Perioperative management of a CADASIL type arteriopathy patient

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We report the anaesthetic management of a patient suffering from an ischaemic arteriopathy of the CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy) type. The anaesthetic implications of this pathology are discussed. By analogy with other cerebral arteriopathies, the aim of our management was to keep mean arterial blood pressure and end-tidal carbon dioxide so as to prevent any cerebral ischaemic or vasospastic phenomenon. We preserved the cerebral venous return by avoiding excessive head-down position. We used a balanced anaesthetic technique because it allows easier titration of the depth of anaesthesia with regard to mean arterial pressure. There is no contraindication to the use of loco-regional anaesthesia.

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We describe the anaesthetic management of a 30-yr-old patient who needed urgent laparoscopy for torsion of a Fallopian tube. This patient also suffered from an ischaemic arteriopathy of the CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy) type. The anaesthetic implications of this pathology are discussed. This disorder is rare and its precise incidence is currently unknown.

Case description

A 30-yr-old woman presented for urgent laparoscopy with suspected torsion of a Fallopian tube. Her medical history included the following: (i) total thyroidectomy for the treatment of Graves disease, complicated by severe symptomatic post-operative hypoparathyroidism, which triggered one episode of seizures; (ii) benign ventricular extrasystole; and (iii) CADASIL disease, diagnosed after childbirth when she was 28 yr old. As a consequence of post-partum haemorrhage, systemic hypotension and fainting were followed by confusion and drowsiness for several hours. When the drowsiness had diminished, complete amnesia of the event and throbbing hemicranial headache accompanied by nausea and vomiting were observed. Since then, the headache had persisted almost uninterruptedly. Moreover, disabling photophobia and acouphobia set in progressively.

The clinical and neurological examination, carried out in the emergency room, was normal. The preoperative blood
examination yielded normal results. The following medica-
tions were taken at home: thyroxine 200 μg, aspirin 160 mg,
rocaltril and calcium carbonate 8 g.

After premedication with ranitidine 50 mg and metoclo-
pramide 10 mg i.v., the patient was taken to the operating
theatre. With standard monitoring (ECG, pulse oximetry,
non-invasive blood pressure, gas analyser and capnography)
and pre-oxygenation, a rapid sequence induction with
cricoid pressure using propofol, sufentanil and succinylcho-
line was carried out. Neuromuscular block was achieved
with atracurium and controlled with train-of-four monitor-
ing (ToF-Watch®; Organon International IWC, NJ, USA).
Anaesthesia was maintained by controlled ventilation with
an oxygen/air/desflurane mixture and the lungs were
mechanically ventilated. After insufflation of the pneu-
monoperitoneum, the patient was placed in a 30° head-down
position.

Because it was an emergency case and no information or
recommendations concerning the anaesthetic manage-
ment of patients with CADASIL arteriopathy were available in
textbooks or on the internet, we decided to keep mean
arterial blood pressure greater than 60 mm Hg (=8 kPa) and
end-tidal carbon dioxide around 40 mm Hg (=5.3 kPa) so as
to prevent any cerebral ischaemic or vasospastic pheno-
mena. Moreover, the cerebral venous return was preserved by
restricting the head-down position to the minimum needed
for the surgery and the head was kept in a neutral position.
Surgery and recovery were uneventful. The neurological
examination in the recovery room and later in the ward was
normal.

Discussion

The CADASIL syndrome1–5 is an inherited neurological
condition caused by non-atherosclerotic and non-amyloi-
dotic micro-angiopathy. Linkage has been demonstrated
with chromosome 19p13.1. 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. 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 theCACNL1A4 calcium channel gene, which carries
the causal mutation of familial hemiplegic migraine and
type II familial episodic ataxia. On the basis of the efficacy
of acetazolamide (inhibitor of carbonic anhydrase) in
channelopathies such as episodic ataxia, this treatment has
been tried with some success in the prevention of migraine
attacks in patients suffering from CADASIL.

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. This material is observed in brain tissue, in
nerves and also in the dermis:6,7 this is why a skin biopsy is
recommended to confirm the diagnosis of CADASIL.
Moreover, in addition to establishing the diagnosis in the
patient, skin biopsy also allows the screening of asympto-
matic relatives.

From a clinical point of view, this disease has a natural
history of recurrent ischaemic episodes affecting the white
substance (71%). The signs and symptoms of the disease
are: (i) migraine, with or without accompanying neuro-
logical signs (38%); (ii) cognitive problems (48%); (iii)
epileptic attacks (10%); (iv) psychiatric symptoms (30%);
and (v) dementia (28%), which is frequently accompanied
by walking difficulties, urinary incontinence and pseudo-
bulbar syndrome.

So far no treatment8-9 has proved to be efficient in
influencing the natural evolution of this disease. From a
purely empirical point of view, an anti-aggregant treatment
may be proposed, on the basis that it may have a
prophylactic effect on ischaemic attacks. It is essential to
keep in mind that cerebral arteriography is highly inadvis-
able, 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.

From the anaesthetic point of view, the frequent use of
acetazolamide in these patients requires the preoperative
measurement of blood electrolytes. In the case of general
anaesthesia in patients with a cerebrovascular disease, it is
important: (i) to keep the mean arterial blood pressure
within the limits of cerebral autoregulation (as these limits
are unknown in CADASIL disease, we used the limits used
in non-hypertensive patients because the patient was not
hypertensive); and (ii) to maintain normocapnia, to avoid
both hyper- and hypocapnia, although the cerebral reactivity
to carbon dioxide seems to be reduced in CADASIL
disease.10

In our patient, we used balanced inhalation anaesthesia
instead of an i.v. technique because the consequences of the
cerebral vasoconstriction due to propofol are unknown in
CADASIL disease. Moreover, the use of balanced anaes-
thesia allows easier titration of the depth of anaesthesia with
regard to mean arterial pressure. Although cerebral auto-
regulation is better preserved with low-dose sevoflurane in
patients with cerebrovascular disease,11 we did not use
sevoflurane because neither EEG nor bispectral monitoring
was available to diagnose any subclinical seizure-like
activity, which may occur with high concentrations of
sevoflurane.12 Isoflurane would have been the ideal choice
but it was not available in the emergency room, and we
therefore used desflurane.

Systemic blood pressure is best maintained by avoiding
hypovolaemia. Should vasoconstrictors be necessary, no
experimental or clinical data are available and it is probably
better to use direct vasoconstrictors (such as norepinephrine
and neosinephrine) instead of indirect vasoconstrictors. 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. Obstructions to the cerebral venous return and the head-down position should be avoided as much as possible. There is no contraindication to the use of loco-regional anaesthesia. Peripheral nerve blocks do not constitute a problem, but if central nerve blocks are used it is important to keep the mean arterial blood pressure within the limits of cerebral autoregulation and the usual precautions should be taken if the patient is on anti-aggregant therapy. Regarding postoperative analgesia, paracetamol, non-steroidal anti-inflammatory drugs can be used. Tramadol,13 given at a dose of 1 mg kg⁻¹ i.v. over 10 min to prevent vomiting, has no effect on intracranial pressure and cerebral perfusion pressure and can be used to provide postoperative analgesia.

In conclusion, we describe the anaesthetic management of a young patient with CADASIL syndrome undergoing emergency laparoscopy. 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.

References