CASE REPORT

Diffusion MRI findings of cytomegalovirus-associated ventriculitis: a case report

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ABSTRACT. Cytomegalovirus (CMV) ventriculoencephalitis is a rare but serious potential complication of CMV infection in immunocompromised patients. Characteristic diffusion-weighted imaging findings can be helpful for the diagnosis of CMV ventriculitis, as in this case report.

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Cytomegalovirus (CMV) usually exists as a latent infection in the adult population, but it can provoke opportunistic infection and be fatal in immunocompromised patients [1]. Ventriculoencephalitis is the main central nervous system (CNS) pathology because CMV tends to localise to ependymal and subependymal regions [1]. On MRI, it can show subependymal signal changes along the lateral ventricles, septum pellucidum, corpus callosum and fornices owing to the necrotic changes of ventriculitis. However, the subependymal signal changes are hard to see on conventional T_1 and T_2 weighted images even with contrast enhancement. We present a case of CMV ventriculoencephalitis in a leukaemia patient, in whom there were typical findings of ventriculitis and ependymitis on a diffusion-weighted image (DWI) and an apparent diffusion coefficient (ADC) map. This is the first case describing the restricted diffusion along the ependymal linings in CMV ventriculitis on DWI.

Case report

A 20-year-old male patient was admitted to our haematology unit with persistent fever and progressive leg weakness. He had previously been diagnosed with acute lymphoblastic leukaemia (ALL) approximately 18 months ago and was in complete remission (CR) after chemotherapy. However, he relapsed and received re-induction chemotherapy. CR was again achieved and the patient underwent cord blood transplantation (CBT) 1 year after the initial diagnosis. 1 month after CBT, he received treatment for bacterial infection and CMV antigenaemia. Despite treatment with intravenous

foscarnet, the number of CMV RT-PCR (reverse transcription polymerase chain reaction) copies increased exponentially. During this admission for persistent fever and leg weakness, the patient showed pancytopenia and a second relapse was diagnosed. On the eleventh day after admission, CT and MRI of the brain were performed for the evaluation of his acute decreased awareness and dysarthria. A brain CT showed sulci and cisternal spaces that were rather prominent for his age, suggesting brain atrophy and mild ventricular dilatation. On T_1 and T_2 weighted, there were multiple high-signal intensity nodular lesions in both subcortical and periventricular deep white matter, both basal ganglia and both medial temporal lobes (Figure 1a,b). Also, curvilinear high signal changes were detected along both lateral ventricular walls on fluid attenuated inversion recovery (FLAIR) (Figure 1c), which also showed subtle subependymal contrast enhancement (Figure 1d). These lesions along the ventricular wall showed strikingly increased signal intensities (Figure 1e and 2a) on DWI and low ADC values (Figure 1f and 2b), suggesting diffusion restriction or cytotoxic oedema.

Clinically, he was diagnosed with CMV ventriculoencephalitis. He then developed further episodes of altered mentality with decreased blood O_2 saturation. His caregivers refused further treatment and the patient died as a result of concurrent septic pulmonary complications.

Discussion

CMV as a source of congenital intrauterine infection presents unique radiological findings, such as microcephaly, gyral anomalies, cerebellar hypoplasia, focal white matter lesions, hippocampal abnormalities, ventriculomegaly, hydranencephaly, porencephaly and paraventricular cysts with bilateral periventricular calcification in infants. However, radiographic findings of opportunistic CMV ventriculoencephalitis in the adult

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Figure 1. Axial (a) T_1 and (b) T_2 weighted MRI (566/16, 5000/93; repetition time/time to echo) show mild ventricular dilatation and multiple tiny nodular T_2 high-signal intensity lesions in basal ganglia and right frontal subcortical white matter without definite periventricular signal change. (c) Axial fluid attenuated inversion recovery image (9900/126) shows thin curvilinear high-signal intensities along the walls of both lateral ventricles and multifocal faint high-signal intensities at right frontal and basal ganglia regions. (d) Axial contrast enhanced T_1 weighted image (600/16) shows subtle subependymal enhancement (arrow). (e,f) Diffusion weighted image (7000/90) shows striking curvilinear high-signal intensities along the ventricular wall with a subtle low apparent diffusion coefficient value (arrow).

population are non-specific. Almost all cases reveal no abnormality with a few showing diffuse or patchy increased signal intensities in white matter owing to

demyelination and enhancement in the periventricular subependymal lining along the lateral ventricles, septum pellucidum, corpus callosum and fornices owing to

Figure 2. (a,b) Diffusion weighted image (7000/90) at the occipital horn level shows striking curvilinear high-signal intensities along the ventricular wall of occipital horns with definite low apparent diffusion coefficient value (arrow).

ventriculitis [2]. A previous report of CMV ventriculoencephalitis showed diffuse cerebral atrophy, progressive ventriculomegaly and a variable degree of periventricular or subependymal abnormality and emphasised that FLAIR sequencing was the most sensitive method in the detection of periventricular abnormality [3].

In the current case, the high-signal intensities along the ependymal lining (Figure 1e and 2a) were identified on DWI with low ADC values (Figure 1f and 2b). These subependymal abnormalities were better visualised on DWI than FLAIR (Figure 1c) or contrast enhanced T_1 weighted imaging (Figure 1d). This peculiar CMV ventriculitis finding with subependymal cytotoxic oedema is the first to be reported in the literature for CMV ventriculoencephalitis.

Kiroglu et al [4] explained that congestion with perivascular cuffing and thrombus formation of viral encephalitis is responsible for the cytotoxic oedema that leads to restricted diffusion and low ADC. We postulated that in the case of CMV infection, the enlargement in cellular size owing to intranuclear and intracytoplasmic inclusion particles leads to increased intracellular osmolarity and the shift of water from extracellular fluid (ECF) to intracellular fluid (ICF). The increase in cellular size and decrease of extracellular volume impedes the distribution or mobility of water, and may result in the restricted diffusion of water. Therefore, the decreased ADC value along the ependymal layer, as described in this case, could be a radiological finding suggestive of CMV-induced ventriculitis.

CMV, a member of the herpes virus family, is the most frequent cause of foetal and neonatal viral infection and is latent in a large percentage of the general adult population. The reactivation of this virus often causes a subclinical or mild infection resembling mononucleosis. Less often encountered is the disseminated form of the disease, which can be fatal in immunosuppressed patients with acquired immunodeficiency syndrome (AIDS), haematological disease or transplant patients [5, 6]. CMV retinitis and gastrointestinal tract involvement are common forms of CMV infection, but neurological manifestations, including meningoencephalitis, encephalitis, ventriculoencephalitis, radiculomyelopathy and peripheral neuropathy, can be identified in less than 1% of all patients with CMV infection. Ventriculoencephalitis is the most common form of CNS involvement in CMV infection and is characterised by ependymitis along the inner surface of ventricles. CMV ventriculoencephalitis was identified in approximately one-third of autopsies of AIDS patients [2, 7, 8]. Clinical symptoms of CMV ventriculoencephalitis include confusion, disorientation, apathy, withdrawal, cranial neuropathies and nystagmus. These clinical symptoms develop in a subacute form over several weeks [1]. Most cases of autopsy-diagnosed CMV encephalitis are either not recognised *in vivo* or only suspected on the

basis of CMV isolation from blood or other specimens [9]. In these circumstances, a final diagnosis can be based on clinical and imaging features characteristic of CMV infection. Salazar et al [10] reported that a diagnosis of CMV ventriculoencephalitis can be reached if there are MRI findings that are suggestive of ventriculitis in AIDS patients with altered neurological status, CMV viraemia, retinitis or hypoglycorachia. Until recently, there was no effective treatment for CMV encephalopathy, including intravenous ganciclovir or foscarnet; the prognosis is still poor [11–13]. To prevent recurrence, maintenance therapy should be considered [13].

In the current case, a severely immunocompromised patient with relapsed ALL and CBT history presented with CMV ventriculoencephalitis with striking subependymal diffusion restriction.

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