

# High signal in the cerebrospinal fluid following prior gadolinium administration in a patient with renal impairment

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## ABSTRACT

Increased signal intensity in the cerebrospinal fluid (CSF) on magnetic resonance imaging due to the presence of gadolinium is rarely observed, but has been seen in patients with brain or spinal pathology or underlying renal impairment. We report this phenomenon in a 66-year-old woman with diabetic nephropathy and discuss the possible pathogenesis of the scan findings. Recognition of this unusual finding, and features distinguishing it from other causes of high CSF signal intensity, such as subarachnoid haemorrhage and protein in the CSF, are emphasised to help prevent diagnostic errors.

**Keywords:** cerebrospinal fluid, gadolinium, magnetic resonance imaging, renal insufficiency

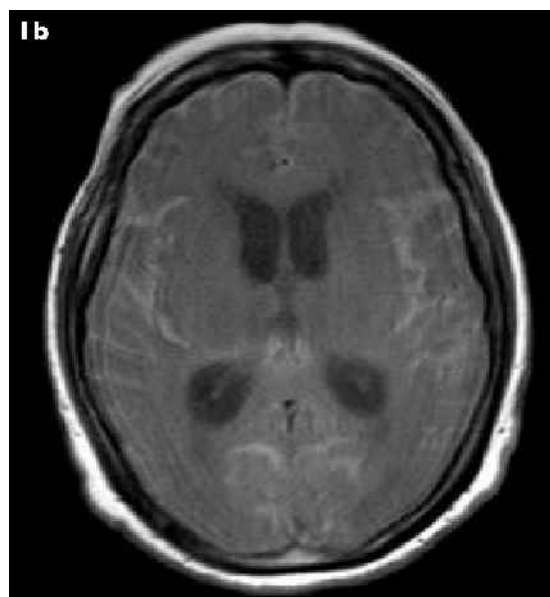
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## INTRODUCTION

High signal intensity in the cerebrospinal fluid (CSF) on magnetic resonance (MR) imaging may be due to subarachnoid haemorrhage, raised CSF protein content, or rarely, the presence of gadolinium within the CSF. We report a case showing high signal intensity in the CSF from the presumed persistence of gadolinium in a patient with diabetic nephropathy. We also discuss the possible pathogenesis of the scan findings.

## CASE REPORT

A 66-year-old woman with a background of hypertension, hyperlipidaemia, congestive cardiac failure and diabetes with nephropathy, presented with an acute history of altered behaviour, slurred speech and memory loss. Clinical examination revealed left dysdiadochokinesis with past pointing. Her blood pressure was 172/65 mmHg. Computed tomography (CT) of the brain on admission showed bilateral chronic subcortical white matter ischaemic changes. Serum creatinine on admission was 271  $\mu\text{mol/L}$



**Fig. 1** (a) Sagittal and (b) axial T1-weighted MR images show diffusely increased signal intensity in the subarachnoid spaces.

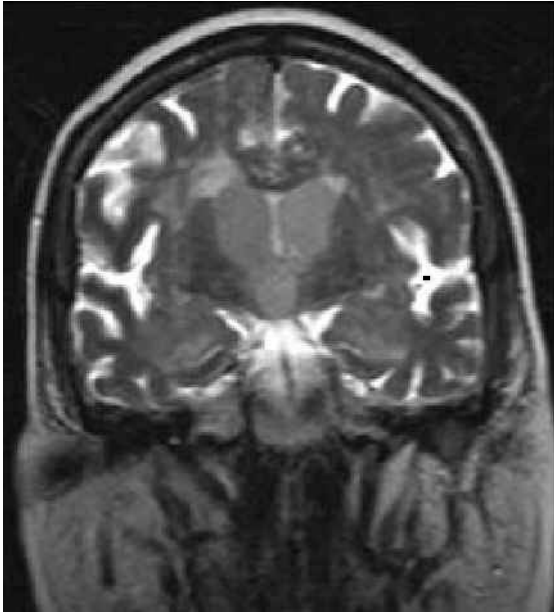
and there was azotaemia with serum ammonia of 63.8  $\mu\text{mol/L}$  (normal range 9–33  $\mu\text{mol/L}$ ). She developed bilateral lower limb weakness over the next few days and MR imaging of the spine done

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**Fig. 2** Coronal T2-weighted fast FLAIR image shows failure of CSF signal suppression, with high signal seen in the subarachnoid spaces and some increased signal in the ventricles. Hyperintense signal noted in the periventricular white matter is due to chronic microvascular ischaemia.

five days after admission showed myelomalacia in the lower cervical cord, unchanged from a previous MR imaging done four years ago following surgical decompression for an epidural abscess. 13 ml (0.1 mmol/kg) of Magnevist (Bayer Schering, Berlin, Germany), containing gadopentetic acid dimeglumine salt in aqueous solution, was given during the study. No spinal or epidural abscess was detected and no abnormal meningeal enhancement was seen.

Unenhanced MR imaging of the brain performed the following day, showed an acute small infarct in the left cerebellar hemisphere, which was the probable cause of her symptoms. Strikingly increased signal intensity was seen diffusely in the subarachnoid spaces on the T1-weighted images (Fig. 1). T2-weighted fast fluid-attenuated inversion-recovery (FLAIR) images revealed failure of CSF signal suppression with high signals seen in the subarachnoid spaces and some increased signals in the ventricles (Fig. 2). CT performed later on the same day showed no subarachnoid haemorrhage. Lumbar puncture was subsequently performed and CSF analysis revealed 0.6 g/L of protein (normal range 0.1–0.4 g/L), 3 white cells/ $\mu$ L and < 1 red cell/ $\mu$ L. CSF cultures were negative. The CSF signal hyperintensity was consequently attributed to the persistence of gadolinium in the CSF from the prior spine MR imaging.

## DISCUSSION

The presence of gadolinium in the CSF resulting in high signal intensity on MR imaging is a rare phenomenon that has been described in a number of patients with renal impairment,<sup>(1-4)</sup> brain tumours,<sup>(5)</sup> intracranial or spinal infection,<sup>(6)</sup> and acute stroke.<sup>(7)</sup> It has been postulated that this is due to the breakdown of the blood brain barrier (BBB) from intracranial pathology, and that the rate of accumulation in the CSF is proportional to the size of the area of disruption.<sup>(5)</sup> It has also been shown that there is higher enhancement of the CSF closer to the area of pathology.<sup>(5,8)</sup>

Gadolinium can also enter the CSF due to increased dose or accumulation from poor clearance due to renal impairment.<sup>(1-4)</sup> Follow-up MR imaging after dialysis showed resolution of the changes,<sup>(9)</sup> suggesting impaired gadolinium excretion as the likely cause for the accumulation. Gadolinium is an extracellular contrast medium which is excreted by glomerular filtration. It has a mean elimination half-life of 1.3 hours in healthy subjects.<sup>(9)</sup> In subjects with renal impairment, the mean elimination half-life increases according to the severity of renal impairment. It has been postulated that the poor excretion of gadolinium in patients with renal impairment results in the accumulated gadolinium being equilibrated among the body's extracellular compartments, including the CSF. The exact site of leakage of gadolinium into the CSF has not been ascertained. The brain capillaries contain tight junctions forming the BBB, which highly restrict the passage of solutes like gadolinium. However, the fenestrated capillaries of the choroid plexus and uveochoroid membrane of the eye may allow the passage of gadolinium from plasma into the CSF.<sup>(2)</sup> The latter may explain why gadolinium diffusion into the ocular globes has been observed in patients with chronic renal disease. Alternative sites of entry into the CSF include the circumventricular organs, ependymal surfaces and the pia-glial membrane.<sup>(2)</sup>

Although our patient had a small left cerebellar infarct, the diffuse distribution of the T1 and FLAIR hyperintensity in the CSF suggests that the underlying renal impairment probably played the major role in the development of this phenomenon, rather than BBB breakdown. The hyperintense appearance of the CSF in the subarachnoid spaces, and to a lesser extent in the ventricles, on FLAIR imaging is a striking feature in our case. Animal models have demonstrated the extreme sensitivity of FLAIR imaging to changes in the T1 relaxation of CSF.<sup>(10)</sup> Gadolinium typically shortens the repetition time (TR) of tissues leading to high signal on T1-weighted images.<sup>(11)</sup> The FLAIR sequence, on the other hand, produces heavily T2-

weighted images with CSF signal suppression by using an inversion recovery pulse and acquiring the image data after a suitable time delay (the inversion time), when the longitudinal magnetisation of the signal from CSF is zero. Any other tissue with TR similar to that of CSF then also appears strongly attenuated.<sup>(12)</sup> If there is gadolinium in the CSF, this would significantly change the TR of the CSF water molecules. Thus, if standard inversion times were used, this would result in incomplete suppression on the FLAIR image and result in hyperintensity of the CSF.<sup>(12)</sup> Mathews et al have shown how FLAIR is sensitive to T1 shortening with gadolinium and that FLAIR is superior to T1-weighted images in detecting superficial lesions, such as in the subarachnoid spaces.<sup>(11)</sup> There have also been suggestions that the relatively decreased enhancement of the ventricular CSF with gadolinium is due either to dilution of the CSF in the ventricles, or to increased diffusion through the meninges into the extraventricular subarachnoid spaces due to a larger surface area compared to the ependyma and choroid plexus.<sup>(3)</sup> This corresponds with the appearance on our FLAIR images.

Other causes of high signal in the CSF include subarachnoid haemorrhage and high concentration of protein.<sup>(2)</sup> In our case, the CT scan and CSF analysis done following the MR imaging showed no evidence of subarachnoid haemorrhage, thus excluding this as the cause of CSF hyperintensity. The diffusely increased FLAIR signal within the ventricles is also not typical for intraventricular haemorrhage, which tends to appear as a fluid-fluid level and is more heterogeneous. In addition, intraventricular haemorrhage would be evident on other MR imaging sequences, especially gradient-recalled echo images, and CT. The presence of protein within the CSF, of which meningitis is a common cause, may result in hyperintense T1 and FLAIR signals as well. However, Melhem et al have shown that the threshold for FLAIR hyperintensity is 125 mg/dL of protein for echo times (TE) of 150 ms and below.<sup>(13)</sup> The mildly-elevated CSF protein level in our case (0.6 g/L) is thus unlikely to be the cause

of CSF hyperintensity, given the FLAIR imaging parameters used (TR 9500 ms, TE 122 ms).

In conclusion, high signal intensity in the CSF may be seen on MR imaging in patients with renal impairment, and in those who have had recent gadolinium-enhanced imaging. It may also be seen in cases with underlying intracranial or spinal pathology. Correlation of the imaging appearance with laboratory findings is useful in distinguishing this entity from other causes of increased CSF signal intensity.

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