephalopathies and in Leigh’s syndrome. Although dystonia may be prominent in Leigh’s syndrome,3 the presence of other features such as retinopathy, peripheral neu- ropathy, and dysmorphism help to distin- guish it from GA-1. In addition, enlarged frontotemporal CSF spaces are not found in Leigh’s syndrome. To confirm a diagnosis of GA-1, glutaryl CoA dehydrogenase activity must be measured in cultured skin fibro-blasts or blood lymphocytes.1 It is usually undetectable in homozygotes.

GA-1 is thought to be rare in adults, but there are almost certainly unrecognised cases among populations of adults with sta- ble neurological deficits acquired in childhood. This report illustrates the clinical and neuroradiological findings that may be seen in adults and extends the clinical range of GA-1.