was fully alert. Serum and urinary osmolarity became normal, urinary specific gravity was 1005-1025. She recovered from ovarian hyperstimulation syndrome and laparotomy during the next month.

Brain MRI and CT performed during the next five years were normal, as were repeated neurological and psychiatric examinations. The patient's IQ was 126-130.

Severe seizures with ascites and hydrothorax due to ovarian hyperstimulation syndrome and haemoperitoneum due to tubal pregnancy, with hypovolaemia, anaemia, and hypoproteinaemia serum concentration masked an SIADH that was heralded by seizures, followed by a prolonged lehargic state. Collateral evidence of SIADH was obtained by normal creatinine clearance with urine hyperconcentration. The symptoms of CNS water intoxication, as usual, appeared during a sudden decrease in Na+ serum concentration, and were treated slowly to avoid central pontine myelinolysis. During SIADH, CT showed several patchy areas of hypoperfusion, resembling severe lesions of acute hypoxic-ischaemic encephalopathy with brain oedema. Hypoxic-ischaemic lesions are, however, usually caused by residual neurological or psychiatric deficit, and CT shows evolution of lesions, with ventricular enlargement and leucomalacia. In this patient the hypoproteinaemia disappeared, the patient had no neurological or psychiatric alterations, and later CT and MRI did not show residual areas of altered signal corresponding to early hypoproteinaemias. Furthermore, unlike the situation in hypoxic-ischaemic lesions, the basal ganglia did not seem to be involved, and the ventricular system was not narrowed as in severe brain oedema. We concluded therefore that water intoxication induced CT images of patchy hypoproteinaemias rather than the expected homogeneous hypoproteinaemia.

DONATO MELCHIONDA
TOMMASO FULGENTE
State University of Chieti,
Correspondence to: Professor Marco Melchionda,
Clinica Neurologica, Ospedale ex Pediatrico, Via Martiri Lancianesi 6, 66100 Chieti, Italy.

Letters to the Editor

A 46 year old woman was admitted with blood in the suprasellar cisterns and the left Sylvian fissure. Two days later she developed a subarachnoid haemorrhage with changes in urine production during surgery. However, from day 12 onwards she again developed a progressive polyuria of up to 21 200 ml per day (on day 22) and a 24 hour renal sodium loss of 2630 mmol. The plasma atrial natriuretic protein concentrations were within the normal range (up to 11·1 pmol/l, normal 3·23 pmol/l), atrial natriuretic protein in CSF was found in diuresis of 75%. Both a reactive increase of CSF production and a decrease in the perivascular autonomic and the arterial and temporal white matter on both sides, mainly in the periventricular and adjacent subcortical regions (fig 1).

Family history showed that the mother of the patient died at the age of 52 with a history of a subarachnoid haemorrhage. The son had M1R changes similar to the index patient, and one had had recurrent episodes of aphasia, headache, and hemianopia. Six members of this family, three affected and three healthy, have been genotyped with eight chromosome 19 markers spanning the CADASIL locus. No linkage was found with any of those markers. Maximum lod scores were obtained with markers D19S226, D19S253, and D19S119, strongly suggesting that this family is linked to the CADASIL locus.

A patient with cerebral autosomal dominant arteriopathy with subcortical infarcts and leuкоencephalopathy (CADASIL) confirmed by sural nerve biopsy

"Cerebral autosomal dominant arteriopathy with subcortical infarcts and leuкоencephalopathy" (CADASIL)1 is a newly defined syndrome characterised, in the absence of hypertension, by recurrent subcortical ischaemic strokes and by peculiar non-amyloid, non-arteriosclerotic angiopathy of cerebral vessels. On MRI circumscribed subcortical ischaemic lesions and diffuse areas of leukoaraiosis are seen both in symptomatic and asymptomatic family members.2 Recently, genetic linkage analysis in two families with CADASIL has assigned the disease locus to chromosome 19q12 with the most likely location of the disease gene between D19S221 and D19S222.3

A few postmortem studies have been reported, showing predominant involvement of the cerebral white matter with diffuse myelin loss, multiple small infarcts, and occasional haemorrhages. As first reported by Baudrimont et al., the small subcortical and leptomeningeal arteries and arterioles display fibrous thickening and an eosinophilic, periodic acid-Schiff (PAS) positive, granular material in the muscle layer. Electron microscopy shows swollen myocytes in the media surrounded by collagen, elastin, and a compact electron dense material.1

The arteriopathy of CADASIL is apparently not restricted to brain vessels as identical vascular lesions have been found in small myocardial arteries and sural nerve.4 We present a 55 year old woman with a history of recurrent pulmonary embolism from the age of 55. At the age of 40 she experienced a feeling of heaviness in her left arm for about two days. Fifteen years later the patient described episodes of a burning sensation on her tongue and tinnitus as well as weakness of the left side of her face and her left arm. Six months later she complained of numbness and weakness of her left arm and leg, from which she recovered slowly. No risk factors such as arterial hypertension, diabetes, or migraine were reported. Neurological examination showed a slight left sided ataxia, hemiparesis, and hypaesthesia of the left upper and lower extremities. MRI showed reduced cognitive performance and flexibility, a deficit in learning and memory, and abnormal visual constructional abilities which were compatible with a subcortical dementia. Brain M1RI showed extensive hypersensitivity of the cerebral white matter with diffuse ischaemic changes in the basal ganglia, thalamus, and occipital lobes. Treatment with fludrocortisone had no effect on renal sodium loss. Despite the low serum sodium, serum ADH concentrations were normal. The mean intraoperative fluid (CSF) production was 600-700 ml/h, and the mean plasma sodium was also normal. The patient remained conscious and she gradually recovered from a mild aphasia and right facial weakness. However, from day 12 onwards she again developed a progressive polyuria of up to 21 200 ml per day (on day 22) and a 24 hour renal sodium loss of 2630 mmol. The serum creatinine was 86 μmol/l (normal 50-100 μmol/l) and the colloidal osmotic pressure was between 18·7 and 24·0 mm Hg. Serum ADH concentrations were normal. The presence of granular electron dense deposits in the media of the sural nerve was processed for light and electron microscopy. Six fascicles were present. Around 120 small and large vessels were counted in the endoneurial and epineurial spaces. The largest endoneurial and epineurial arteries (size up to 100 μm) appeared normal. Small epineurial and perineurial vessels were unchanged in paraffin sections. The arteriolar wall was not thickened on semi-thin sections and no increase in number of nuclei was evident. The perineurium was not thickened and there was no increase of endoneurial connective tissue. The density of myelinated fibres was 6600/mm2 (normal range for the sural nerve for this age 6000-8000/mm2). Myelin degradation products were not encountered.

Electron microscopy showed changes in a few epineurial vessels, consisting of electron dense material in the perineurial areas and especially along the outer aspects of the vessel walls (fig 2A). Most of these granules were on the abluminal surface of pericytes and less often on endothelial cells. Most granules measured 0·2 to 0·5 μm in diameter. However, some measured up to 1·2 × 0·8 μm. Dense deposits were frequently located in thickened basal laminae and were often pushing back the cell membrane of an adjacent pericyte (fig 2 B and C). Most dense deposits were round or oval but some were flat or disc shaped and oriented parallel to the cell surface. For thin sections the number of dense deposits ranged from none to five or six along a single vessel. Some were found in very small arterioles but most were in large capillaries or meta-arterioles (size 14–15 μm) consisting of endothelial cells surrounding by a circumferential layer of pericytes without the presence of smooth muscle cells. In some vessels, the basal lamina surrounding the endothelial cells was clearly redundant and tortuous (not shown). Many pinocytic vesicles were found along and underneath the surface of cell membranes. Their density was not altered at the site of close apposition to the cell membrane with the electron dense granular deposits. The presence of granular electron dense