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CLINICAL REPORT

Reversible cerebral vasoconstriction syndrome with limb myoclonus following intravenous administration of methylergometrine

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Abstract Neurological deficits associated with methylergometrine have been reported primarily as a result of reversible cerebral vasoconstriction syndromes (RCVS). RCVS are characterized by reversible multifocal vasoconstrictions of the cerebral arteries heralded by acute severe headache with or without neurological deficits. Here, we present the first case of suspected RCVS with transient limb myoclonus following the intravenous administration of methylergometrine during cesarean section. A 31-year-old woman who received slowly infused intravenous methylergometrine during a cesarean section suddenly reported severe occipital headache after 40 min, followed by apnea and unconsciousness for 8 min. A second administration of methylergometrine to treat the weakness of her uterine contractions resulted in a repeated loss of consciousness within minutes and the development of limb myoclonus. No abnormalities were detected by brain computerized tomography, magnetic resonance imaging, and electroencephalogram. She fully recovered spontaneously within 12 h. We consider that the transient limb myoclonus in our patient appeared as a result of RCVS caused by the intravenous administration of methylergometrine.

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Introduction

Transient neurological deficits, such as headache, seizures, consciousness disturbances, visual disturbances, or muscle weakness, have been reported to be associated with methylergometrine administration [1, 2]. Most such events developed as a result of reversible cerebral vasoconstriction syndromes (RCVS). However, limb myoclonus following methylergometrine administration has not been reported, although limb myoclonus may be induced by hypoperfusion and/or ischemia in the central nervous system [3].

RCVS are a group of disorders characterized by reversible multifocal vasoconstrictions of the cerebral arteries with acute severe headache. They cover a variety of syndromes, including the Call–Fleming syndrome, benign angiopathy of the central nervous system, migrainous vasospasm, thunderclap headache with vasospasm, postpartum angiopathy, and drug-induced cerebral vasoconstriction. Various neurological symptoms could occur in dependence upon the site and severity of cerebral artery vasoconstriction [4].

Here, we report a case of suspected RCVS with transient limb myoclonus following the intravenous administration of methylergometrine during a cesarean surgery.

Case description

A 31-year-old woman, gravida 2, para 1, underwent an elective cesarean section at 38 and 1/7 weeks gestation

because of a prior history of cesarean section 3 years earlier. Her first cesarean section was performed due to arrest of labor and was uneventful. Throughout her second pregnancy, she was normotensive and did not experience edema, proteinuria, seizures, or headaches. She had no history of migraine, epilepsy, or drug allergies. Review of the medical history and the physical examination revealed no abnormalities prior to the cesarean section.

After routine monitoring, an epidural catheter was placed at the Th12–L1 interspace, and spinal anesthesia was performed at the L3–L4 interspace with 2 ml of 0.5% tetracaine and 10 μg of fentanyl. Ten minutes after the injection, the bilateral sensory block level was under Th1. The cesarean delivery of a healthy male neonate was uncomplicated. After umbilical cord clamp, 0.2 mg of methylergometrine was slowly administered intravenously to induce uterine contraction. One minute after the administration, she complained of nausea and breathing difficulty. Her oxygen saturation (SpO_2) was 98%, blood pressure was 120/70 mmHg, and heart rate was 60–70 beats per min. She experienced difficulty in breathing, which became progressively worse, but had no motor blockade in her upper extremities. Approximately 40 min after the initiation of methylergometrine administration, she complained of a sudden severe occipital headache without hypertension and promptly thereafter became unconscious and stopped breathing. Bag-mask ventilation of 10–12 breaths/min was performed with 6 l/min of 100% O_2 for 8 min until she recovered consciousness and recommenced breathing. She was normal except for slight headache for the following 20 min—until the second administration of methylergometrine. During the first recovery period her breathing was stable.

She received a second dose of 0.2 mg of methylergometrine after the operation because her uterine contraction was weak and again experienced difficulty in breathing without any change in respiratory rate. Eight minutes after the second administration of methylergometrine, she once again lost consciousness and stopped breathing. Bag-mask ventilation was performed again to maintain her oxygenation status, and 5 min later, she recovered partial consciousness, but bilateral myoclonus of the upper extremities commenced. Examination by a neurologist revealed normal findings apart from decreased muscle tonus of both lower extremities because of spinal anesthesia. Periods of unconsciousness and breathing difficulty lasting approximately 5 min were repeated three times, and she experienced myoclonus of the upper extremities during consciousness.

The brain computerized tomography (CT) scan conducted immediately following the operation showed no evidence of hemorrhage, and no abnormal signals could be detected on the sensitive diffusion-weighted magnetic resonance imaging (MRI) scan of the brain performed 3 h after presentation of the initial symptoms. No paroxysmal epileptic discharges were detectable on the electroencephalogram (EEG). After her transfer to the intensive care unit (ICU), her occipital headache continued for 5 h, and the myoclonus continued intermittently for 12 h after the first administration of methylergometrine. She was discharged from the ICU on post-operative day 1 without neurological deficits.

Discussion

Methylergometrine has vasoactive functions and transiently induces vasoconstriction, resulting in coronary spasm, hypertension, or cerebral vasoconstriction [2, 5]. Since methylergometrine is primarily used in the field of obstetrics, the cerebral vasoconstriction due to methylergometrine used to be called postpartum angiopathy. However, more recently, reversible cerebral vasoconstrictions followed by severe acute headache have been grouped together under the unified classification of RCVS, which also includes postpartum angiopathy.

Reversible cerebral vasoconstriction syndromes are characterized by reversible multifocal narrowing of the cerebral arteries heralded by severe acute headache called "thunderclap headache" with or without other neurological deficits, such as visual defects, seizure, or paresis [2, 6]. Other neurological symptoms depend on the location and severity of the vasoconstrictions in the cerebral arteries. Patients with RCVS are usually women between the ages of 20 and 50 years. One of the conditions associated with RCVS is pregnancy and puerperium, and one of the risk factors is methylergometrine [1, 4]. There are no validated criteria for the diagnosis of RCVS, but some key elements with facilitate the correct diagnosis are thunderclap headache, reversibility, multifocal segmental cerebral artery vasoconstrictions documented by contrast CT or magnetic resonance angiography (MRA), no aneurismal subarachnoid hemorrhage, and normal or near-normal cerebrospinal fluid analysis. The results of brain CT and MRI are frequently normal. Although neurological deficits are reversible in RCVS in most cases, some cases develop ischemic stroke, intracerebral hemorrhage, or subarachnoid hemorrhage during and after severe cerebral vasoconstriction [6, 7].

In the present case, the patient complained of sudden severe headache following the administration of methylergometrine and developed apnea, disturbance of consciousness, and myoclonus of both upper extremities, from which she fully recovered within 12 h. The temporal relation between symptoms and drug administration was obvious in this case because the same neurological

symptoms appeared several minutes after the initiation of intravenous administration of methylergometrine on two separate instances. The symptoms after the second administration of methylergometrine were more obvious than those after the first administration.

The initial symptoms in our patient appeared within 1 min after the administration of methylergometrine, which is consistent with the therapeutic onset of methylergometrine. However, her symptoms lasted 12 h after the first administration, which is far beyond the mean terminal half-life of methylergometrine, namely, 120 min [8]. Vasoconstriction in patients with RCVS is known to be detectable on MRA images for several days up to weeks, once initiated [2, 4]. In this context, methylergometrine may act as a trigger for the subsequent vasoconstriction.

We believe that neurological dysfunction should be induced by vasoconstriction of cerebral arteries. Brain CT and MRI did not detect any evidence of subarachnoid hemorrhage, cerebral venous thrombosis, ischemic stroke, or reversible posterior leukoencephalopathy syndrome, all of which frequently cause severe headache with or without other neurological symptoms. The EEG showed no epileptic discharge, which could indicate eclampsia. Taken together, our findings strongly suggest that the two intravenous administrations of methylergometrine induced reversible cerebral vasoconstriction, which in turn caused transient severe headache and other neurological symptoms in our patient.

The limb myoclonus observed in our patient has not been reported to be a symptom of RCVS. Myoclonus, defined as a sudden, brief, jerky muscle constriction, may arise from anywhere in the central nervous system, from the spinal cord, to the brain stem or in the cerebral cortex [3]. In our patient, the neurological symptoms, including occipital headache, unconsciousness, apnea, and limb myoclonus, may have been caused by constriction of the posterior circulation, including the vertebral, basilar, and posterior cerebral arteries which primarily supply the brainstem and occipital lobe [9]; however, we could not determine the location of cerebral vasoconstriction.

Methylergometrine usually acts selectively on the uterus, but it can also cause hypertension, coronary vasospasm, and cerebral vasoconstriction [5]. The mechanism of methylergometrine-induced vasoconstriction is unclear. As well as having muscle-stimulating activity on the uterus, methylergometrine acts as a weak alpha-adrenergic receptor agonist and as a 5HT-1 and dopamine receptor agonist [10]. Alpha-adrenergic and 5HT-1 receptors, but not dopamine receptors, are known to be involved in the regulation of vascular smooth muscle constriction [11]. The stimulation of either the 5HT-1 receptors or, to a lesser extent, alpha-adrenergic receptors may have caused the cerebral artery constriction in our patient.

Interestingly, our patient had a history of safe administration of methylergometrine during her first cesarean section 3 years before, despite no differences between the previous and present anesthesia in terms of other vasoconstriction inducible factors. In this sense, a past history of safe administration does not assure safety of repeated administration of this drug. Five patients reported in previous studies with RSVS in association with methylergometrine administration also had no candidate risk factors affecting vasoconstrictions, such as preeclampsia, gestational diabetes mellitus, advanced age, or history of migraine [2, 12–15]. Therefore, the good health of a pregnant woman does not assure safety of administration of this medicine.

Due to the frequent use of methylergometrine in peripartum and its association with adverse events, we recommend that careful observation is needed following its administration.

Conflict of interest The authors certify that there is no actual or potential conflict of interest in relation with this article.

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