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Case Report

Vessel wall enhancement in the diagnosis and management of primary angiitis of the central nervous system in children

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Abstract

We describe two cases of primary angiitis of the central nervous system in children (cPACNS) diagnosed by vessel wall contrast enhancement on magnetic resonance imaging (MRI). Both patients developed acute cerebral infarction after fever and malaise. In patient 1, a 7-month-old boy, MRI revealed extensive cerebral infarction in the right middle cerebral artery (MCA) area and stenosis at the M1 portion of the right MCA. Oral glucocorticoid therapy was initiated. Vessel wall enhancement was ameliorated 3 months after onset, and stenosis was mostly restored. Patient 2, a 5-year-old boy, suffered from cerebral infarction in the left MCA area, and stenosis was identified in the left internal carotid artery, left MCA, and left posterior cerebral artery. Although vessel wall enhancement was reduced after glucocorticoid therapy, vessel wall enhancement of left MCA re-emerged, accompanied by increased erythrocyte sedimentation rate (ESR) and, decreased cerebral blood flow (CBF) in the affected hemisphere. Intravenous methylprednisolone therapy followed by oral glucocorticoid and mycophenolate mofetil resulted in resolution of these findings.

Vessel wall enhancement is a promising finding in the diagnosis of cPACNS. Disease flares occur rarely in medium-to-large vessel cPACNS during dose tapering. Vessel wall enhancement, ESR, and CBF may be useful for the assessment of the activity of angiitis.

Keywords: Primary angiitis of the central nervous system (PACNS); Vessel wall enhancement; Medium-to-large vessel angiitis of the CNS

1. Introduction

Primary angiitis of the central nervous system in children (cPACNS) is an idiopathic angiitis that affects CNS vessels without evidence of systemic vasculitis. It is assumed to be rare, but is nonetheless important as a treatable etiology of cerebral infarction in children.

Several distinct phenotypes have been identified; 1) progressive, angiography positive (medium-to-large vessel) cPACNS; 2) non-progressive, angiography positive (medium-to-large vessel) cPACNS; and 3) angiography-negative (small vessel) cPACNS. The 'progressive' type has been defined as aggravation of findings of vasculitis at 3 months after initial angiography [1]. Magnetic resonance angiography (MRA) can detect the stenosis of medium-to-large vessels in cPACNS, and gadolinium

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enhancement on 3D spin echo T1-weighted images with blood suppression magnetic resonance imaging (MRI) has been also useful in adult patients with PACNS for detecting vessel wall inflammation [2,3]. Brain biopsy is necessary for small vessel cPACNS that appears normal on MRA to prove the presence of vascular inflammation. However, the proportion of false negative results in brain biopsy is higher in cases of medium-to-large vessel cPACNS.

Nonspecific symptoms such as headache, malaise, and fever are often the initial symptoms in cPACNS. Blood and cerebrospinal fluid (CSF) examination often reveals inflammatory activity [1,4].

Immunotherapy is often effective for both adult and cPACNS, and the treatment regimen is different for each clinical phenotype. Non-progressive medium-to-large vessel cPACNS is treated with short-term corticosteroids, not in combination with cyclophosphamide (CYC), which is often chosen for adult PACNS. Progressive medium-to-large vessel cPACNS and small vessel cPACNS require a further 2 years of immunotherapy with immunosuppressive agents [4]. Despite these immunotherapy options, certain children with PACNS experience relapse or disease flares during treatment, with novel clinical symptoms or new lesions in MRI, often resulting in neurological deterioration.

Here, we report two cases of medium-to-large vessel cPACNS for which assessment of pyrexia, vessel wall enhancement, and erythrocyte sedimentation rate (ESR) were effective in monitoring disease activity.

2. Case reports

2.1. Patient 1

The boy developed normally until the age of 7 months, when he developed left hemiparesis within 3 days of pyrexia and malaise (Suppl. Fig. 1A). On admission, he was alert, babbled well, and showed interest in his surroundings. Pyramidal signs were positive on the left toe, but deep tendon reflex was normal bilaterally. We noted transient left hemispatial neglect. No cutaneous eruptions or vesicles were present. Brain MRI revealed an extensive infarct in the right middle cerebral artery (MCA) area (Fig. 1A and B), and MRA revealed stenosis at the M1 portion of the right MCA (Fig. 1C and E). Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) levels were 31 mm/h and 0.17 mg/dL, respectively. CSF cell count and protein level were normal. Another MRI on hospitalization day 15, with gadolinium enhancement on 3D spin echo T1-weighted images with blood suppression revealed segmental vessel wall thickening and contrast enhancement at the stenosis site (Fig. 1G–J). Signal intensity of the stenotic vessel wall before enhancement was comparable to the contralateral vessel site (not shown). Screening investigations for the cause of angiitis were all negative, including serum and CSF titers of varicella zoster virus, blood levels of ferritin, coagulation/fibrolytic markers and autoantibodies, plasma amino acids, urinary organic acids, urinalysis, and cardiac and carotid ultrasonography.

Although the patient's hemiparesis gradually improved, vessel wall enhancement persisted and he experienced repeated, intermittent fever accompanied by elevated CRP and ESR levels (Suppl. Fig. 1A). Under a diagnosis of cPACNS, we administered low-dose corticosteroids (prednisolone [PSL]; 1 mg/kg/day) from day 35. After initiating corticosteroid therapy, he had no recurrence of fever, and vessel wall enhancement became less evident at 3 months compared to onset (Fig. 1D, F, K–N).

2.2. Patient 2

The boy developed normally until age 5, when he developed right hemiparesis and dysarthria preceded by headache, slight fever, and malaise (Suppl. Fig. 1B). On admission, he followed verbal instructions but had aphasia. We noted right flaccid hemiparesis including the facial muscles. Right Babinski sign and ankle clonus were positive by day 2. Brain MRI revealed extensive infarction in the left MCA area (Fig. 2A, C, and D), and MRA revealed extensive stenosis in the intracranial part of left internal carotid artery (ICA), the M1 portion of left MCA, and the P1 portion of the posterior cerebral artery (PCA) (Fig. 2E and F, arrows and arrowheads). ESR and CRP levels were 35 mm/h and 0.30 mg/dL, respectively. CSF showed mild pleocytosis (7 cells/mm^3) and a normal protein level. Low-dose aspirin and heparinization were administered, but hemiplegia progressed on day 4 of admission, when findings of re-infarction were evident on MRI (Fig. 2B). On day 18, vessel wall enhancement was revealed at each stenotic portion on 3D spin echo T1-weighted images with blood suppression (Fig. 2H–J, L). Screening investigations for the cause of angiitis were all negative as in patient 1.

Under a diagnosis of cPACNS, we initiated low dose corticosteroid therapy (PSL; 1 mg/kg/day). Thereafter, vessel wall enhancement in the left ICA persisted, but enhancement of the MCA and PCA became less evident (Fig. 2K and M). After tapering the glucocorticoid dosage, vessel wall enhancement in the left insular (M2 and M3) MCA branches re-emerged (Fig. 2N). Despite methylprednisolone pulse therapy (30 mg/kg/day) and mycophenolate mofetil (MMF) (300 mg/m^2), enhancement of the MCA persisted. Furthermore, cerebral blood flow (CBF) in the affected hemisphere further reduced at 6 months after onset (not shown). We increased the dosage of MMF to 450 mg/m^2, which reduced the degree of vessel wall enhancement and