CASE REPORT:

Patient Presents for Emergency Appendicectomy, and Has Thin Hollow Spaces between the Bones of her Hands with Pronounced Thenar and Hypothenar Muscle Atrophy: What Anesthesia Technique must be used?

(Case year 2000, report written 2021-6-10)

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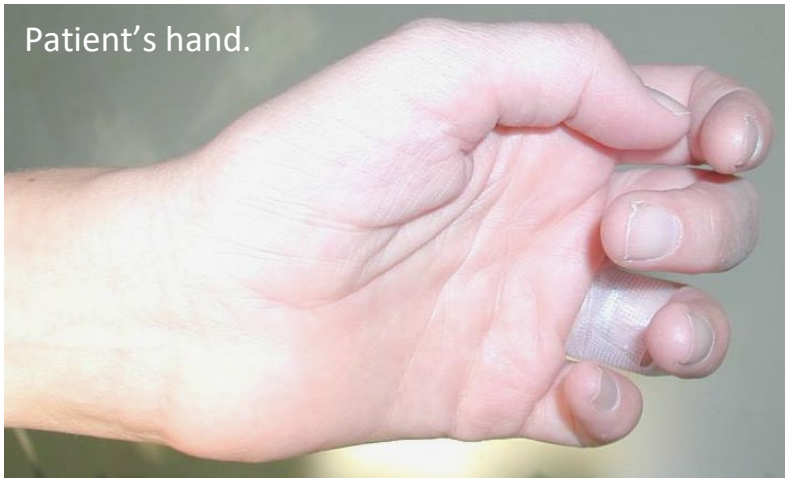
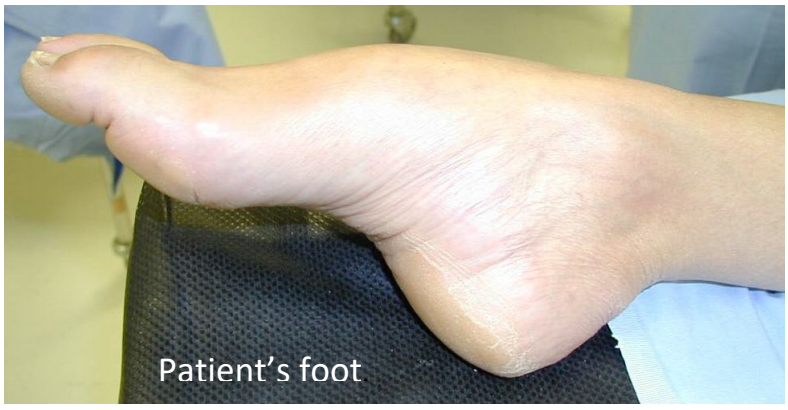
CASE:

A 45-year-old lady presented in the evening with a clinical picture of abdominal pain compatible with the diagnosis of acute appendicitis. The surgeon wished to operate immediately. History taking and a swift general physical assessment yielded no worrisome information.

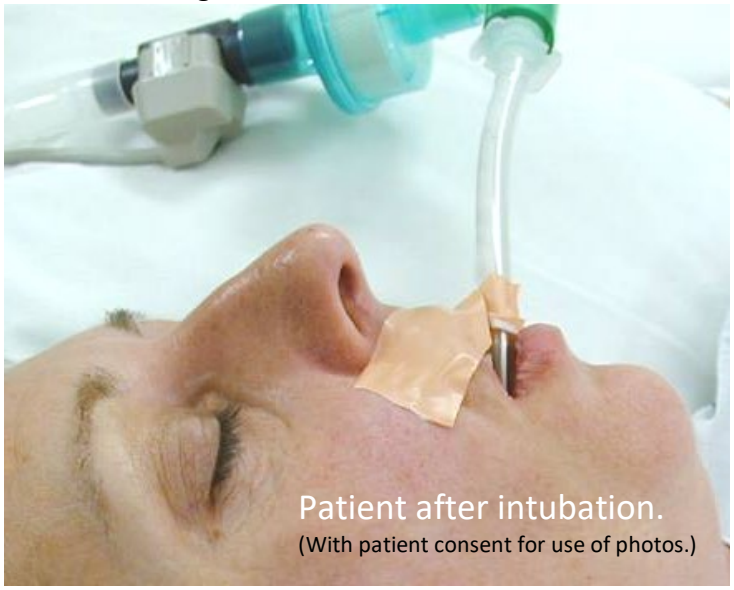
Whilst inserting an intravenous cannula into one hand, the anesthesiologist noted both hands looked strange. The thenar and hypothenar spaces were very thin indicating wasted muscle. The fingers were in a clawed position. The feet had high arches and slight hammer toes formation. On further questioning, the patient admitted to having many daily life challenges relating to the weakness in her feet and hands. Sometimes she dropped cups, she struggled with zips and buttons and stumbled often. She had a normal touch sensation.


Patient's hand.


Patient's foot

The anesthesiologist labeled her tentatively as having an *undefined myopathy*, thus necessitating regarding her as having risk for malignant hyperthermia. Due to her having an intestinal ailment and the surgery being urgent she was also regarded as having a full stomach necessitating either rapid sequence intubation, or awake intubation.

Furthermore, there was concern for her having any lingering pharmacological muscle weakness at the end of surgery superimposed on her clear clinical signs of muscle weakness.


Patient after intubation.
(With patient consent for use of photos.)

Standard anesthesia monitoring was used, with additional neuromuscular junction function monitoring. The anesthesia machine was made free of sources and traces of volatile anesthetic drugs. The rapid sequence intubation protocol included having suction at hand, good pre-oxygenation, and the use of cricoid pressure. Succinylcholine was avoided. Induction drugs were propofol 2.5 mg/kg IV, and Remifentanil 100 μg IV. The remifentanil dose was administered half before the propofol and half immediately after propofol. Twenty seconds were waited before intubating, and the tracheal intubation was easy. The vocal cords were relaxed in a neutral position, and the patient did not respond or move in any way to laryngoscopy and tracheal intubation. When the endotracheal cuff was inflated, she gave a single very weak cough.

Anesthesia was maintained with a single 5mg dose of cisatracurium a very predictable duration drug independent of organs for its elimination, a remifentanil infusion run at 0.5μg/kg/min, propofol infusion run at 2.5mg/kg/h, and an air-oxygen gas mixture was used with a FiO2 of 50%. No volatile anesthetics were used.


Laparoscopic view of patient's appendix about to be clipped at its base.

The surgeon's skin-to-skin laparoscopic operating time was 20-minutes, and the diagnosis of acute appendicitis was confirmed. Muscle relaxation was fully reversed as measured clinically and with NMJ monitoring, and an intravenous NSAID and anti-emetic drug was administered at the conclusion of surgery.

In addition, an intraperitoneal regional-anesthesia block was injected through a laparoscopic port. A solution was prepared: (1) 30ml of 0.5% bupivacaine with 1:200 000 epinephrine (adrenaline), (2) 70ml of 0.9% saline, and (3) 1.25ml of 8.5% Sodium bicarbonate. The sodium bicarbonate was added to the local anesthetic solution at the last minute to avoid causing drug precipitation in the solution. Twenty ml of the local-anesthetic concoction solution was used to inject the abdominal wall at each laparoscopic port site. The other 80 ml of local anesthetic concoction was injected intraperitoneal via the last laparoscopic port to be removed, and the

patient kept in a head-down position until she was ready for tracheal extubation. That assured the intra-peritoneal pool of local anesthetic drug would bath the region of the Coeliac plexus.

The surgery, anesthetic, and post-operative recovery were fully uneventful and uncomplicated. The patient reported no postoperative abdominal pain for 20 hours, after which the mild pain was treated with non-opiate analgesics. Neurologist consultation with extensive special tests, including muscle biopsies for Malignant Hyperthermia risks, were done. She had had no test evidence of vulnerability to develop malignant hypothermia. She was formally diagnosed as suffering from Charcot-Marie-Tooth (CMT) disease. It was on that evidence, together with a full family history, then also strongly assumed her one of her two children had the disease too, and one of her parents as well. The family had never had this disease diagnosed before.

The patient's CMT disease was diagnosed only because the anesthesiologist had to insert the IV cannula into the patient's hand, and observed its deformities closely.

DISCUSSION

It is controversial as to whether Charcot-Marie-Tooth (**CMT**) disease-carrying patients have a risk for malignant hyperthermia or not. Single anecdotal reports exist of patients with myopathies labeled as that of CMT, having developed malignant hyperthermia after exposure to volatile anesthetic gasses and succinylcholine. There are passionate scientific reports, one from an anesthesiologist, disputing that CMT is a risk disease for malignant hyperthermia[1]. There are case reports of the safe use of regional anesthesia in CMT patients without inducing malignant hyperthermia, nor with worsening of their peripheral neuropathies[2,8].

The association of malignant hyperthermia with CMT disease has been a trail of possibilities converted by repetitive presumed facts into a considered fact. It demonstrates many medical scientists reading abstracts only of the scientific references that they use. For example:

- **Soulilioti** in 2021 describes the anesthesia management of a CMT patient with malignant hyperthermia safe anesthetic practice. The patient was managed safely and well. Soulilioti states factually that CMT can cause malignant hyperthermia if depolarizing muscle relaxants are used, and only references a case managed by Ducart. Soulilioti's case report however does not validate the claimed malignant hyperthermia risk for CMT patients. It only implicitly propagates a possible myth.
- **Ducart** in 1995 describes a case with myopathy who develops malignant hyperthermia following sevoflurane anesthesia, later confirmed by contracture testing of muscle biopsies for malignant hyperthermia susceptibility. Ducart's patient did a *not get neurologist verified diagnosis* for the alleged CMT disease she carried. Ducart in his scientific discussion states that association of CMT and malignant hyperthermia is unknown, and references the Roelofse case report that states the same point. In addition, Ducart references the Antognini study that specifically excluded the likelihood of CMT patients having malignant hyperthermia susceptibility, which Ducart echoes in his phrase that a link between CMT and malignant hyperthermia susceptibility in "considered unlikely".
- **Roelofse** in 1985 describes the Anesthesia management of a patient believed to have CMT, with a malignant hyperthermia safe non-depolarizing muscle relaxant. Roelofse states that malignant hyperthermia, to that time, had *never been associated* with CMT. Their primary reason for avoiding succinylcholine was to avoid precipitating serum potassium changes due to the secondary muscle

atrophy that CMT patients have. In that year CMT was regarded as primary myopathy rather than primary neuropathy. All patients having any *primary myopath*y raised a thought about possible malignant hyperthermia risks with anesthesia.

- Thus, the myth that CMT was linked to malignant hyperthermia susceptibility got propagated.

It is possible some of the exceedingly few cases reported as having CMT and developing malignant hyperthermia, were actually sufferers of other diseases than CMT. A leading example of another disease misdiagnosed as CMT is Central Core Disease. The muscle weakness of Central Core Disease ranges from zero to mild, but rarely it is severe. Muscle weakness tends to be either more proximal and worst in the upper torso, or generalized. Skeletal abnormalities are common, such as kyphoscoliosis, hip dysplasia, joint contractures, and foot deformities. Forty percent of Central Core Disease patients have cardiac conditions such as dysrhythmias and mitral valve problems. Central Core Disease patients are 100% susceptible to developing malignant hyperthermia.

CMT disease characteristically is practically purely a motor disease, affecting the feet first and the hands only by mid-life and later. Sensory signs with CMT, if any are few, minimal, and only appear late in the person's life. The weakness in a limb strongly tends to only involve the most distal limb parts as in the hands and feet, and not hips, knees, elbows, and shoulders. It is a wise matter to subject any CMT patient for muscle tests for malignant hyperthermia, just to eliminate that concern for anesthesiologists. It is also wise to have an expert neurologist make a firm statement of diagnosis of CMT.

CMT is one of the more common inherited peripheral neuropathies with an incidence report as 1 in 2500. CMT is the group name of a large cluster of related, but slightly different illnesses. It is also clinically very heterogenous and has a large range of different genetic markers. Genetic testing can currently verify the diagnosis of a large majority of CMT sufferers[3],[4]. There is however a single gene marker that seems to be common to nearly all CMT variants[5]. The end injury is inflammation within a nerve that can become so swollen that it can be clinically palpable in some shallow nerve's cases[6].

CONCLUSION.

Some anesthesia commentators have made a personal argument that in any disease manifesting muscle wasting such as CMT can cause, it is wise to always err on the safe side and perform malignant hyperthermia safe anesthesia, because the diagnosis of CMT may be erroneous[7]. Antognini reviewed 161 anesthetics for all of the surgeries done on 86 patients with CMT and despite succinylcholine being used 41 times and volatile anesthetics 71 times not a single malignant hyperpyrexia event was identified[8]. It must be concluded on available evidence that CMT, is not an inherent risk disease for the development of malignant hyperpyrexia. The risk is that CMT is *wrongly diagnosed* as CMT, when it is a muscle-wasting disease like Central Core Disease, with a 100% risk for malignant hyperpyrexia (MH) if administered the MH triggering anesthesia drugs.

Wrongly labeling a patient as being malignant hyperpyrexia susceptible may be a momentary practical decision, as was in this case report. A malignant hyperpyrexia susceptibility diagnosis is however *not a trivial diagnosis* across a lifetime, and all patients deserve having

genetic testing to verify they truly have CMT as suspected. The verification of having CMT may be considered as proof of not having malignant hyperpyrexia susceptibility. Equally, a proposed diagnosis of malignant hyperthermia susceptibility needs contracture testing for verification. That will all greatly make all anesthesia options and clinical decisions easier, thus making anesthesia safer overall.

Accordingly, this author makes the following recommendations;

- If the patient's diagnosis of CMT was made by a *respected and qualified neurologist*, the anesthetic drugs and techniques chosen may be *anything* that is best suited to the surgery and the patient's total co-morbid diseases. Genetic testing for CMT afterwards at a convenient time is recommended.
- If there is an element of uncertainty or lack of appropriate validation of the diagnosis of CMT and *surgery is urgent*, it is wiser to utilize MH-safe anesthesia techniques and drugs. With the extensive numbers of drug classes and options available in 20210, that should be only a matter of trivial to zero consequence.
- For any patient where *surgery is elective* and CMT is only suspected, and unconfirmed, it is wisest to obtain a *pre-surgical neurological* formal assessment of the patient's musculoskeletal defects, including genetic testing. Strong consideration should also be given to doing a muscle biopsy for malignant hyperthermia testing as well.

This case report patient fully illustrates all of the above recommendations.

There are no grounds to believe that correctly diagnosed CMT carries any associated risk of the patient also having malignant hyperthermia susceptibility.

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The author.

Dr. Robert M Raw MD is a physician anesthesiologist. He has 7-years of experience as a rural African general medical physician, including doing obstetrics, surgery, and anesthesia. He has two degrees in primary care medicine and emergency room medicine. He has two degrees in anesthesiology. He founded a national regional anesthesia society, worked 13 years as a private practicing anesthesiologist, followed by entering American university anesthesiology practice for 12 years becoming a full professor. He has won teaching awards twice and has lectured in many countries. At his last university he was consistently assessed as being a master clinician in his annual performance reviews.