

# Longitudinally extensive spinal cord infarction in CADASIL

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## INTRODUCTION

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary small-vessel disease caused by mutations in the *NOTCH-3* gene. Characteristic features include early onset lacunar stroke, migraine usually with aura and cognitive impairment with early onset subcortical dementia.<sup>1</sup> Pathological studies show involvement of small arteries throughout the body,<sup>2</sup> although these symptoms are typically confined to the central nervous system.

## CASE REPORT

A 48-year-old woman presented with a rapidly progressive spastic paraparesis. Following the sudden onset of severe back pain, she experienced left leg spasms and hyperacute left leg weakness that progressed over 12 h. Over the subsequent 24 h, her right leg was similarly affected and she developed urinary retention.

She had no past history of neurological or psychiatric illness and took no regular medication. Her family history was noteworthy: her maternal grandmother developed migraines at the age of 40 and paraparesis later in life; her mother experienced migrainous headaches from the age of 50; her brother suffered a stroke aged 40 and her son had migraines.

On examination, there was no obvious cognitive impairment (Addenbrooke's Cognitive Examination Revised 84/100 with English as a second language; lower limit of normal for native English speaker of similar age group 86<sup>3</sup>) and normal cranial nerve and upper limb function. She had an almost complete spastic paraparesis with an asymmetric sensory level to T1 on the left and T5 on the right. Proprioception was absent in the lower limbs.

Investigations, including serum B12, methylmalonic acid, homocysteine, copper studies, HIV serology, syphilis

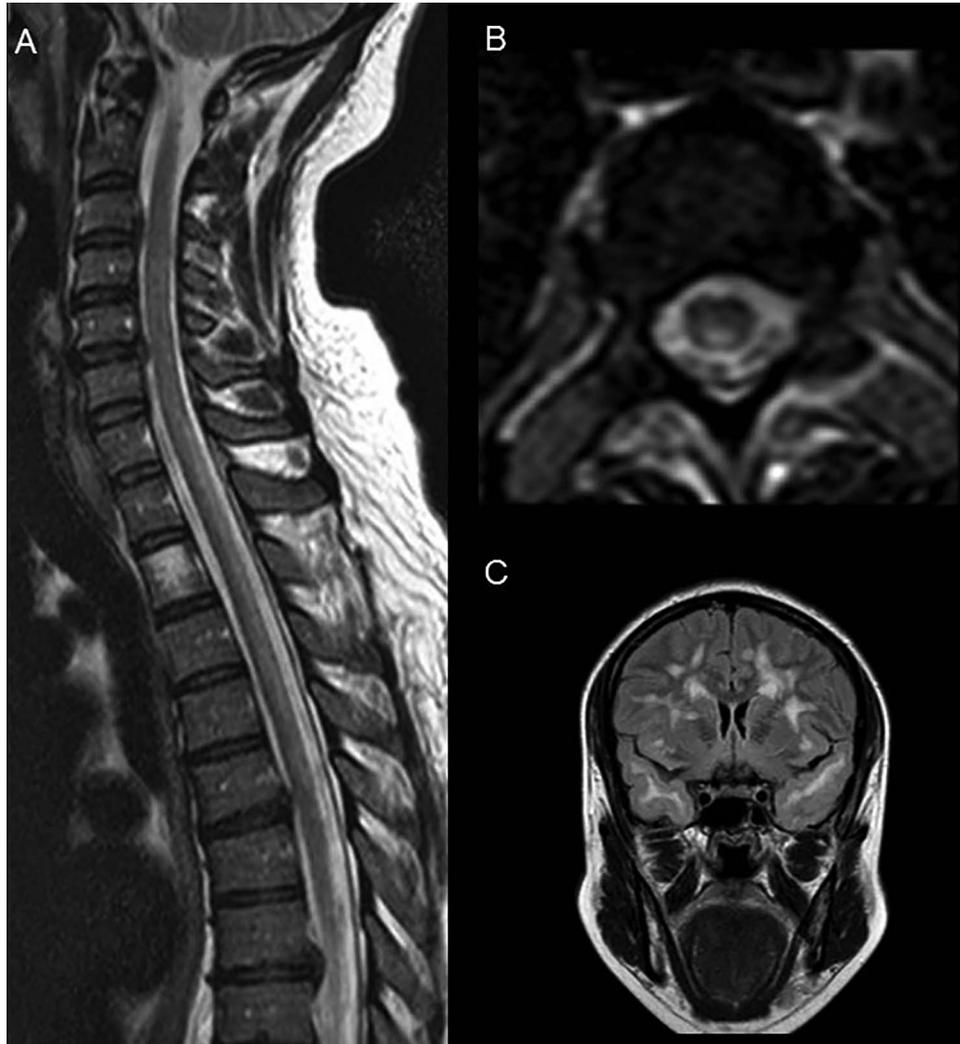
serology, anti-nuclear antibody, anti-myelin oligodendrocyte glycoprotein and anti-aquaporin-4 antibodies were all normal or negative. Initial MRI of the spinal cord was normal. Repeat imaging 2 days later with gadolinium showed T2 hyperintensities from C3 to T6, mainly posteriorly, but also extending into the central grey matter. There was no significant cord enlargement (figure 1). MR brain imaging showed widespread T2 hyperintensities throughout the white matter with marked involvement of the anterior temporal lobes, as well as in the basal ganglia, thalamus, midbrain and pons (figure 1). Cerebrospinal fluid (CSF) was acellular, with normal protein, glucose and cytology and negative PCR for viruses. There were no oligoclonal bands in the CSF. *NOTCH-3* gene analysis showed heterozygosity for the c.268C>T (p.Arg90Cys) mutation, a previously reported pathogenic CADASIL mutation.<sup>4</sup>

In view of an initial differential possibility of an inflammatory event, the patient received a short course of high-dose corticosteroids followed by an oral taper over 6 weeks. Aspirin was also commenced. She improved within the first week and could walk a few months later. Repeat MRI approximately 1 month after her initial presentation showed the spinal cord lesion had improved.

## DISCUSSION

We report an unusual case of genetically proven CADASIL presenting in the 5th decade with posterior spinal cord infarction. There was no evidence of inflammation within the CSF, and the acute onset, as well as MRI, favoured an ischaemic aetiology.

Spinal cord infarction represents only around 1% of ischaemic strokes. The vascular anatomy of the spinal cord consists of one anterior spinal artery and two posterior spinal arteries, supplied in the



**Figure 1** MR scans of brain and spine: (A) sagittal T2 image showing signal change in the posterior spinal cord between C3 and T6. (B) Axial T2 image highlighting the posterior nature of the signal change at level T3. (C) Coronal FLAIR MR scan of brain showing widespread white matter hyperintensities with marked involvement of the anterior temporal lobes, suggesting cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). FLAIR, fluid attenuated inversion recovery (sequence).

cervical region from the vertebral arteries and in the lumbar region from intercostal arteries, mainly via the Adamkiewicz artery. Most commonly affected are the anterior and lower regions of the spinal cord.<sup>5 6</sup>

**Spinal Cord Infarction (~1% of strokes) [5;6]**

**Localisation:**

1. Anterior (30%)
2. Unilateral ant./ post. (15-20%)
3. Posterior (7-15%)
4. Central (8-11%)

**Etiology:**

1. Unknown (30-70%)
2. Radicular artery occlusion with spinal disease (~50%)
3. Hypoperfusion in pre-existing arterosclerotic disease
4. Embolic, Vascular malformations, Fibrocartilaginous embolism, etc.

The posterior spinal cord contains longer perforating arteries that might be more susceptible to the

effects of CADASIL vasculopathy. This explains the clinical (predominantly dorsal column involvement and motor deficit) and imaging features compared with those in the more common anterior spinal cord infarction (predominantly spinothalamic tract involvement and motor deficit). The stepwise progression could be explained by sequential involvement of perforating spinal cord arteries. Her clinical improvement is likely attributable to the combination of corticosteroid-responsive peri-ischaemic inflammatory changes and natural recovery.

Spinal cord involvement in CADASIL is well recognised but rare. In a UK cohort of 200 patients, there were no cases of spinal cord infarction.<sup>1</sup> An anterior spinal cord infarct occurred in an Irish patient with probable CADASIL who had a history of severe migrainous headaches.<sup>7</sup> A cervical spinal cord MRI study showed no abnormalities in 25 symptomatic CADASIL patients.<sup>8</sup> However, compared with 14 healthy controls, patients with CADASIL showed

impaired magnetisation transfer, suggesting there were diffuse spinal cord changes beyond the resolution of conventional MRI.<sup>8</sup> In 2011, two sisters with a novel cysteine altering *NOTCH-3* mutation were found to have spinal cord pathology.<sup>9</sup> Both had a previous history of migraines, and one of them experienced a relapsing–remitting brainstem–cord syndrome.

More recently, a 53-year-old woman was described as having a *NOTCH-3* mis-sense mutation and a progressive paraparesis, developing over 6 months and responding to corticosteroids.<sup>10</sup>

The present case highlights the importance of brain imaging and of taking a detailed family history in cord pathology as well as the need to consider CADASIL in the differential diagnosis of spinal cord infarction—particularly posterior cord infarction—even with no previous history of migraines or other features more typical of CADASIL.

**Contributors** SH, SN, DB and HSM: revision of manuscript, care of patient. MG: manuscript draft, care of patient. GQ: preparation of images for article, review of MRI. AS: revision of manuscript, overall responsibility for care of patient.

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**Patient consent** Obtained.

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