## A small deep infarct revealing leukoencephalopathy, calcifications and cysts in an adult patient

Leukoencephalopathy with intracranial calcifications and cysts (LCC) is an uncommon entity; it was first described in 1996 in three unrelated children.<sup>1</sup> Following this report, six other cases have been reported, including one adult-onset case.<sup>2-5</sup> The clinical presen-

**Figure 1** Leucoencephalopathy with calcifications and cysts. Axial computed tomography image (A) shows thalamic and caudate calcifications with leucopathy and a right parietal cyst. Diffusion-weighted image (B) shows an acute ischaemic lesion of the left internal capsule. T2-weighted images turbo-spinecho (C) and gradient echo (D) show diffuse leucopathy surrounding hyperintense cysts (C) and hypointense calcifications (D). T1-weighted images before (E) and after (F) contrast show ring enhancement of the cyst walls and adjacent to calcifications.

tations of this cerebral disorder include progressive extrapyramidal, cerebellar, pyramidal signs, slowed cognitive performances and/or seizures.<sup>1-5</sup> LCC is characterised by a striking triad of neuroimaging findings: asymmetric calcifications, diffuse abnormal white-matter signal and parenchymal brain cysts.<sup>1-5</sup> Histopathological examination in LCC reveals "angiomatous-like rearrangements of the microvessels", with proliferation of abnormal small vessels associated with Rosenthal fibres, gliosis and calcifications.<sup>1</sup> The admitted primary pathological feature of LCC is cerebral angiomatous rearrangements involving the microvessels, whereas perivascular foci of calcifications, hyaline deposits and formation of Rosenthal fibres appear compatible with secondary changes.<sup>1 3 5</sup> Extensive cerebral calcifications and leukoencephalopathy have been also reported in another rare disorder, "Coats plus", which is characterised by additional features: intrauterine growth retardation, bilateral retinal telangiectasias and exudations (Coats disease), sparse hairs, dysplastic nails, and occasionally skeletal abnormal-



ities, pancytopenia or intestinal bleeding.4 Neuropathologic examination in patients with "Coats plus" shows abnormal small vessels with angiomatous proliferation and extensive calcinosis, similar to LCC.4 Recently, Linnankivi et al. reported patients showing LCC, and retinal vascular abnormalities, skeletal changes and haematological abnormalities, which overlap with features of the previously reported patients with "Coats plus" syndrome and LCC.<sup>4</sup> This strongly suggests that LCC and "Coats plus" belong to the same spectrum.4 The occurrence of affected siblings and consanguinity in parents strongly suggests that these microangiopathic affections are autosomal-recessive disorders.<sup>2</sup> <sup>4</sup>

We report herein an adult-onset LCC case revealed by an acute hemiparesis due to a small, deep cerebral infarct. This presentation expands the clinical spectrum of this condition.

#### **CASE REPORT**

A 30-year-old woman was admitted due to an acute right-sided hemiparesis. Her family history was negative for neurological or ophthalmological illnesses, and no consanguinity was known. She had a past history of migraine without aura, according to the International Headache Society criteria, since the age of 25 years, without associated cardiovascular risk factors, mood disorders or cognitive dysfunction. On admission, 8 hours after onset, there was a right hemiparesis with an ipsilateral Babinski sign. Sensation to pain and touch was impaired on the right side. There was no cognitive dysfunction, visual-field defect or dysphasia. Her score on the National Institute of Health Stroke Scale was 6. The optic disk and retinal vessels were normal. Her blood pressure was 130/80 mm Hg. The routine laboratory workup was normal, including blood cell count, coagulation tests, creatinine, glucose, sedimentation rate, calcium, phosphate, alkaline phosphatase and lactate levels. Brain computed tomography (CT) showed numerous foci of calcifications scattered in the right thalamus, the left basal ganglia and the right part of the cerebellum, associated with a cystic formation on the right parietal lobe and asymmetric diffuse leucopathy (fig 1A). Magnetic resonance imaging (MRI) diffusionweighted imaging revealed the presence of an acute ischaemic lesion in the posterior limb of the left internal capsule (fig 1B). T2weighted imaging showed asymmetric white-matter hypersignals, always surrounding cysts and calcification foci (fig 1C). Gradient echo imaging revealed the extent of the calcifications, which were not seen on CT or conventional MRI (fig 1D). Ring-contrast enhancement of the cysts walls and adjacent to calcifications was observed (fig 1E-1F). Cerebral MRI angiography was normal. Electrocardiogram, cervical and transcranial Doppler, and transoesophageal echocardiography,

were also normal. Spinal MRI was normal, as well as cervical, thoracic and abdominal CT examinations. Complementary biological tests were obtained, including antinuclear, anticardiolipids and anti-\beta2GP1 antibodies, antithrombin III, protein C and S. prothrombin (G20210A) and factor V mutations (Leiden), cholesteroaemia, homocysteinaemia, endocrinology tests (including parathyroid hormone) and serological tests for cysticercosis, human immunodeficiency virus (HIV-1 and -2), Treponema pallidum haemagglutination and Venereal Disease Research Laboratory (TPHA/VDRL) tests. All these tests were negative or in the reference range. Cerebrospinal fluid studies were normal. Treatment with aspirin was prescribed. Eight months later, the patient has only slight weakness in her right hand.

### DISCUSSION

This young adult patient shows the classical LCC neuroradiological triad-namely, asymmetric calcifications, asymmetric abnormal white-matter signal and parenchymal brain cvsts. However, she did not show any of the clinical symptoms that were previously reported in LCC, such as progressive extrapyramidal, cerebellar, pyramidal signs, slowed cognitive performances or seizures.1-5 Surprisingly, clinical onset was unusual as the patient presented an acute hemiparesis due to a small, deep, cerebral infarct. To our knowledge, this type of clinical manifestation has not been reported in LCC patients even in adult cases.<sup>1-5</sup> We strongly believe that this lacunar infarct is a consequence of the disease as no other cause of cerebral infarct has been identified in this patient despite thorough investigations, and because LCC is characterised by a cerebral obliterative microangiopathy. In conclusion, these data suggest that LCC belongs to the group of hereditary causes of ischaemic smallvessel diseases of the brain, which already include Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), Cerebral Autosomal Recessive Arteriopathy with Infarcts Subcortical and Leukoencephalopathy (CARASIL), cerebroretinal vasculopathy, Hereditary Endotheliopathy with Retinopathy, Nephropathy, and Stroke (HERNS) and familial amyloid angiopathy.

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# Measuring the effect of amantadine in chronic anoxic minimally conscious state

The effect of pharmacological agents on recovery in chronic disorders of consciousness remains unsatisfactory.<sup>1</sup> Amantadine, a dopaminergic agonist, has been suggested to behaviourally improve recovery from both a vegetative state (VS) and a minimally conscious state (MCS).<sup>2 °</sup> Here, we report the effect of amantadine in a chronic anoxic MCS patient using standardized behavioural evaluations, actigraphy and serial positron emission tomography.

## CASE REPORT Patient

A 23-year-old man was found comatose after ventricular fibrillation. A brain computed tomography scan was normal and electroencephalography showed an alphacoma pattern. Somatosensory-evoked potentials detected no cortical (N20) responses. After 3 weeks, the patient evolved to a vegetative state (VS) and was transferred to a rehabilitation centre (where no cognitiveenhancing interventions were given). He returned home after 6 months, having been diagnosed as being in a VS. After 2 years, the family contacted us for re-evaluation. Using the Coma Recovery Scale-Revised (CRS-R),<sup>4</sup> the patient was recognised as being in a minimally conscious state (MCS; that is, presence of visual pursuit). After written informed consent from the patient's legal representative, amantadine treatment (200 mg per day) in an ABAB design was proposed in conjunction with weekly CRS-R assessment, actimetry monitoring and serial FDG-PET (fluorodeoxyglucose-positron emission tomography) (3 weeks baseline period, amantadine administrated during 6 weeks, stopped during 6 weeks and again resumed for 6 weeks). Throughout the observational period, the patient remained free of other centrally acting drugs. The study was approved by the Ethics Committee of the University of Liège.



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