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Anesthetic Management and Postoperative Care of a Patient with CADASIL (Cerebral Arteriopathy, Autosomal Dominant, with Subcortical Infarcts and leukoencephalopathy) for Cesarean Section

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Abstract

CADASIL (cerebral arteriopathy, autosomal dominant, with subcortical infarcts and leukoencephalopathy) is an infrequent inherited small artery disease that could have anesthetic implications. However these have rarely been reported. We present an anesthetic experience of a female patient previously diagnosed with CADASIL, who had suffered an ischemic vascular cerebral accident with a MRI compatible with leukoencephalopathy, and who was dependent for daily activities, mood alterations, apathy, and urine incontinence. We discuss anesthetic management of CADASIL patient, considering protection from further cerebral ischemia.

Keywords: Cerebral Arteriopathy, Anesthetic Management, Pregnancy

Case description

We describe the anesthetic management and postoperative care of a 36 years old pregnant woman with CADASIL disease who needed urgent cesarean section. According to her past medical history, she was already diagnosed as CADASIL syndrome 3 years ago. Her medical history included left hemi lateral paresis, accompanied by walking difficulties, urinary incontinence, psychiatric symptoms, apathy, diabetes mellitus, hypertension, and ovarian cyst. CADASIL diseases, was diagnosed after a hemi paretic attack when she was 32 years old. As a consequence of headache, was followed by neurologic symptoms. After admission to hospital, the clinical and neurological examination, MRI and CT-scan, and by genetic examinations, CADASIL disease was diagnosed. She got one dilatation and curettage due to a missed abortion pregnancy under sedation, 2 years ago at a primary care clinic.

Now, her symptoms associated with CADASIL were intermittent headache and left hemi lateral paresis, and hypertension. She was taking methyldopa and aspirin (80 mg daily). Her diabetes was controlled by Insulin during pregnancy. She admitted to the Alzahra hospital due to hypertension one day ago. She received 5mg hydralazine and stopped aspirin. On preoperative evaluation, there were no abnormalities in laboratory tests and radiologic evaluations except slightly elevated U/A protein 1+. Her brain CT was checked two months ago revealed the confluent low densities at the subcortical and deep white matter of both cerebral hemispheres and several small old infarctions in both basal ganglia and thalami. But the neurologist who examined the patient after admission judged her still neurologically normal.

Because of recent aspirin medication, we decided to conduct general anesthesia with informed consent. After premedication with ranitidine 50 mg and metoclopramide 10 mg IV, the patient was taken to the operating room. With standard monitoring (ECG, pulse oximetry, non-invasive blood pressure, and capnography) and pre-oxygenation, a rapid sequence induction with cricoid pressure using fentanyl, thiopental, and succinylcholine was carried out. For intubation used a cuffed 7.0 mm ETT. Neuromuscular block was achieved with atracurium, and anesthesia was maintained by controlled ventilation with an oxygen/N2O 50%/50% and isoflurane 1% mixture.

With recommendations concerning the anaesthetic management of patients with CADASIL arteriopathy, we kept mean arterial blood pressure greater than 60 mm Hg and end-tidal carbon dioxide around 40 mm Hg so as to prevent any cerebral ischemic or vasospastic phenomenon. Patient's blood sugar within the perioperative was in the normal range. Moreover, the cerebral venous return was preserved by the patient received 8 ml/kg of ringer's solution in the left lateral position. The condition of neonate was assessed by apgar score at 1st and 5th after delivery who was 8 and 9 respectively. Mother received oxytocin 5 IU by continues infusion after delivery. Surgery and recovery were uneventful. The neurological examination in the recovery room and later in the ward was normal. There was no headache and other neurological symptoms during recovery.

After surgery, the patient was transmitted to obstetric ICU for continuous and precise hemodynamic and end-tidal CO2 monitoring. For prevention of cerebral ischemia, head down position was avoided and continuous neurological examinations were performed. After 3 days,

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she discharged from ICU with good condition and without any complications.

Discussion

The CADASIL syndrome is an inherited neurological condition caused by non-atherosclerotic and non-amyloidosic micro-angiopathy (1,2). The disease appears in adult life. Its manifestations are virtually restricted to the central nervous system, especially the brain, and are caused by the progressive development of disseminated white matter lesions in association with small infarcts - lacunes - in subcortical areas. Migraine with aura and focal neurologic deficits caused by these lacunar infarctions are characteristic forms of presentation in young or middle age. Over the years, mood disorders, diverse neurological deficits and cognitive disturbances add up. To the extent that the total volume of lesions increases and cerebral atrophy develops, the frequency and severity of motor difficulties and cognitive dysfunction also increase (3).

Definitive diagnosis is confirmed in patients with clinical and radiological features by the finding of mutations in the notch-3 gene, located on chromosome 19p13.1 (4,5). At the molecular level, strongly stereotyped mutations in repetitive EGF-like domains in the extra-cellular portion of the trans-membrane notch-3 protein are observed (5,6). All these mutations result in the loss or gain of a cysteine residue, which suggests that the disease could result from abnormal disulphide bridge formation in the secondary or tertiary structure of the proteins. It is interesting that the locus of the Notch -3 gene is near that of the Cacnl1a4 calcium channel gene, which carries the causal mutation of familial hemiplegic migraine and type II familial episodic ataxia (2,5). At the histological level, the characteristic that is considered specific for CADASIL-type arteriopathy is the presence, on electronic microscopy, of dense osmophilic granular material in contact with the smooth muscular cells of the arterioles (7). This material is observed in brain tissue, in nerves and also in the dermis. Thus, a skin biopsy is recommended to confirm the diagnosis of CADASIL (8,9). The disease has a natural history of recurrent ischemic episodes affecting the white substance. The signs and symptoms of the disease are migraine, with or without accompanying neurological signs, cognitive problems, epileptic attacks, psychiatric symptoms, and dementia, which is frequently accompanied by walking difficulties, urinary incontinence and pseudo bulbar syndrome (3-5). Typical neuroradiological findings on magnetic resonance imaging (MRI): multifocal and bilateral FLAIR, hyperintensities in the periventricular and deep white matter, with lesions mainly affecting the anterior temporal pole, frontal and parietal lobes, external capsule, pons and basal ganglia; focal hyperintensities (lacunar infarcts) and lesions suggestive of micro hemorrhages or gradient-echo (3,4) (Figure 1).

CADASIL is sometimes not even considered in differential diagnosis for several reasons, especially lack of MRI availability and apparently negative family history. Computed tomography (CT) clearly shows the subcortical infarcts - typically lacunar, but also larger lesions and also shows white matter lesions, especially in more advanced cases (3). No specific treatment is available. However, anti-platelet agents such as aspirin, dipyridamole, or clopidogrel might slow down the disease and help prevent strokes. Given the propensity for cardiovascular and cerebrovascular complications, minimizing vascular risk factors and implementing therapy for primary or secondary prevention of stroke and myocardial infarction seems prudent (2,3). It is essential to keep in mind that cerebral arteriography is highly inadvisable, for it is likely to induce vasospasm. Obviously, no fibrinolytic therapy should be attempted in the case of acute neurological deficit. The hormonal and cardiovascular changes related to pregnancy do not seem to influence CADASIL disease but, to our knowledge, this issue has not yet been described (2).

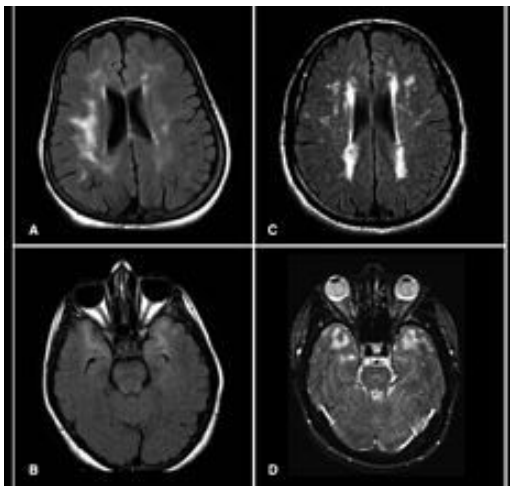

Figure 1. Brain MRI from patients with CADASIL showing multiple lesions.

In the case of general anesthesia in patients with a cerebrovascular disease, it is important to keep the mean arterial blood pressure within the limits of cerebral autoregulation. We used the limits used in non-hypertensive patients because the patient was not hypertensive; and to maintain normocapnia, to avoid both hyper- and hypocapnia, although the cerebral reactivity to carbon dioxide seems to be reduced in CADASIL disease (10). It should be reasonable to keep normocapnia because hyper and hypocapnia affected cerebral blood flow.

All of the volatile anesthetics can be dose-dependent cerebral vasodilators, and suppress the cerebral metabolic rate with the exception of halothane. Nitrous oxide is also a cerebral vasodilator. It was known that nitrous oxide and volatile anesthetics, when administered as components of a balanced anesthetic technique in combination with narcotics, can be used in most elective and many emergency neurosurgical procedures (11). Although cerebral autoregulation is better preserved with low-dose sevoflurane in patients with cerebrovascular disease (12), we did not use sevoflurane. Isoflurane would have been the ideal choice because is less likely to be associated with

uterine atony in clinical practice (13), we therefore used.
In case of hypertensive problems, one should administer vasodilators such as sodium nitroprusside or nimodipine: by analogy to cerebral vasospasm, nimodipine is probably the first choice. Systemic blood pressure is best maintained by avoiding hypovolemia. Should vasoconstrictors be necessary, no experimental or clinical data are available and it is probably better to use direct vasoconstrictors (such as norepinephrine and neosynephrine) instead of indirect vasoconstrictors.
Therefore, at a circumstance that most of anesthesiologists use modern volatile anesthetics like isoflurane, sevoflurane, and desflurane, we agree with the recommendation that efforts should be focused on maintenance of physiologic parameters rather than use of a specific anesthetic for the purpose of brain protection in the clinical setting including cerebrovascular insufficiency, like CADASIL patients. There is no contraindication to the use of regional anesthesia (14). It is important to keep the mean arterial blood pressure within the limits of cerebral autoregulation. We did not use spinal anesthesia because the patient is on antiaggregant therapy (Aspirin).
Regarding postoperative analgesia, paracetamol, non-steroidal anti-inflammatory drugs can be used. It has no effect on intracranial pressure and cerebral perfusion pressure and can be used to provide postoperative analgesia (13,15). This patient received Apotel (paracetamol), every 6 hours in the intensive care unit.

Conclusion

We describe the anesthetic management of a parturient with CADASIL syndrome undergoing cesarean section.
Many aspects of cerebral autoregulation in patients with this non-atherosclerotic cerebrovascular pathology are still unknown. By analogy with other cerebral arteriopathies, we propose maintaining normocapnia and keeping mean arterial pressure within the limits of normal cerebral autoregulation.

Ethical issues

The local ethics committee approved the study.

Conflict of interests

We declare that we have no conflict of interests.

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