Isolated Angiitis of the Central Nervous System First Presenting as Intracranial Hemorrhage during Cesarean Section

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A case of isolated angiitis of the central nervous system (CNS) which first presented as intracranial hemorrhage during cesarean section is reported. Only one case of isolated angiitis of the CNS in post partum has been reported to date. Although a headache in labor and puerperium usually suggests subarachnoid hemorrhage, isolated angiitis of the CNS should be considered in the differential diagnosis.

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Introduction

Isolated angiitis of the central nervous system (CNS) is an uncommon entity with a lesion which is restricted to small and medium size arteries and venules of the brain and spinal cord (1, 2). The prognosis was previously considered poor, but there are several reports suggesting that treatment with corticosteroids plus cyclophosphamide is effective (1, 3, 4).

This case first presented as intracranial hemorrhage during cesarean section. To date, only one case of isolated angiitis of the CNS in postpartum has been reported (5). When persistent headache occurs in labor and puerperium, isolated angiitis of the CNS should be considered in the differential diagnosis.

Case Report

A 27-year-old female, para 0, gravida 1, was admitted at 40 week's gestation for cesarean section, because of cephalopelvic disproportion. She had no symptoms suggestive of preeclampsia. During the operation she developed severe hypertension (220/110 mmHg), but her blood pressure returned to normal after the operation. After she awoke from the operation, she complained of a severe headache. No muscle weakness or sensory disturbance was seen. The headache persisted for 10 days after the operation. She was then referred to our hospital because of blurred vision and persistent slight fever following the operation.

The patient was alert, but calculation was slightly disturbed. Eye movement was normal with no anisocoria. Light reaction was prompt and no hemianopsia was detected. Other cranial nerves were also normal. She had no hemiparesis. Deep tendon

reflex was normal and no pathologic reflex was seen. There was no superficial or deep sensory disturbance. Stereoagnosia was not seen. Signs of meningeal irritation or extrapyramidal dysfunction were absent. There was no dressing apraxia, constructional apraxia, ideational apraxia or unilateral spatial neglect, but slight topographical amnesia was present.

On admission, a complete blood count, routine blood tests, coagulation studies, luetic serology, blood culture and urinalysis were unremarkable. C-reactive protein and rheumatoid factor were negative. Antinuclear antibodies, anti-DNA antibodies, serum immunoglobulin levels, complement levels and angiotensin-converting enzyme were normal. However, circulating immune complex and ESR were elevated to 4.1 µg/dl (normal: below 3.0 µg/dl) and 35 mm/hr, respectively. Herpes simplex, herpes zoster, cytomegalovirus, mycoplasma, and toxoplasma titer were all normal in serum and cerebrospinal fluid (CSF). CSF analysis revealed an opening pressure of 120 mm water, 1 WBC (lymphocyte)/cu mm, a protein concentration of 26 mg/dl and a glucose level of 54 mg/dl. Cultures of CSF were negative. There were no abnormal findings in electromyogram, peripheral nerve conduction velocity, or EEG. CT scan disclosed a hematoma in the right parieto-occipital lobe (Fig. 1). Carotid and vertebral angiogram demonstrated areas of stenosis and irregularity of intracranial arteries (Fig. 2 ABC). There was no abnormality in the branches of external carotid arteries. Systemic angiogram showed no evidence of systemic vasculitis. Biopsy of the temporal artery was normal.

Treatment with prednisolone was started immediately after admission; 60 mg/day for 2 weeks and 50 mg/day for 1 week. ESR decreased to 10 mm/hr, but slight fever continued and the second carotid and vertebral angiogram showed no improve-

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Fig. 1. CT scan disclosed a hematoma in the right parieto-occipital lobe.

ment. Therefore treatment with prednisolone (40 mg every other day) plus cyclophosphamide (100 mg/day) was carried out. Circulating immune complex on the 30th and 58th day after treatment with prednisolone and cyclophosphamide became 3.5 and 1.9 $\mu\text{g/ml}$, respectively. Angiogram on the 56th and 330th day after treatment with prednisolone and cyclophosphamide showed a marked improvement of angiitis (Fig. 2 DEF). She continued to be healthy without any neurological defects for 15 months. Prednisolone was tapered and cyclophosphamide was stopped. Thereafter she complained of headache and showed slight fever again. ESR and circulating immune complex were elevated (25 mm/hr, 3.7 $\mu\text{g/ml}$, respectively). Prednisolone was increased and cyclophosphamide was administered again. She became afebrile, and ESR and circulating immune complex was normalized (9 mm/hr, 2.0 $\mu\text{g/ml}$, respectively) 1 month later.

Discussion

This patient first presented as intracranial hemorrhage during cesarean section and showed no findings suggestive of autoimmune disease except for high immune complex titer. Neurologically, she showed only headache, blurred vision and slight topographical amnesia which is concerned with the small size of right parieto-occipital lobe hematoma. Carotid and vertebral angiogram demonstrated striking areas of stenosis and irregularity of all intracranial arteries and systemic angiogram showed no evidence of systemic vasculitis. As the lesion was confined to the intracranial arteries and no factor which induces vasculitis, for example, infections, malignancy, autoimmune diseases and chemical factors, was not present, this

case can be diagnosed as isolated angiitis of the CNS (1, 2).

Isolated angiitis of the CNS was previously considered as a fatal disease (1, 2). Several reports showed that the disease progressed despite treatment with corticosteroids (6, 7) or corticosteroid and azathioprine (7). But some patients showed a transient improvement with corticosteroids, and required the addition of the cyclophosphamide to maintain the remission (1). A recent study showed that treatment with a combination of cyclophosphamide and corticosteroids is effective; Moore reported 5 cases who showed improvement, and recommended the following treatment regimens for the initial 6 weeks of therapy: 1) prednisone 40 to 60 mg/day, and 2) cyclophosphamide 100 mg/day (3). Moreover, Vanderzant et al reported a case who showed improvement with cyclophosphamide plus corticosteroid (4). The present case did not improve with corticosteroid alone, but showed marked improvement with cyclophosphamide plus corticosteroid. Treatment with a combination of cyclophosphamide plus corticosteroid is rewarding in isolated angiitis of the CNS.

To date, only one case of isolated angiitis of the CNS in the postpartum has been reported. The case in the report of Langlois et al (5) 1 month postpartum, developed a severe headache associated with subarachnoid hemorrhage and was treated with corticosteroid alone. She showed improvement temporarily, but resulted in a flare later because cyclophosphamide was not administered. The present case also showed a severe headache during cesarean section associated with cerebral hemorrhage, and responded to cyclophosphamide plus corticosteroid. But she showed slight fever and elevation of ESR and circulating immune complex again by tapering of corticosteroid and cessation of cyclophosphamide, and showed

Fig. 2. Carotid (A, D; right, B, E; left) and vertebral (C, F) angiogram showed striking areas of stenosis (arrowhead) and irregularity of many intracranial branches before treatment. After treatment marked improvement of the angiitis was seen (A, B, C; before treatment, D, E, F; after treatment).

improvement again by readministration of corticosteroid and cyclophosphamide. Therefore our case can be differentiated from peripartum cerebral angiopathy whose etiology is considered as vasoconstriction (8, 9). Moreover, isolated angiitis of the CNS in a young female on the contraceptive (10) has been reported. As it is well known that estrogens alter plasma proteins making blood more coagulable, it is possible that a female hormone may induce isolated angiitis of the CNS.

From now on isolated angiitis of the CNS should be considered in the differential diagnosis of intrapartum and postpartum headache.

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