Fig 1

adrenoleukodystrophy presenting as spino-cerebellar degeneration from spinocerebellar degeneration.

Adrenoleukodystrophy (ALD) is a sex-linked recessive, peroxisomal disorder that causes diffuse demyelination of the central nervous system. ALD presenting as spino-cerebellar degeneration (SCD), a variant form of ALD, has been recognised.⁵ The brain computed tomography (CT) finding most commonly seen in this form of ALD is atrophy of the brain stem and the cerebellum.⁷ However, MRI has not previously been reported.

A 29 year old man was admitted to our hospital because of gait disturbance. His parents were not consanguineous. His mother was asymptomatic though neurological examination revealed mild spasticity of both legs. At age 26, the patient complained of dysarthria and gait disturbance, and these symptoms were slowly progressive. Impotency, incontinence, and weight loss developed.

He was euphoric and mildly pigmented. Neurological examination revealed slow slurred speech, considerably increased deep tendon reflexes, extensor plantar responses and, ataxia of all limbs. His gait was markedly

spastic and ataxic and he could not walk without support. His total IQ on Wechsler adult intelligence scale was 76.

The following laboratory data were normal or negative: full blood picture, electrolytes, liver function, kidney function, plasma glucose, creatine kinase, serological tests for syphilis, tests for SLE, anti-HIV antibody, anti-HTLV-I antibody, lymphocytes lysosomal enzyme activities including beta-galactosidase, beta-hexosaminidase and aryl-sulfatase A. Fasting plasma ACTH was 81 pg/ml (normal less than 65 pg/ml) while cortisol was normal. Serum cortisol response to ACTH (rapid ACTH test) showed a low response pattern. Cerebrospinal fluid was normal except for a raised protein (61 mg/dl). Very long-chain fatty acids in plasma sphingomyelin fraction were considerably increased, that is C24:0/C22:0 was 1.171 [normal (SD), 0.735 (0.131)], C25:0/C22:0, 0.0380 [0.0143 (0.0039)], C26:0/C22:0, 0.0199 [0.0057 (0.0017)]. Brain CT showed atrophy of the cerebellum and the brain stem. MRI revealed abnormal intensity areas in both corona radiata, internal capsules, cerebral peduncles and white matter around the dentate nuclei of the cerebellum (fig 1) in addition to atrophy of the cerebellum and the brain stem (fig 2).

Pathological findings for ALD presenting as SCD include diffuse demyelination of the cerebellar white matter and the brain stem involving the internal capsule, corpus callosum and optic nerves.⁴ Marked loss of Purkinje cells and neurons of the dentate nuclei, and lesions in superior cerebellar peduncles have also been reported.⁹ In this patient, MRI clearly showed lesions in the pyramidal tracts and cerebellar white matter adjacent to the dentate nuclei, consistent with the clinical findings. The cerebellar lesions seen in this patient also shows one of the common pathological findings in the classic type of ALD, because a discrete lesion involving the cerebellar white matter adjacent to the dentate nucleus was reported in five of 17 necropsy cases.⁸ MRI in the classic type

ALD has shown diffuse lesions in the cerebellar white matter including the pyramidal tract, and the auditory and visual pathways.^{3,6} Areas of abnormal intensity in the internal capsule have been reported in adrenomyeloneuropathy.^{1,2} Thus, ALD presenting as SCD and classic type ALD differ in extent of lesions though the basic abnormality in lipid metabolism is common to both.

The lesions in the cerebellar white matter and the pyramidal tracts may be responsible for the symptoms in this patient which CT failed to detect. A common CT finding in ALD presenting as SCD is atrophy of the brain stem and the cerebellum, which is indistinguishable from that in SCD.⁷ In SCD, however, MRI abnormality suggesting the existence of demyelination as seen in this patient, has not been reported. Thus patients with cerebellar ataxia should be examined with MRI for the possibility of ALD.

We thank Dr Ryoko Koike, Department of Neurology, Brain Research Institute, Niigata University, for measuring very long-chain fatty acids in plasma sphingomyelin fraction from the patient.

I MIYAI
H FUJIMURA
T UMEKAGE
K WATASE
S UENO
S YORIFUJI
M TAKAHASHI*
S TARUI

The Second Department of Internal Medicine,
Osaka University Medical School
Department of Neurology,*
Kinki University Medical School,
Osaka, Japan

Correspondence to: Ichiro Miyai, Second Department of Internal Medicine, Osaka University Medical School, 1-1-50, Fukushima, Fukushima-ku, Osaka 553, Japan.

- 1 Bewermeyer H, Bamborschke S, Ebhardt G, Hunermann B, Heiss WD. MR imaging in adrenoleukomyeloneuropathy. *J Comput Assist Tomogr* 1985;9:793-6.
- 2 Komori T, Nagashima T, Hirose K, Tanabe H, Tsubaki T. Adrenomyeloneuropathy associated with congenital cataracts—report of a family with MRI study. *Clin Neurol* 1988;28:532-5.
- 3 Kumar AJ, Rosenbaum AE, Naidu S, et al. Adrenoleukodystrophy correlating MR imaging with CT. *Radiology* 1987;165:497-504.
- 4 Kuroda S, Hirano A, Yuasa S. Adrenoleukodystrophy-cerebello-brainstem dominant case. *Acta Neuropathol* 1983;60:149-52.
- 5 Marsden CD, Obeso JA, Lang AE. Adrenoleukomyeloneuropathy presenting as spino-cerebellar degeneration. *Neurology* 1982;32:1031-2.
- 6 Nishio H, Kodama S, Tsubota T, Takahashi T, Yokoyama S, Matsuo T. Adrenoleukodystrophy without adrenal insufficiency and its magnetic resonance imaging. *J Neurol* 1985;232:265-70.
- 7 Ohno T, Tsuchida H, Fukuhara N, et al. Adrenoleukodystrophy: a clinical variant presenting as olivopontocerebellar atrophy. *J Neurol* 1984;231:167-9.
- 8 Schamburg HH, Powers JM, Raine CS, Suzuki K, Richardson, Jr EP. Adrenoleukodystrophy. A clinical and pathological study of 17 cases. *Arch Neurol* 1975;32:577-91.
- 9 Takada K, Onoda K, Takahashi K, Nakamura H, Taketomi T. An adult case of adrenoleukodystrophy with features of olivopontocerebellar atrophy: I. Clinical and pathological studies. *Japan J Exp Med* 1987;57:53-8.

Myasthenia gravis and thymoma in multiple endocrine neoplasia (MEN-1) syndrome

Multiple endocrine neoplasia (MEN-type 1) or Werner's syndrome is characterised by the

Fig 2

presence of neoplasms or hyperplasia involving endocrine glands. The organs most often affected are the parathyroids, pancreatic islets and pituitary gland.¹ Occasionally neoplasms of the thymus gland have been reported in this syndrome.²⁻⁴ Myasthenia gravis is frequently associated with thymic hyperplasia and approximately 10-15% of the patients have a thymic tumour.⁵ Our patient presenting with myasthenia gravis had a thymoma and characteristic features of MEN-1 syndrome.

A previously healthy 28 year old male was admitted to hospital with a six weeks history of progressive speech disturbance, problems with mastication and nasal regurgitation, followed by diplopia. There was a progression of symptoms during the day and after exertion and reduction after rest. There was no weakness in the extremities. He suffered from nocturnal dyspnoea. Micturition and sexual functions were normal. There were no symptoms of hypoglycaemia. The patient's mother had been operated on in the past because of hyperparathyroidism.

Physical examination showed a slightly overweight man (height 1.72 m, weight 85 kg) with little facial hair. Internal investigations including the genital organs were normal. Neurological investigation revealed slight dysarthria, bilateral ptosis, facial weakness and paresis of abduction and elevation of both eyes. These symptoms fluctuated, depending on the degree of exertion. Leg raising was possible for 45 seconds, no other limb muscle weakness was present. Deep tendon reflexes were normal. The functional capacity of the lungs by spirometry was within normal limits.

Laboratory investigations demonstrated serum calcium level of 3.19 mmol/l; phosphate 0.84 mmol/l; chloride 101.4 mmol/l; chloride/phosphate ratio 102 mol/mol (N: less than 103 mol/mol); parathyroid hormone level of 11.7 pmol/l (N: less than 5 pmol/l); prolactin 4.68 U/l (N: less than 0.3 U/l); glucose 4.4 mmol/l; insulin 29 U/l (N: 5-25 U/l); insulin/glucose ratio 10 (N: less than 9); serum gastrin and glucagon were normal, as 5HIAA in daily urinary excretion. Circulating antibodies to acetylcholine receptors were elevated 97 nM (N: less than 2 nM). Anti-striated muscle antibodies were positive. There was a normal EMG pattern of the abductor digiti quinti muscle after repetitive (3 Hz) and tetanic (20 Hz) stimulation. Edrophonium chloride (Tensilon) 10 mg given intravenously resulted in a marked temporary improvement of signs and symptoms. Computerised tomography (CT) of the thorax revealed a large dense, partly cystic, anterior mediastinal mass. CT of the sella turcica showed a pituitary tumour. On echocardiography and CT of the abdomen no tumour of the pancreatic islets was seen.

The patient had a median sternotomy. A mediastinal tumour (12.5 × 8 × 3 cm) was completely excised. Microscopically the classic histological features of a benign thymoma were present with both epithelial and lymphoid cells without argentaffinity or mitoses. The tumour cells stained positively with cytokeratin and antibodies to insulin, no other endocrinological activity could be demonstrated. Furthermore, a parathyroid adenoma was removed (1.5 × 0.5 × 0.5 cm) in the same session, the other parathyroid glands were normal. The patient made a slow recovery from thymectomy; some days he required intubation and mechanical ventilation because of respiratory insufficiency. On

repeated postoperative examination his calcium, phosphate, insulin level and insulin/glucose ratio had normal values, the antibodies to acetylcholine receptors were reduced to 24 nM; anti-striated muscle antibodies were still positive. Nine months later he was considerably improved taking pyridostigmine 60 mg four times daily, and bromocriptine 2.5 mg twice daily.

This case represents the combination of myasthenia gravis, a benign thymoma, hyperparathyroidism and a pituitary tumour, probably a prolactinoma. The coexistence of hyperparathyroidism and a pituitary tumour is characteristic of MEN-1 syndrome. The evolution of this syndrome may take years and it is inherited as an autosomal dominant trait with a very high degree of penetrance.¹ The mother of our patient also had hyperparathyroidism. Less common findings reported in patients with MEN-1 syndrome included lipoma, carcinoid tumours, thymic tumours and pinealoma.¹⁻⁴ The neoplasms of thymic origin mainly concern carcinoid tumours with a relatively poor prognosis.²⁻⁴ None of these cases had myasthenia gravis.

Only one other patient has been described with the combination of myasthenia gravis, thymoma and hyperparathyroidism; a sporadic *forme fruste* of the MEN-1 syndrome was suggested by the author.⁶ Moreover, our patient had a pituitary tumour which underlines the diagnosis of MEN-1 syndrome. The insulin level and insulin/glucose ratio were slightly elevated, these values, however, did not prove to be a pancreatic islet tumour. Perhaps the thymoma was responsible for this disturbance as the tumour cells reacted positively with antibodies to insulin and the value returned to normal post-operatively.

The importance of this remarkable finding is not clear, but cell surface receptors for some polypeptide hormones have been mentioned in thymoma cells.⁷ This reaction was negative in five other thymomas that we have investigated in recent years. The association of tumours of the thymic and parathyroid gland is not surprising as these structures have a common embryonic origin from the third pharyngeal pouch.

LJHM VROEGINDEWEIJ-CLAESSENS
CC TIJSSEN

Department of Neurology,

GJM CREEMERS

JHM LOCKEVEER

Department of Internal Medicine

ILJM TEEPEN

Department of Pathology,

St Elisabeth Hospital, Tilburg,

The Netherlands

Correspondence to: LJHM Vroegindewij, Department of Neurology, St Elisabeth Hospital, PO Box 90151, 5000 LC Tilburg, The Netherlands.

- 1 Lips CJM, Vasen HFA, Lamers CBHW. Multiple endocrine neoplasia syndromes. *CRC Crit Rev Oncol Hematol* 1984;2:117-84.
- 2 Floros D, Dosios TH, Tsourdis A, Yiatromanolakis N. Carcinoid tumor of thymus with multiple endocrine adenomatosis. *Path Res Pract* 1982;175:404-9.
- 3 Rosai J, Higa E, Davie J. Mediastinal endocrine neoplasms in patients with multiple endocrine adenomatosis. A previously unrecognized association. *Cancer* 1972;29:1075-83.
- 4 Manes JH, Taylor HB. Thymic carcinoid in familial multiple endocrine adenomatosis. *Arch Pathol* 1973;95:252-5.
- 5 Oosterhuis HJGH. Myasthenia gravis. A survey. *Clin Neurol Neurosurg* 1981;83:105-36.

- 6 Palmer FJ, Sawyers TM. Hyperparathyroidism, chemodectoma, thymoma and myasthenia gravis. *Arch Intern Med* 1978;138:1402-3.
- 7 Arya S, Gilbert EF, Hong R, Bloodworth Jr GMB. The thymus. In: Bloodworth Jr GMB, ed. *Endocrine Pathology*. 2nd ed. Baltimore: Williams and Wilkins, 1982:801.

MATTERS ARISING

Korsakoff's psychosis in the presence of multiple sclerosis: an unusual cognitive state

After the publication of our letter in your journal,¹ some inaccuracies were brought to our attention by Professor E K Warrington in whose department the patient was tested.

The difference between the WAIS IQ and the estimated premorbid IQ (NART) indicates a decline in the performance on non-verbal tests rather than general intellectual ability as stated in the article. A score of 19/30 in the McKenna and Warrington Graded Naming Test is within the average range and not indicative of nominal dysphasia. The statement: "in both Korsakoff's syndrome and multiple sclerosis verbal IQs decline more than performance IQs ..." is erroneous and it would be correct to say that the performance IQ is more likely to deteriorate.

Finally, although not an inaccuracy, the Camden Memory Tests quoted in the letter are still in the process of development and low scores should be interpreted as corroborating poor performance on the standard memory tests. These corrections in no way detract from the conclusions of our letter and we feel that it is worth highlighting the need to search for other pathologies in patients with alcohol related brain damage if their clinical presentation is in anyway unusual.

MARIA A RON
ANTHONY FEINSTEIN
The National Hospital for Nervous Diseases,
Queen Square,
London WC1N 3BG, United Kingdom

- 1 Ron MA, Feinstein A. Korsakoff's psychosis in the presence of multiple sclerosis: an unusual cognitive state. *J Neurol Neurosurg Psychiatry* 1989;52:540.

Magnetic resonance imaging in patients with progressive myelopathy following spinal surgery

The explanation by Mr Adams¹ of the post-operative myelopathy with a biomechanical mechanism producing postoperative traction of the dura and the spinal cord during cervical movements is an adjunct to our paper,² in