was fully alert. Serum and urinary osmolality 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 neurologic 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 hyposmolar serum concentra-

tions masked an SIADH that was heralded by seizures, followed by a prolonged leu-
goemic state. Collateral evidence of SIADH was obtained by normal creatinine clearance with urine hyperconcentration. The symp-
toms 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 hypolucency, resembling severe lesions of acute hypoxic-ischemic encepha- lopathy with brain oedema. Hypoxi-

colic lesions are, however, usually caused by residual neurological or psychiatric deficits, and CT shows evolution of lesions, with ventricular enlargement and leucoma-

lacy. In this patient the hypolucencies 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 hypolucencies. Furthermore, unlike the situation in hypoxic-ischemic 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 hypolucencies rather than the expected homogeneous hypolucency.

Hashimoto's encephalopathy. This was originally postulated to be a distinct disease entity by Brain et al in 1966 and there have subsequently been case reports substantiat-
ing the hypothesis that it represents a unique condition. The characteristic features are a subacute onset of confusion with altered consciousness and focal seizures, and events that respond to steroids and which occur in the context of high anti-microbial antibody titres. To date all the patients reported have been either euthyroid or hypothyroid at the time of presentation. We present a case of Hashimoto's encephalopathy with pronounced thyrotoxi-

cosis, that was successfully managed with steroids, carbimazole, and propranolol. A 49 year old woman presented with a six month history of weight loss and a three month history of proximal arm pain and hand tremor. Two weeks before admission she developed a progressive left sided weak-

ness involving the arm and leg in conjunc-
tion with a left hemianesthesia. On examination at admission she was flushed, feverish, and tachycardic with a hyperdy-

namic circulation. Her thyroid gland was slightly enlarged but there was no associated

bruit. Cranial nerve examination disclosed left visual inattention as the only abnormal-

ity. Limb examination showed a moderately severe hypokinetic left side sensory inat-

ention, generalised hyperreflexia, and bilat-
erally extensor plantar responses.

She had wasting of the shoulder girdle muscles and adhesive capsulitis of the shoulder joints bilaterally. In the days immediately after admission she became more confused and had florid visual hallucinations, while independently having runs of paroxysmal atrial fibrillation. As a result of the original negative findings (see later) dexamethasone (12 mg/day) and acyclovir were started with the presumptive diagnosis of an encephalitis or vasculitis. On this regime she made a dra-

matic improvement, which was further enhanced by the treatment of her thyrotoxi-

cosis on receipt of her thyroid function tests. The introduction of carbimazole and propranolol was then followed by a reduction in the dexamethasone and in the dose of acyclovir. Attempted steroid weaning over subsequent days provoked a recrudescence of her focal symptoms on two occasions, with weakness of her right arm. Eventually the patient was stabilised on prednisolone (40 mg/day) and dexamethasone, which slowly reducing course with no relapses three months after discharge.

Investigations performed during her inpa-
tent stay showed that full blood count, cry-
throcite sedimentation rate, urea, electrolytes, liver function tests, and serum immunoglobulins were normal.

Protein electrophoresis showed an acute phase response with a C reactive protein of 52 mg/l. Her autoantibody screen and VDRL/TPHA serology were negative, but her thyroid function tests showed her to be thyrotoxic with TSH less than 0.03 U/l, free T4 >80 pmol/l, and free T3 41 pmol/l. Her thyroid microsomal antibodies were positive at a titre of 1:6400. Her CSF analysis was normal with negative oligoclonal bands and repeated CSF cultures were negative. Her chest radiograph was normal but her ECG showed a sinus tachycardia with episodes of paroxysmal atrial fibrillation. Her EEG showed occasional brief bursts of frontal slow activity which spread posteriorly and brain CT with contrast and MRI with gadolinium were normal. In addition a

transthoracic and transoesophageal ECG along with MRI of her heart were all normal.

These results show that she had a pro-

nounced thyrotoxicosis with antimicrobial antibodies. There was no evidence for any fixed structural lesion within the CNS accounted for her clinical picture. This is as evidenced by her normal brain CT and MRI.

Autoimmune thyroid disease can be con-

sidered as a range of clinical disorders reflecting the variety of autoantibodies present. Hashimoto's disease is characterised by the presence of thyroid antimicrobial anti-

bodies and has rarely been associated with an encephalopathic process of unknown aetiology. All previously described patients have either been euthyroid or hypothyroid and this is the first description of an encephalopathy in combination with thyrotoxi-

cosis. As the mechanism of encephalopa-
	hy is uncertain the term thyroid related encephalopathy is preferable. Although atrial fibrillation was present in our patient, the normal heart and head imaging argues against an embolic cause for her condition. Furthermore, her remarkable steroid respons-

iveness suggests an autoimmune cause for her fluctuating multifocal encephalopathy.

Various mechanisms have been postulated to account for this unusual condition. One possibility is demyelination, which can virtu-

ally be discounted on the basis of our results as both MRI and CSF were normal. More likely explanations are either a multifocal abnormality of cerebral perfusion or a patchy defect of cerebral autoregulation.

This patient completes the repertoire of thyroid states seen in thyroid related encephalopathies and emphasises the need to assess thyroid function and autoantibody status in patients presenting with encephalopathy and stroke-like events in the absence of structural or infective aetiology.

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Cerebral salt wasting syndrome

Excessive natriuresis, resulting in hypona-

 tremia and polyuria, is an often recognised complication after subarachnoid haemor-

rhage. Initially this was attributed to inap-

propriate antidiuretic hormone (ADH) secretion resulting in water retention, but

Thyrotoxic Hashimoto's encephalopa-

thy

Thyroid disease is associated with several neurological disorders, of which one of the rarest and least well understood is
Letters to the Editor

A 46-year-old woman was admitted with haemorrhage who showed remarkable traumaemia in the cerebral salt wasting syndrome characterised, in the absence of hypertension, by recurrent subarachnoid haemorrhage and by peculiar small and large vessels having a characteristic angiographic appearance. The patient had fully recovered two years after operation. Repeated measurements of the cerebrospinal fluid for the cerebral salt wasting syndrome, especially in more severe cases.

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

"Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy" (CADASIL) 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 circumscript subcortical ischaemic lesions and diffuse areas of leukoaraiosis are seen both in symptomatic and asymptomatic family members.1 Recently, genetic linkage analysis in two unilineal families has assigned the disease locus to chromosome 19q12 with the most likely location of the disease gene between D19S221 and D19S222.

A few postmortem studies have been reported, showing predominant involvement of the cerebral white matter with diffuse myelin loss, multiple small deep infarcts, and occasional haemorrhages.2 As first reported by Baudrimont et al.,1 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.

The arteriopathy of CADASIL is apparently not restricted to brain vessels as identical vascular lesions have been found in small myocardial arteries3 and sural nerve.4 We present a 55-year-old woman with a history of recurrent pulmonary embolism from the age of 35. At the age of 40 she had MRI changes similar to the index patient and, one had had previous 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. The patient 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 2 cm long segment 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 epineurial arteries (size up to 100 μm) appeared normal. Small epineurial and subepineurial vessels were unchanged in paraffin sections. The arteriolar wall was not thickened on semi-thin sections and there was 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, PAS positive, granular material in the outer aspect 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 lamina and were often pushing back the cell membrane of an adjacent pericyte (fig 2B and C). Most dense deposits were round or oval but some were flat or disc shaped and oriented parallel to the cell surface. The diameter of the core of the dense deposits ranged from none to five or six around 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 a lumen 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 pinoctytic 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

recently it has become clear that hyponatraemia in the cerebral salt wasting syndrome is accompanied by hypovolaemia.1,2 We report a patient with cerebral salt wasting after aneurysmal subarachnoid haemorrhage who showed remarkable changes in the cerebral salt wasting after aneurysmal subarachnoid haemorrhage in man. Acta Neurochir (Wien) 1990;106:18–23.


A 46-year-old woman was admitted with haemorrhage who showed remarkable traumaemia in the cerebral salt wasting syndrome characterised, in the absence of hypertension, by recurrent subarachnoid haemorrhage and by peculiar small and large vessels having a characteristic angiographic appearance. The patient had fully recovered two years after operation. Repeated measurements of the cerebrospinal fluid for the cerebral salt wasting syndrome, especially in more severe cases.

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