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Gadolinium enhancement of cerebrospinal fluid in a patient with renal failure

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Abstract  
Gadolinium based MRI contrast agents are considered very safe due to their well known pharmacologic properties and elimination mechanisms. In this paper, we present a unique case in whom transient enhancement of CSF with contrast is seen. Severe renal failure is demonstrated to be responsible for this finding. The diagnostic criteria for everyday clinical setting and possible clinical implications are discussed.

Keywords  
Gadolinium · Contrast agents · Cerebrospinal fluid

Introduction

Transient gadolinium enhancement of cerebrospinal fluid (CSF) on fluid attenuation inversion recovery (FLAIR) images can be seen in subjects without significant meningeal disease [1]. However, detection of CSF enhancement on conventional T1-weighted images usually implies extensive meningeal or superficial brain disease [2–4]. To our knowledge, such a phenomenon has not been reported in the absence of a meningeal disease process. We present a case of CSF enhancement by gadolinium on T1-weighted and FLAIR images which we believe was due to a combination of a high dose of gadolinium and renal failure.

Case report

This 70-year-old female patient with multiple medical problems including CREST syndrome, chronic renal failure, hypertension, and coronary artery disease had ongoing Clostridium difficile diarrhea for almost 8 months, with worsening renal failure (creatinine levels being elevated to 2.7 from the baseline value of 1.9 mg/dl). Although the renal sonogram showed small and echogenic kidneys, her complicated medical course and slow recovery raised a suspicion of underlying renovascular disease, prompting magnetic resonance angiography (MRA) of the renal arteries at an outside institution. Renal MRA performed following an injection of 0.2 mmol/kg of Gadoteridol revealed no significant abnormality. The patient presented to our institution the following day with declining mental status without any focal neurological findings. At the same time she had also developed severe pancytopenia with toxic megacolon. MRI of the brain revealed that both the ventricular and subarachnoid CSF had diffusely increased signals on FLAIR images (Fig. 1a). The T1-weighted images demonstrated increased signal of the subarachnoid CSF (Fig. 1b). Additionally, there was enhancement in the nasal and nasopharyngeal mucosa, superior sagittal sinus, small vessel related infarcts and perivascular spaces (Fig. 1a, c). Lumbar puncture done on the same day revealed clear-colorless CSF, normal cytology, normal cell count (two white and three red blood cells), glucose of 64 mg/dl (serum glucose same day 98 mg/dl), protein 60 mg/dl (normal range in our laboratory being 15–45 mg/dl). After excluding the possibilities of meningitis, subarachnoid hemorrhage or meningeal carcinomatosis by laboratory analysis of CSF we performed MR imaging of the CSF.
Fig. 1  a Axial FLAIR image TR/TE/IT: 9002/154/2200 shows hyperintense CSF in the ventricles and extra-axial spaces. The relatively low signal of ventricular CSF compared with the extra-axial spaces may be due to dilution effects.  b Axial T1-weighted image TR/TE: 550/16 shows diffuse CSF hyperintensity in the subarachnoid spaces and perivascular spaces, and enhancement of old white-matter infarcts. Low signal of CSF in the ventricles is maintained. Enhancement is seen in the superior sagittal sinus.  c Sagittal T1-weighted image TR/TE: 550/16 shows diffuse hyperintensity of subarachnoid CSF. Note the enhancement of nasal mucosa sample, which revealed increased layering signal in the dependent part on T1-weighted spin-echo images compared with normal saline, as seen in Fig.2, suggestive of gravity effects of gadolinium. The patient was dialyzed the following day without improvement in her mental condition. Repeat MRI of the brain demonstrated resolution of CSF signal abnormalities on FLAIR and T1-weighted images (Fig.3a, b). Her condition deteriorated gradually and she died a few days later of complications from toxic megacolon.

Discussion

Gadolinium products have been in clinical use for more than a decade. Among the different products available, their efficacy, utility and safety have been extensively studied, including their use in patients with renal failure [5–7]. It is generally agreed that gadolinium agents do not cross intact blood–brain and blood-CSF barriers, and the enhancement in pathological areas is largely related to disruption of these barriers [8–9].

Previous reports have suggested gadolinium enhancement of CSF on T1-weighted images in patients with brain tumors and leptomeningeal metastasis, meningeal carcinomatosis and cryptococcal meningitis [2–4]. In all these cases higher than normal diffusion of gadolinium in CSF was suspected, due to disruption of the blood–brain barrier. However, in an animal experiment, Knutzon et al. detected in vitro T1-shortening of CSF in normal dogs following intravenous gadolinium administration [10]. This finding indicates that although it is possible for gadolinium to diffuse along an intact blood–brain barrier, it is not likely that a sufficiently high concentration is achieved for detection on post-contrast T1-weighted images. On the other hand, FLAIR images are extremely sensitive to T1-shortening effect, and can show CSF enhancement at a much lower concentration of gadolinium in CSF. Mamourian et al.