Owing to the large variety of pathogens causing acute aseptic meningitis, clinicians rely on rapid laboratory confirmation of suspected cases by standard methods such as RT-PCR or the plaque reduction neutralisation test (PRNT). Nowadays, PRNT is rarely used owing to its complexity and time consuming nature, while RT-PCR appears inadequate because of the short duration of the viraemia.[1 2] Recently developed EIA formats can establish the presence of infection by detecting specific IgM in acute phase samples and were able to confirm TOSV infection in this case. With millions of travellers and increasing TOSV infections around the Mediterranean basin, commercially available EIA methods will be of growing importance. In addition to other severe travel related diseases, TOSV infections now need to be considered by physicians.

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Intracerebral haemorrhage in CADASIL

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) is a rare hereditary disease characterised by recurrent transient ischaemic attacks, strokes, and vascular dementia. Pathological studies reveal multiple small infarcts and diffuse white matter changes as well as vascular alterations most prominent in small arteries.[1] The presence of granular osmiophilic material in arterial walls on ultrastructural examination is pathognomonic. Mutations in the notch3 gene located on chromosome 19 are associated with the disease.[2] Here we report a patient with an unusual clinical course with recurrent intracerebral haemorrhage.

Case report

A 47 year old woman was admitted after a fall at home, followed by several minutes of unconsciousness. Her past medical history was uneventful. In particular, there was no history of migraine or depression, and she was not taking any drugs. On admission, her husband reported memory deficits for several weeks. Initially, the patient complained about headaches and mild dysarthria. Moderate left sided hemiataxia and pronation of the left arm were present. Blood pressure was raised to 220/120 mm Hg

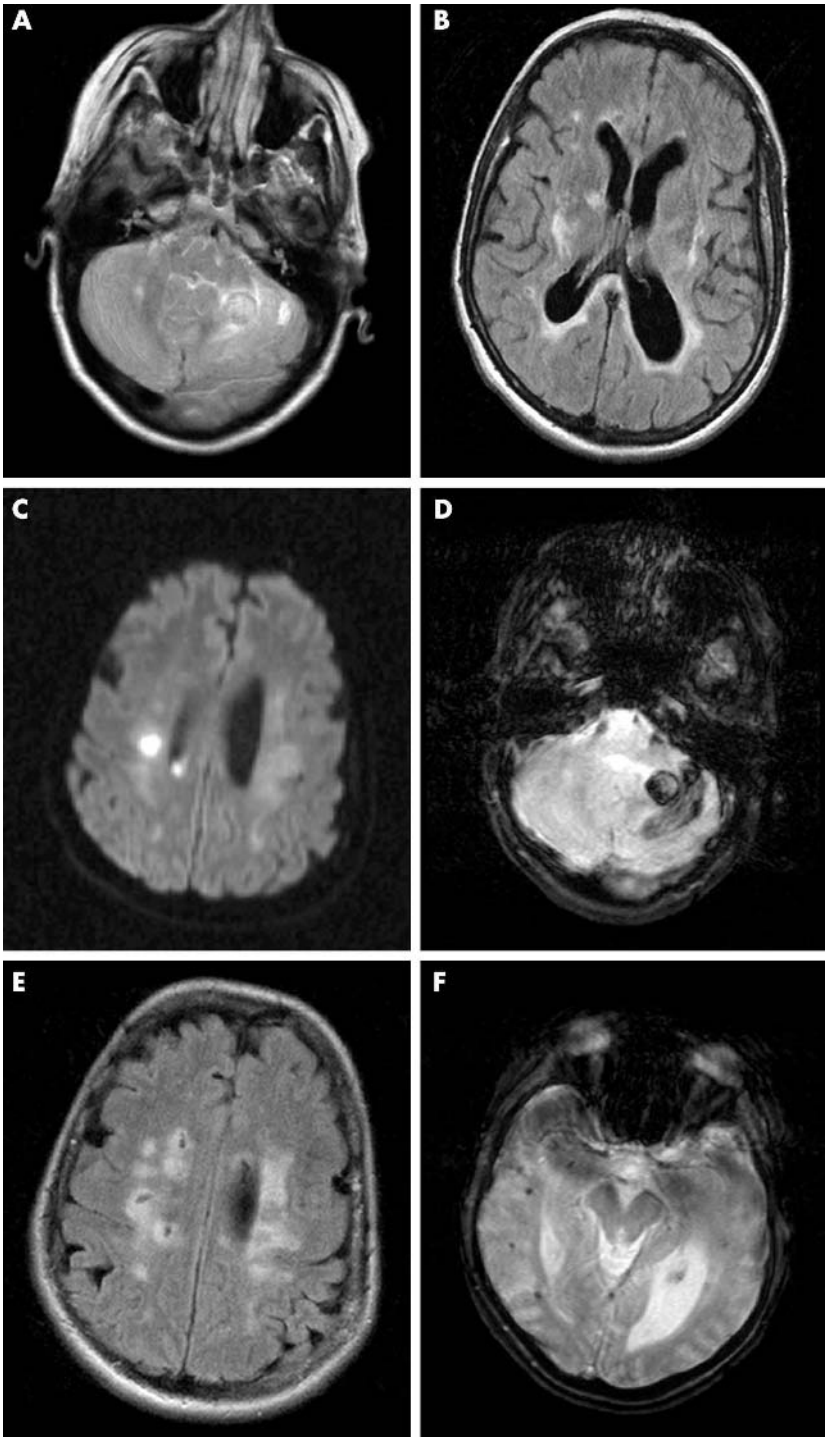

Figure 1 Bleeding in the left cerebellar hemisphere as shown in pd+T2 tse (A) and T2* (D). White matter lesions in the FLAIR sequence (B, E): note the lesions in the external capsule which are often present in CADASIL (B). (C) Acute ischaemic lesions in the right hemisphere in a diffusion weighted image. (F) Multiple microbleeds shown in T2*. CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy; FLAIR, fluid attenuated inversion recovery.

without a known history of arterial hypertension. Neuropsychological deficits were prominent in impaired semantic, visual-spatial, and episodic memory, and in deterioration in cognitive speed. Concentration and mathematical problem solving were also reduced, indicating severe cognitive impairment. Initial cranial computed tomography revealed a haemorrhage of 20 mm diameter in the left cerebellar hemisphere. Subsequent magnetic resonance imaging (MRI) with T2* gradient echo (GE) showed more than 25 small haemorrhages distributed over the entire brain. T2 weighted scans showed white matter lesions with periventricular emphasis (fig 1). Serum markers for vasculitis and coagulation indices were normal, as was the cerebrospinal fluid. An ophthalmological examination showed hypertensive changes. Ultrasound sonography of the extracranial and intracranial vessels revealed arteriosclerotic vessel walls but no stenosis. Electronmicroscopic examination of a skin biopsy showed granular osmiophilic material (GOM) in the basal lamina of small arterioles, establishing the diagnosis of CADASIL. Direct bidirectional sequencing of all exons coding for epidermal growth factor (EGF)-like repeat domains (exons 2 to 24) of *notch3* did not reveal any mutation.

After stepwise normalisation of arterial blood pressure, the patient gradually improved over the following weeks. Headaches, ataxia, and dysarthria resolved gradually, but severe neuropsychological deficits remained, rendering her unable to take care for herself. A follow up examination three months after discharge showed further amelioration of gait without any other focal neurological symptoms. The neuropsychological deficits had improved slightly, but there were still severe memory deficits. The patient was aware of these deficits and she reacted in a depressive manner. Activities of daily life were moderately impaired. Follow up MRI showed no new lesions.

Comment

The clinical course of this case with intracerebral bleeding in combination with excessive blood pressure values was consistent with hypertensive intracerebral haemorrhage. Although there was no history of known arterial hypertension, the changes of the retina supported this diagnosis. Hypertension is the most common cause of intracerebral haemorrhage, accounting for 50–70% of cases. Hypertensive bleeding into the cerebellum, however, is relatively rare (<10%). The finding of numerous cerebral microbleeds on T2*-GE MRI led to the suspicion of amyloid angiopathy, a common cause of intracerebral haemorrhage in the elderly. On the other hand, the relatively young age of the patient and the family history (mother and two sisters suffering from migraine; father died at 47 years from unknown cause) was compatible with an autosomal dominantly inherited condition, for example, CADASIL. The finding of GOM in the basal lamina of small vessels is pathognomonic of this disease and confirmed the diagnosis. Mutations in exons 2 to 24 of the *notch3* gene are found in approximately 95% of patients, but were not detected in this case.[2]

While transient ischaemic attacks and ischaemic strokes, along with the development of vascular dementia, are common, major intracerebral haemorrhages are not a common feature of CADASIL. There have been sporadic reports of intracerebral hemorrhages,[4 5] but the significance of these observations remains unclear, given the absence of intracerebral haemorrhage in large patient series.[6 7] In a recent study with GE T2* weighted scans, microbleeds (up to 22 in a single subject) ranging from 2 to 10 mm in diameter were found in 69% of CADASIL patients examined, but no major ICH was found.[8] Another study found microbleeds in 31% of all CADASIL patients examined, and an increased risk of intracerebral haemorrhage was predicted. The presence of microbleeds correlated with age and the use of antiplatelet drugs.[9] CADASIL leads to degeneration of small arterioles, thus increasing the probability of vessel rupture in arterial hypertension. Compared with the patients in the studies cited above, our patient showed even more microbleeds (25), possibly indicating a greater risk of intracerebral haemorrhage in patients with CADASIL in combination with arterial hypertension. While the white matter pathology in our patient may appear relatively sparse, lesions in the external capsule and the temporal lobe typical of CADASIL were present.

We conclude that CADASIL should be considered in patients with cerebral haemorrhage, and careful blood pressure management is particularly important in CADASIL patients, as the risk of vessel rupture and subsequent intracerebral haemorrhage appears to be further increased compared with patients with arterial hypertension alone. While there is no effective treatment for CADASIL, control of arterial hypertension could at least slow the rate of deterioration in this disabling and dementing disorder.

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Catastrophic primary antiphospholipid syndrome presenting as status epilepticus

Antiphospholipid syndrome (APS) is defined as the occurrence of arterial or venous thrombosis or recurrent miscarriage, with raised titres of antiphospholipid antibodies, namely lupus anticoagulant (LA) or anti-cardiolipin antibodies (aCL). An accelerated form of APS is catastrophic antiphospholipid syndrome (CAPS) or Asherson's syndrome. Proposed diagnostic criteria for definite CAPS are: multiorgan failure, development of manifestations within 1 week, demonstration of antiphospholipid antibodies and histopathological evidence of microthrombosis (positive predictive value 99.4%).[1] Precipitants include infection, surgery, and childbirth. Patients typically develop widespread thrombotic vasculopathy with marked thrombocytopaenia. Clinically apparent cerebral infarction occurs much less frequently than in uncomplicated APS but the major pathological manifestation of CAPS is cerebral microthrombosis at postmortem examination.

CASE REPORT

A 30 year old woman delivered her first child following a full term uncomplicated pregnancy. Three weeks later, she developed headache and transient hemiparesis. The following day she had an episode of speech arrest, bit her tongue, and held both arms stiffly in the air for about 1 minute. On admission to hospital, she was pyrexial and developed generalised tonic clonic seizures. There was no relevant previous medical history and she was not taking any medication. Blood tests, including erythrocyte sedimentation rate (ESR) and C reactive protein (CRP), were normal. Computed tomography scan of the brain and analysis of the cerebrospinal fluid (CSF) were normal. Gynaecological examination showed no retained products of conception. The seizures proved refractory to treatment with intravenous lorazepam. She was transferred to a specialist neurological centre that day.

On arrival she was agitated, disorientated and pyrexial (38°C). Generalised tonic clonic seizures continued. Neurological examination was normal except that all limb reflexes were pathologically brisk and plantar responses were extensor. General examination was unremarkable. Despite being given ''loading'' doses of phenytoin, phenobarbitone, and magnesium sulphate, the seizures continued. She was anaesthetised and intubated, and mechanical ventilation was introduced.