responsiveness to glucocorticoid therapy seems unlikely to be due to chance.[10]

The initial meningo-encephalitic type presentation of our patient in 1987 was probably the first manifestation of HE in view of clinical findings and laboratory data (Mild CSF pleocytosis is not unusual in HE.[3]) There was a delay of 14 years before the diagnosis was first established, in spite of several hospital admissions. The initial relapses after diagnosis responded well to steroids, confirming the diagnosis of HE. Whether the current episode was precipitated by the sudden withdrawal of oral steroids or the chest infection itself, for which they were prescribed, is unclear.

Our patient illustrates the possibility of steroid resistance in an established case of HE and the need to consider further immunomodulatory therapy. Intravenous immunoglobulins are a safe, convenient, and effective treatment in such circumstances.

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References

1 **Lord Brain**, Jellinek EH, Ball K. Hashimoto's disease and encephalopathy. *Lancet* 1966;**2**:512–4.
2 **Shaw PJ**, Walls TJ, Newman PK, *et al*. Hashimoto's encephalopathy: a steroid-responsive disorder associated with high anti-thyroid antibody titre – report of 5 cases. *Neurology* 1991;**41**:228–33.
3 **Peschen-Rosin R**, Schabet M, Dichgans J. Manifestation of Hashimoto's encephalopathy years before onset of thyroid disease. *Eur Neurol* 1999;**41**:79–84.
4 **Ferraci F**, Moretto G, Candeago RM, *et al*. Antithyroid antibodies in the CSF. Their role in the pathogenesis of Hashimoto's encephalopathy. *Neurology* 2003;**60**:712–4.
5 **Boers PM**, Colebatch JG. Hashimoto's encephalopathy responding to plasmapheresis. *J Neurol Neurosurg Psychiatry* 2002;**73**:601.
6 **Henchey R**, Cibula J, Helveston W, *et al*. Electroencephalographic findings in Hashimoto's encephalopathy. *Neurology* 1995;**45**:977–81.
7 **Chaudhuri A**, Behan PO. The clinical spectrum, diagnosis, pathogenesis and treatment of Hashimoto's encephalopathy (recurrent acute disseminated encephalomyelitis). *Curr Med Chem* 2003;**10**(19):1945–53.
8 **Bohnen NI**, Parnell KJ, Harper CM. Reversible MRI findings in a patient with Hashimoto's encephalopathy. *Neurology* 1997;**49**:246–7.
9 **Mahmud FH**, Renaud DL, Reed AM, *et al*. Steroid-resistant encephalopathy associated with Hashimoto's thyroiditis in an adolescent with chronic hallucinations and depression: case report and review. *Pediatrics* 2003;**112**(3 Pt 1):686–90.
10 **Chong JY**, Rowland LP, Utiger RD. Hashimoto's encephalopathy. Syndrome or myth? *Arch Neurol* 2003;**60**:164–71.

Spontaneous lobar haemorrhage in CADASIL

CADASIL is an autosomal dominant form of arteriopathy, primarily affecting cerebral vessels, and predominantly caused by point mutations in the *Notch3* gene on the short arm of chromosome 19.[1] Affected individuals develop subcortical strokes and cognitive deficits in their 50s and 60s.[2] Brain magnetic resonance imaging (MRI) shows large areas of leukoencephalopathy and multiple subcortical lacunar infarcts. Small arteries and capillaries are characterised histologically by a non-atherosclerotic, non-amyloid angiopathy with accumulation of granular osmiophilic material (GOM) within the smooth muscle cell basement membranes and extracellular matrix.[3] While CADASIL is considered a primarily ischaemic form of vascular dementia, microhaemorrhages have recently been reported in 31% of symptomatic *Notch3* mutation carriers, suggesting that structural fragility of the arterial walls may lead to leaking of haem products.[4] Lobar haemorrhage in the absence of other risk factors for haemorrhage has previously been reported in one patient with CADASIL.[5] Here we report a second case.

Case report

A 56 year old man who had been diagnosed with multiple sclerosis six years earlier was admitted to the hospital with an acute change in mental state. He had collapsed at home and was unresponsive when rescue arrived. In the emergency room he had a depressed level of consciousness and difficulty following commands, with paucity of speech, dysarthria, and hypophonia. There was no evidence of head trauma. His blood pressure was 100/63 mm Hg and his temperature was 36.1°C.

Past medical history included chronic obstructive pulmonary disease, prostate resection for prostate cancer, and a history of nicotine and alcohol dependence. He had no history of hypertension, diabetes mellitus, or coagulopathy. His drug treatment included ipratropium, ranitidine, methyprednisolone, and albuterol. His mother, now deceased, had been diagnosed as having multiple sclerosis and had migraines with auras, stroke-like symptoms, and dementia. He had eight siblings, three with headaches and one with recent transient ischaemic events.

Computed tomography (CT) of the head in the emergency department showed an area of high attenuation in the right frontal lobe consistent with an acute intraparenchymal haemorrhage (fig 1A). There was no evidence of trauma on head CT. Gradient echo MRI sequences of the brain done on hospital day 2 showed a 2×2.5 cm area of haemorrhage in

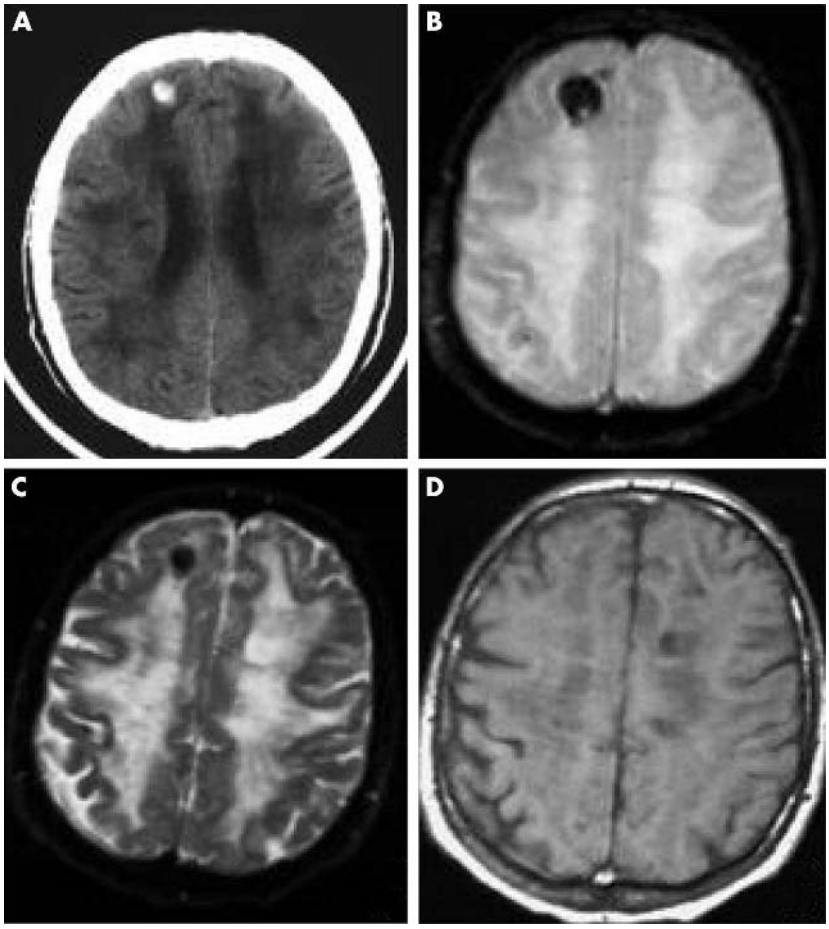

Figure 1 (A) Non-contrast computed tomography of the head done in the emergency room showing an area of high attenuation in the right frontal lobe consistent with acute haemorrhage. The other panels show non-contrast magnetic resonance imaging done on hospital day 2: (B) Gradient echo sequence demonstrating a 2×2.5 cm area of haemorrhage in right frontal lobe, a microhaemorrhage in the right parietal region, and extensive white matter disease. (C, D) The area of haemorrhage is hypointense on T2 and isointense on T1 weighted imaging, consistent with an acute haemorrhage.

the superior-anterior aspect of the right frontal lobe white matter as well as a microhaemorrhage in the right parietal region (fig 1B). The area of haemorrhage was hypointense on T2 (fig 1C) and isointense on T1 weighted sequences (fig 1D), consistent with acute haemorrhage. There was no MRI evidence of a cavernous haemangioma, arteriovenous malformation, or tumour. Magnetic resonance angiography was not done.

A brain biopsy of the right frontal lobe done on the seventh hospital day showed degeneration of small and medium sized arteries. Vessel walls were thick and hyalinised in the grey matter, white matter, and meninges. PAS staining was positive and the muscular coat of the large vessels revealed degenerative changes. Electron microscopy showed the granular osmiophilic material characteristic of CADASIL. *Notch*3 gene testing revealed a R133C mutation in exon 4, consistent with the diagnosis of CADASIL. The patient remained normotensive throughout his hospital stay. On the fifth hospital day he developed aspiration pneumonia requiring mechanical ventilation. He died eight days later as a result of this pneumonia.

Comment

This is the second report of spontaneous cerebral haemorrhage in a patient with CADASIL. In 1977, Sourander and Walinder reported a 29 year old man with hereditary multi-infarct dementia on anticoagulants, with a large haemorrhage in the right hemisphere.[5] This family was thought to be one of the first with CADASIL; however, recent testing for *Notch3* mutations in the family has not confirmed that diagnosis.[6] In 1992, Baudrimont *et al* reported a case of massive left cerebral haematoma involving the caudate nucleus, internal capsule, and thalamus in a 40 year old normotensive woman who was a member of a large CADASIL family. She had no known history of other risk factors for haemorrhage.[7]

The index patient in this report had no evidence of coagulopathy and no history of previous hypertension, cerebral haemorrhage, or anticoagulant therapy. The patient could have experienced a haemorrhagic contusion related to a closed head injury during his unwitnessed fall before admission, but there was no evidence of trauma on physical examination or on head CT. On MRI there was no evidence of a cavernous haemangioma, arteriovenous malformation, or neoplasm. Necropsy was not carried out.

Ultrastructural analysis of small arteries in human postmortem brain and skin in patients with CADASIL shows breakdown of the arterial wall cytoarchitecture, which may help explain the propensity for microhaemorrhages.[8] The first *notch3* transgenic mouse shows early widening of the subendothelial and intra-smooth-muscle spaces in the vascular smooth muscle cells, denoting weakening of the arterial wall and increasing susceptibility to micro- and macrohaemorrhages.[9]

This case report supports the growing evidence for both ischaemia and haemorrhage in a variety of small artery diseases including amyloid angiopathy and CADASIL.[10 11] Clinicians may need to consider the possibility of haemorrhage when evaluating new events and deciding on treatment for stroke prevention in patients with CADASIL.

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References

1 **Joutel A**, Corpechot C, Ducros A, *et al*. Notch3 mutations in CADASIL, a hereditary adult-onset condition causing stroke and dementia. *Nature* 1996;**383**:707–10.
2 **Dichgans M**, Mayer M, Uttner I, *et al*. The phenotypic spectrum of CADASIL: clinical findings in 102 cases. *Annals of Neurology* 1998;**44**:731–9.
3 **Ruchoux MM**, Maurage CA. CADASIL: cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy. *J Neuropathol Exp Neurol*, 1997;**56**:947–64.
4 **Lesnik Oberstein SA**, van den Boom R, van Buchem MA, *et al*. Cerebral microbleeds in CADASIL. *Neurology* 2001;**57**:1066–70.
5 **Sourander P**, Walinder J. Hereditary multi-infarct dementia: morphological and clinical studies of a new disease. *Acta Neuropathol (Berlin)* 1977;**39**:247–54.
6 **Kalimo H**, Ruchoux MM, Viitanen M, *et al*. CADASIL: a common form of hereditary arteriopathy causing brain infarcts and dementia. *Brain Pathol* 2002;**12**:371–84.
7 **Baudrimont M**, Dubas F, Joutel A, *et al*. Autosomal dominant leukoencephalopathy and subcortical ischemic stroke: a clinicopathological study. *Stroke* 1993;**24**:122–5.
8 **Rouchoux MM**, Maurage CA. Endothelial changes in muscle and skin biopsies in patients with CADASIL. *Neuropathol Appl Neurobiol* 1998;**24**:60–5.
9 **Ruchoux MM**, Domenga V, Brulin P, *et al*. Transgenic mice expressing mutant notch3 develop vascular alterations characteristic of cerebral autosomal dominant angiopathy with subcortical infarcts and leukoencephalopathy. *Am J Pathol* 2003;**162**:329–42.
10 **Greenberg SM**. Cerebral amyloid angiopathy and vessel dysfunction. *Cerebrovasc Dis* 2002;**13**(suppl 2):42–7.
11 **Dichgans M**, Holtmannspotter M, Herzog J, *et al*. Cerebral microbleeds in CADASIL: a gradient-echo magnetic resonance imaging and autopsy study. *Stroke* 2003;**34**:376–7.

Urinary retention caused by a small cortical infarction

The cortical representation of micturition is speculated to reside in the medial frontal lobes.[1 2] Lesion pathology, however, varies from acute stroke to a neoplasm, and there is not necessarily a small, distinct lesion.[2] We report a case of urinary retention in which the main presenting symptom is thought to have been caused by a small cortical infarction.

Case report

One morning, a 66 year old, right handed man had difficulty urinating. He had no history of voiding difficulty, diabetes mellitus, injury to the lower urinary tract, or neurological disease. Digital rectal examination and ultrasonography of the prostate detected no enlargement. Urinalysis showed no haematuria or pyuria. He was not taking any medications that cause voiding dysfunction. There was no urinary incontinence, but he had difficulty in voiding even though he felt the bladder was full. At that time, he also had difficulty in lifting his left arm and leg and so was brought to our hospital. Neurological examination in the emergency room found no weakness, and he was sent home. Later, he experienced urinary retention and visited the emergency room again. His post void residual urine volume was 350 ml, and an urinary catheter was inserted. At that time the patient was alert, and his cranial nerves were intact. Limb muscle strength was normal. Sensory examination was unremarkable. Tendon reflexes were normal in all four limbs. Tandem gait and standing on one foot were difficult. He had normal bladder sensation but difficulty in urinating. Drip infusion pyelography revealed no abnormality in the upper urinary tract or the form of the bladder. Filling cystometry showed stable detrusor with normal bladder sensation, whereas acontractile detrusor was noted in the voiding phase. He could void only with strain, having a peak flow rate of 5.0 ml/s and a voided volume of 135 ml. Diffusion weighted MRI, performed on the day of onset, showed a small, distinct, high intensity signal, and T1 weighted imaging showed a low signal in the right caudal part of the anterior cingulate gyrus, indicative of an infarct in the acute stage (fig 1A and C). No definitive infarct was observed elsewhere. MR angiography showed no occlusion or stenosis of the intracranial vessels. An electrocardiogram was normal. Transthoracic echocardiograms showed no abnormal findings. The urinary catheter was withdrawn 3 days after admission, and he had no subsequent difficulty with urination. His gait returned to normal about the same time.

Discussion

In the acute stage of a cerebral vascular accident, the presenting symptom often is urinary retention due to detrusor areflexia,[3] but patients who have this problem usually have a major stroke with severe neurological deficits.

To the best of our knowledge, this is the first report in the English literature of urinary retention, although temporary, caused by a small cortical infarct as shown by diffusion weighted MRI.

Various cortical areas are activated during voiding because a network of brain regions is necessary for voiding modulation.[4] The locations of the primary cerebrum cortical areas for voiding and storage are speculated to be separate, the former being at the para-central lobule.[2] A PET study found normal micturition to be associated with activation of the middle frontal gyrus, superior frontal gyrus, superior precentral gyrus, thalamus, and the caudal part of the anterior cingulate gyrus in the left hemisphere.[5] Another recent PET study showed that increased brain activity related to increasing bladder volume was located in the bilaterally mid-cingulate cortex, while that related to decreased urge to