Regional Anesthesia in a Patient with Familial Mediterranean Fever

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Introduction

Familial Mediterranean Fever (FMF) is a rare hereditary condition characterized by recurrent episodes of painful inflammation. These pain episodes occur most commonly in the abdomen, but can also involve the chest, joints, and rarely the heart, as well as membranes surrounding the brain, spinal cord, and testicles.1,4 Abdominal crisis occurs in 95% of cases, although patients with uncomplicated FMF are usually asymptomatic.4,5 Attacks can be accompanied by fever, rash and headaches1-3,6 and may develop within 1-2 hours following a triggered event such as emotional stress.4,7 Episodes vary in intensity and usually last 12 to 72 hours.3,4,5 The onset of attacks usually occurs prior to age 20 and decrease in frequency with aging.1 FMF predominantly affects people of Armenian, Arab, Turkish, or Jewish descent from the Mediterranean region with a reported prevalence from 1 in 200 to 1,000 in these populations and less common in other populations.1,3,5,6

Patients have developed serositis and fever triggered by the physical and emotional stress from surgery and anesthesia, including spinal anesthesia.4,7 Little is known about the anesthetic considerations to prevent and abort intraoperative pain episodes in patients with FMF. We present a 53-year-old female with FMF who underwent regional anesthesia and monitored anesthesia care (MAC) for bunionectomy.

Case Presentation

A 53-year-old female, American Society of Anesthesiologists classification III, underwent bunionectomy for recurrent left foot bunion. She has FMF and is followed by rheumatology with symptoms of fever and serositis triggered by stress and anxiety. Episodes were controlled for the past six months on outpatient oral colchicine therapy 0.6 mg twice a day. In addition to FMF, past medical history includes hyperlipidemia, bilateral hand arthritis, bilateral partial rotator cuff tears and history of chest pain with negative workup. Her other medications included diltiazem 1% topical gel, atorvastatin, folic acid, and methotrexate. The patient had no known drug allergies and negative family medical history. Prior surgeries included appendectomy, hysterectomy, and prior foot procedures. She reported no previous problems with anesthesia, including an ankle block for her previous left foot metatarsal osteotomy. Review of systems was negative on presentation. Preoperative vital signs were within normal limits: temperature 36.2°C, heart rate 64 beats per minute, respiratory rate 20 breaths per minute, blood pressure 114/56 mmHg and a BMI of 26.1 kg/m2.

Preoperative airway exam demonstrated adequate mouth opening, a Mallampati class II airway, full cervical neck range of motion, midline trachea, and adequate thyromental distance. Physical exam, including cardiac and respiratory exam, was unremarkable. Her ECG was notable for baseline flat t-waves in leads V3 and V4, which the patient had on prior ECG. Echo was unremarkable with trace mitral regurgitation and slightly thickened mitral valve leaflets. Laboratory studies were unremarkable.

Patient was instructed to continue her prophylactic colchicine 0.6 mg tablet twice a day peri-operatively. On the day of surgery, the patient took her home colchicine medication, as instructed. In the operating room, the patient was given oral midazolam for anxiolysis and intravenous fentanyl for pain control prior to the performance of a left ankle peripheral nerve block. The American Society of Anesthesiology standard monitors (pulse oximetry, noninvasive blood pressure, EKG, and capnography) were placed. The patient was positioned supine, head neutral, and had all pressure points padded. All five peripheral nerves of the left ankle were identified by anatomic landmarks and local anesthetic solution of ropivacaine 0.5% and lidocaine 1% mixture was used for the left ankle peripheral nerve block. Padded ankle tourniquet was used to maximize patient comfort. Intravenous propofol was titrated to the patient’s level of sedation during the surgery. The patient maintained spontaneous respirations throughout the procedure with 6 L/min of supplemental oxygen via face mask. The patient’s vital signs remained stable throughout the 3-hour uneventful procedure. At the conclusion of surgery, the patient was transported to the post-anesthesia care unit (PACU) with continued oxygen supplementation at 8 L/min via face mask. She continued to do well in the PACU and was later discharged home the same day.

Discussion

Given the possibility and severity of perioperative pain crises associated with patients with FMF, anesthetic goals should focus on stress and anxiety reduction and the prevention of acute attacks. Careful consideration of each patient’s needs is important in providing high quality and safe anesthesia care.

Preoperative Management

Since the 1970’s, colchicine has been identified as the treatment of choice for FMF.1 It is a lifelong treatment, but is only
effective as prophylaxis and ineffective for acute attacks. The
drug can prevent attacks by controlling inflammation and
halting the development of secondary amyloidosis, the most
serious complication of the disorder, which can eventually lead
to kidney failure.\(^1,2,5\) Specifically, colchicine inhibits neutrophil
chemotaxis, a step necessary for the inflammatory episodes in
FMF.\(^1\)

Because of the medication’s efficacy in preventing acute
attacks, it is ideal to optimize the dosing of the drug prior to
proceeding with surgery. Dosing depends on a patient’s age and
their frequency and severity of symptoms. Children under the
age of five are given a dose between 0.03-0.07 mg/kg/day.\(^1\)
Children beyond the age of ten and adults typically require a
colchicine dose of 1 mg.\(^1,8\) Complicated FMF patients with
frequent crises or identified amyloidosis should receive a higher
daily dose of 2-2.5 mg, with maximum dose up to 3 mg in adults
as tolerated given normal liver and kidney functions.\(^1,8\) We
recommend patients to be compliant with their home colchicine
prior to performing surgery to prevent intraoperative complica-
tions.

Serial monitoring of acute-phase reactants in the blood, such as
fibrinogen, erythrocyte sedimentation rate, serum amyloid A
(SAA) protein, and C-reactive protein (CRP), should be
monitored at least every 3 months and can help to assess patient
compliance and response to their treatment.\(^1,6,8,9\) The progres-
sion to amyloidosis can be prevented by maintaining normal
concentrations of the precursor protein SAA, specifically below
10 mg/L. This is the preferred acute-phase reactant to monitor.\(^8\)
CRP is a nonspecific alternative for monitoring if SAA protein
assays are unavailable.\(^8\)

Non-responding or resistant FMF patients with uncontrolled
attacks despite maximum tolerated dose of colchicine for at
least 6 months should consider alternative treatments. Anti-
interleukin-1 (IL-1) agents should be considered if inflamma-
tion cannot be adequately controlled with colchicine therapy
and are recognized as promising second-line therapies with
reported significant reduction in the frequency of attacks in
small randomized controlled trials.\(^8,11\) IL-1 inhibitors such as
canakinumab (human immunoglobulin G against IL-1 beta) and
anakinra (a recombinant IL-1 antagonist) are currently being
studied for their efficacy against FMF attacks.\(^1,8,9,11\) Given that
there is no current evidence that these alternative biological
therapies can prevent the development of amyloidosis in
patients with FMF, colchicine should be co-administered to
combat the risk of amyloidosis despite the persistence of pain
episodes.\(^8\) There are also reported refractory FMF cases
successfully treated with spinal cord stimulation with reduced
frequency of pain crises.\(^3\)

Intraoperative Management
Stressful factors, including the administration of anesthesia and
surgery, can lead to FMF crises despite prophylactic use of
colchicine.

One report of an intraoperative FMF episode developed
following administration of spinal anesthesia for a patient
receiving pilonidal sinus surgery.\(^4,7\) The 20-year-old male
patient reported severe intraoperative abdominal pain similar to
the pain of an FMF attack.\(^4,7\) He had been taking colchicine 2
mg/day for treatment of FMF for 3 years without exacerbation of
attacks within the last year prior to surgery.\(^4,7\) The pain
eventually resolved within 8 minutes after administration of
intravenous fentanyl and diclofenac and the surgery proceed-
ed.\(^4,7\)

There are potential intraoperative problems in patients with
FMF. Prior to the start of surgery, a patient’s level of anxiety
and stress should be assessed. Oral midazolam can be given for
anxiolysis as needed. Patient’s oxygen saturation should be
monitored as it can drop in those experiencing attacks and
supplemental oxygen may be provided as needed.\(^9\) Colchicine
is not used to abort acute episodes and may even lead to diarrhea
and worsening gastrointestinal complaints during a pain crisis.\(^1\)
There are no effective therapies for acute crisis and only
supportive measures can be provided. If an acute crisis occurs,
ensure the patient is in the supine position and deepen the level
of anesthesia in an attempt to alleviate the crisis. Given reports
of intraoperative crisis successfully treated with intravenous
fentanyl, it can be given for prophylactic pain control. Adequate
levels of sedation should be considered prior to administration
of a spinal or regional block.\(^5,7\) Non-steroidal anti-inflammatory
drugs such as diclofenac, indomethacin, and naproxen are also
used for supportive pain therapy.\(^1,8,12\) Several small studies
proposed alternative therapies, including the use of IL-1
inhibitors as an effective treatment for acute attacks, but other
studies report no clear evidence of efficacy.\(^1,8,12\)

One report recommended the avoidance of all types of
anesthesia, including regional anesthesia, in patients with auto-
inflammatory syndromes given that they are more likely to
experience worsening inflammation and/or intracranial
pressure of the meninges.\(^9,13\) However, there is no compelling
evidence for the absolute contraindication of neuraxial blocks
in FMF patients especially given reported cases of uncompli-
cated regional anesthesia.\(^14\)

Conclusion
Although FMF is a relatively rare hereditary condition in the
general population, patients with such disorder may have
serious complications of painful inflammation and fever. These
pain attacks can be triggered by surgery or anesthesia admini-
stration, including spinal anesthesia. Our 53-year-old female
patient with FMF safely underwent regional anesthesia, MAC
anesthesia, and podiatric surgery. However, given the potential
for serious perioperative pain episodes in these patients, it is
important to carefully consider anesthetic goals focusing on
stress and anxiety reduction and prevention of acute attacks as
well as becoming familiar with emergency management.
REFERENCES


