A Benign Form of Isolated Angiitis of the Central Nervous System in Puerperium: An Identical Disorder to Postpartum Cerebral Angiopathy?

Yasuji SUGIYAMA, Akiko MUROI, Mikio ISHIKAWA, Tetsuro TSUKAMOTO and Teiji YAMAMOTO

A case of isolated angiitis of the central nervous system (IACNS) in puerperium with a clinical presentation of bilateral frontal lobe hemorrhage is described. Her symptoms and arteriographic abnormalities were resolved by institution of corticosteroid. After cessation of steroid treatment she showed no evidence of relapse. This case indicates that there appears to be a benign form of IACNS, although the etiology of postpartum IACNS is not known. The postpartum cerebral angiopathy described in the literature may be an identical disorder, since there are no clinical points of specific distinction between them.

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Key words: primary angiitis of the central nervous system (CNS), pregnancy, cerebral hemorrhage, benign clinical course

Introduction

Isolated angiitis/angiopathy of the central nervous system (IACNS) or primary angiitis of the central nervous system is an uncommon disorder restricted to the central nervous system (1-5). Recently, this disease has been increasingly diagnosed by cerebral angiography and considered as a highly fatal disorder if untreated and, even treated, relapse is notoriously common. Most cases of this disease present themselves with manifestations of cerebral ischemia, but rarely intracranial hemorrhage occurs. In addition, a few cases of IACNS have been reported in association with pregnancy or puerperium (6-8).

On the other hand, postpartum cerebral angiopathy (PCA), the clinical symptoms and neuroradiological findings of which are similar to that of IACNS, is a rare neurological complication following a normal pregnancy. We report a patient with IACNS in puerperium, in whom multiple intracranial hemorrhages were the presentation. Since her clinical course was benign, we discuss the conceptual relationship between postpartum IACNS and PCA.

Case Report

A 34-year-old woman, at 3 weeks after cesarean section, was hospitalized with a sudden onset of right frontal throbbing headache on March 20, 1996. Although the initial brain com-

puted tomography (CT) was unrevealing, her headache gradually worsened together with general malaise. On March 22, she was admitted to a local hospital because her repeated brain CT revealed localized high-density areas indicating hemorrhage in the bilateral frontal lobes. Cerebral angiography demonstrated multiple areas of segmental narrowing and dilatation of the intracranial arteries suggesting a vasculitic process. Since the frontal headache that was accompanied by nausea and vomiting did not improve, she was transferred to our neurological service on March 25. She had no previous history of toxemia of pregnancy, collagen-vascular diseases, miscarriage, drug abuse or bromocriptine treatment.

On admission, her body temperature was 36.5°C and blood pressure 102/68 mmHg, pulse 65/min, and regular. The heart was unremarkable to auscultation, and carotid, subclavian or orbital bruit was not audible. Peripheral arterial pulses were all intact to palpation. There was no tenderness of the scalp, cord-like arteries or muscle tenderness suggesting temporal arteritis. The remainder of the physical examination was normal. On neurological examination, she was drowsy but when arose, her speech was normal. Funduscopic examination revealed bilateral choked discs with peripapillary hemorrhages. Pupils were isocoric and promptly reactive to light. The extraocular movements showed bilateral abducens nerve palsy. The rest of the cranial nerves were normal. Motor, sensory and autonomic nervous system findings were unremarkable and deep tendon

From the Department of Neurology, Fukushima Medical College, Fukushima

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Reprint requests should be addressed to Dr. Yasuji Sugiyama, the Department of Neurology, Fukushima Medical College, 1 Hikarigaoka, Fukushima 960-12

reflexes were hyperactive in the right side and plantar response was bilaterally flexor.

The results of blood and biochemical investigations were not indicative of a systemic inflammatory process: white blood cell count $6,600/\text{mm}^3$ (blood picture was normal), erythrocyte sedimentation rate 22 mm/1 hour and C-reactive protein 0.2 mg/dl. Prothrombin time, activated partial thromboplastin time, protein C, protein S, β -thromboglobulin and platelet factor IV were all in normal ranges. Autoantibodies tested, including lupus anticoagulant, anti-nuclear, anti-cardiolipin, anti-DNA, anti-SS-A, anti-SS-B and anti-neutrophil cytoplasmic antibodies, were all negative. Serum immunoglobulins and complements were also within the normal levels. Angiotensin converting enzyme and anti-herpes simplex antibody titers were within

normal ranges. Cerebrospinal fluid (CSF) examination by lumbar puncture was postponed however, in view of the choked discs associated with multifocal hemorrhaging. The lumbar puncture performed two months after the onset revealed the opening pressure of 170 mmH₂O and CSF examinations were unremarkable (cell count was 8/3, protein 20 mg/dl, glucose 20 mg/dl and no oligoclonal immunoglobulin G (IgG) bands).

An emergency brain CT (Fig. 1) performed upon admission disclosed two high density masses due to hemorrhage localized to the bilateral frontal lobes both adjacent to the frontal cortex, the right one larger than the left. Her midline brain structures were shifted to the left side. Magnetic resonance imaging (MRI)s (Fig. 2) performed one month after the onset revealed a hyperintense round area on the T₁-weighted signal image that

Figure 1. Brain CTs without contrast dye show bilateral frontal lobe hemorrhages; the right one is larger than the left. Her midline brain structure was shifted to the left side.

Figure 2. Brain MRIs reveal bilateral frontal lobe hematomas on T₁ and T₂ signal images; the right one is larger than the left.

Figure 3. Cerebral digital subtraction angiography reveals multiple segmental irregular narrowing and dilatation ("beading" appearance) of the arteries of the right anterior and middle cerebral distributions (arrows).

Figure 4. Follow-up cerebral angiography disclosed that the evidence of vasculitis had been totally resolved.

were also hyperintense surrounded by a low intensity rim on T₂ signal image in the right frontal lobe, indicating a hematoma. A similar but smaller mass was identified in the left counterpart. Cerebral digital subtraction angiography (Fig. 3) performed the day after admission revealed multiple segmental areas of irregular narrowing and dilatation ("beading" appearance) of the arteries of bilateral anterior, middle and posterior cerebral distributions. However, there was no evidence of cortical veins or venous sinus thrombosis. Single photon emission computed tomography (SPECT) using ¹²³IMP showed a decreased area of cerebral blood flow in the right frontal lobe on top of a diffuse diminution throughout the cerebral and cerebellar hemispheres.

Clinical course

As soon as the diagnosis of IACNS was made, based on laboratory and neuroimaging studies, hyperosmotic mannitol was intravenously infused in order to lessen the brain edema associated with hematoma; daily oral prednisolone of 40 mg was also instituted. Her headache and papilledema improved gradually, and she became stable neurologically after one month. Cerebral angiography (Fig. 4) repeated one month after the initiation of prednisolone disclosed the radiological evidence of vasculitis had been totally resolved. No neurological residuals have remained. Thereafter she has shown no evidence of relapse of vasculitis during the subsequent 9 months, al-

though corticosteroid was withdrawn after 2 months.

Discussion

This is a case of IACNS in the puerperium, the presentation of which was bilateral frontal hemorrhage. Prior to this event, she had not shown the evidence of toxemia of pregnancy in view of absence of hypertension, proteinuria or eclampsia. The vasculitic process was rapidly reversed, following corticosteroid therapy and no recurrence of the symptoms has appeared after the cessation of corticosteroid. Although the patient had not undergone leptomeningeal/parenchymal biopsy, she was diagnosed as having IACNS on the basis of following points: 1) cerebral angiography showing multi-segmental areas of narrowing and dilatation of those arteries supplying the hemispheres, and, 2) exclusion of such systemic inflammatory disorders as infectious vasculitis, collagen-vascular or granulomatous diseases. The vasculitic process may give rise to either cerebral ischemia, hemorrhage or both. The narrowing of the vascular lumen as shown on arteriography may imply the vasculitic process or associated mural thrombus formation, and the dilatation may be a manifestation of disrupted medial wall of the artery.

Although an uncommon neurologic disorder, IACNS is considered to be a highly fatal disorder when untreated. Moore (2) has recommended to treat the disease by an aggressive immunosuppressive regimen of combined cyclophosphamide

and prednisone, since corticosteroid treatment alone has either a transient or no effect on the course of this disease. However, cases of IACNS characterized by a benign clinical course have appeared in the literature; Shimizu et al (9) reported a self-limited clinical course in IACNS, and Calabrese et al (10), after surveying the English language literature reported through 1990, suggested that there was a distinctive and relatively benign subset of IACNS. They emphasized that the benign subset is characterized by acute onset of headache with or without focal neurologic deficits, female gender, young age and relatively benign cerebrospinal fluid findings (low white cell counts and protein). In addition, they suggested that early diagnosis and therapy may be more important than previously recognized in determining the clinical outcome. Our case is in complete accord with theirs; i.e., prednisolone appeared efficacious in arresting the disease process and preventing the relapse and her clinical course was uneventful even after discontinuation of steroid. We withheld cyclophosphamide in view of her clinical symptoms and because the findings of arteritic process on follow-up cerebral angiography were totally resolved. Therefore, this particular case appears compatible with that of benign IACNS, characterized by Calabrese et al (10).

Only a few cases of IACNS during pregnancy or puerperium have been described to date. The pathogenesis of postpartum IACNS is unknown, although the hormonal factors that are presumably drastically changed during pregnancy or after delivery are assumed to be in part responsible. In fact, there was a case of IACNS following the use of oral contraceptives (11). Also, some aberrant immunological responses to the products of the placenta/fetus that are released into the maternal blood stream might be a possibility.

Cerebrovascular events, presented as cerebral infarction or hemorrhage, have been known in association with pregnancy and puerperium. Eclampsia is known to be the major cause, but PCA, a vague entity described in association with thrombotic and hemorrhagic events, is another consideration (12). PCA is a reversible clinico-radiological syndrome that follows a normal pregnancy, and is characterized by headache, seizure and focal neurologic deficits. Angiographic characteristics are similar to those of IACNS and the clinical outcome is usually favorable. Although the etiology of PCA is unknown, this disorder is reported to be associated with the use of ergot alkaloids and other vasoactive drugs; Comabella et al reported a case of postpartum cerebral angiopathy which developed after bromocriptine treatment (13), and Raroque et al described a PCA case after the use of a sympathomimetic drug (14).

It is not certain if the pathogenesis of PCA differs from that of IACNS. The case presented here is, however, better de-

scribed as a "benign" form of IACNS since the arteritic process was resolved without difficulty. However, the "benign" form may not necessarily be benign, if one assumes that hematoma formation as our case illustrates becomes large enough to be life-threatening. Although it has been considered as a highly fatal disorder, IACNS associated with pregnancy or puerperium is a relatively benign subset and we feel that postpartum IACNS is identical to PCA since there are no clinical points of specific distinction between the two. It is therefore important to recognize the presence of a benign subset of this particular disorder.

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