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Memorable Stories of Malignant Hyperthermia Patient Care

Announcer:
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And now here's your host, Dr. Charles Turck

Dr. Turck:
Malignant hyperthermia is a potentially life-threatening genetic disorder that requires a rapid diagnosis and treatment approach. But what does that actually end up looking like in practice? This is *The Pulse of Emergency Medicine* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss malignant hyperthermia through the lens of two patient cases is Dr. Henry Rosenberg, President of the Malignant Hyperthermia Association of the United States. Dr. Rosenberg, thanks for being here.

Dr. Rosenberg:
My pleasure.

Dr. Turck:
Now Dr. Rosenberg, we're going to be taking a look at two patient cases today, but before we dive into those, would you be able to give us a brief overview of what malignant hyperthermia is?

Dr. Rosenberg:
Certainly. Malignant hyperthermia was first described in the early 1960s. And since that time, when people really didn't understand what it was all about, we found that it's a disorder that's marked by hypermetabolism in response to potent anesthetic agents, such as sevoflurane, desflurane and formerly halothane. In addition, the other drug that's frequently used, that is a stimulus to develop malignant hyperthermia is the relaxant succinylcholine. The disorder is based on some changes that take place within the skeletal muscle, and what happens during an episode of malignant hyperthermia is that the intracellular calcium levels rise as a result of release of calcium from the sarcoplasmic reticulum within the skeletal muscle. That increase in calcium leads to an increase in metabolism, and an increase in contraction of the muscle. And when the muscle contracts, it's noted in various parts of the body, and in addition, the metabolism leads to an increase in the acid-base content of the muscle. Acidosis develops, muscle membrane may break down, patient may develop hyperkalemia, patient may develop myoglobinuria as well. It's a very rapid-acting syndrome, so once the syndrome begins, it's important to recognize it as soon as possible, because fortunately, there is a drug that reverses these changes that cause a malignant hyperthermia. And that drug is called dantrolene. So, in other words, it's a hypermetabolic syndrome that has as its basis an increase in intracellular calcium within the skeletal muscle that produces increase in acid-base changes, breaks down muscle membrane, leading to hyperkalemia, leading to myoglobinemia, and if not recognized and treated fairly promptly, can lead to death. The hyperthermia comes about because of the increase in the metabolism due to the release of calcium within the skeletal muscle.

Dr. Turck:
So with that background in mind, let's turn to our first patient case. Dr. Rosenberg, would you share the details of a memorable case from your experience?

Dr. Rosenberg:
Yes, the case that I'm going to describe was actually a very unusual case that was reported to the Malignant Hyperthermia Association. So this is a story of a 6-year-old boy, who had significant lordosis that was evaluated, but there was no course for it found. Other family

members also had some degree of lordosis. He was pretty normal. And he was exercising and running around and started to complain that his legs were getting very stiff and tight. The mother came and felt the child's head, and thought he was very hot, so she put him in the car and they drove to the nearest hospital. By the time they came to the hospital, not only were his legs stiff, but now he was having trouble speaking because his jaw muscles became stiff as well. So they brought him to the emergency room and the emergency physicians evaluated him and thought that they were concerned that the airway might be compromised. So, what do you do when you have a difficult airway? Well, the first drug they reached for was succinylcholine, or Anectine, in order to relax the muscles. But in the case of malignant hyperthermia, it doesn't do that. What happened was the succinylcholine precipitated further the attack of malignant hyperthermia, and the child's muscles became tighter. The child developed ventricular tachycardia, ventricular fibrillation, hyperkalemia, and died. So, the question was, what was it that caused this particular problem? This was a rare type of case, but the investigation precipitated along the line of, gee whiz, what caused this problem, with this child? And it turned out that other family members with the lordosis – a mild lordosis – had problems with exercise and strenuous activity, as well. And so, the child and the family members were investigated. And the family members who were tested had an abnormal response. Now since that time, there's been more work done to investigate the genetics of malignant hyperthermia, because the syndrome is known to be inherited in an autosomal dominant fashion. Well, this child and his family members who had the lordosis, also had the genetic changes that were typical for malignant hyperthermia. So, the problem was that because of the increase in body temperature, the increase in muscle tone, the administration of succinylcholine was thought to be the appropriate thing to do. And it turns out that that was not the appropriate thing to do, but that was a very difficult decision. More appropriate would have been to give the child dantrolene, that's presuming they had dantrolene available. And if that were the case, and the patient's malignant hyperthermia syndrome would have abated. So now, the family members have an inherited abnormality that's typical for malignant hyperthermia, and so they have to take special precautions when it comes to anesthetic agents.

Dr. Turck:
Thanks for breaking that down for us, Dr. Rosenberg. Now that we have those details, how did you go about diagnosing this patient?

Dr. Rosenberg:
Yes, the diagnosis nowadays, when there is a suspicion of malignant hyperthermia, most people will draw blood and send it to one of the laboratories that are capable of doing genetic testing, to look for the DNA variants that are associated with malignant hyperthermia. Now, although any genetics lab technically can do it, there are a couple of laboratories that have focused on this. One of them is called Prevention Genetics, located in Marshfield, Wisconsin. So that's the usual first step, and if there is no abnormality seen, then the next step would be to do the muscle biopsy and testing in the laboratory. Those are the ways that it's conducted.

Dr. Turck:
And could you tell us a bit more about the importance of diagnosing patients with malignant hyperthermia as quickly as possible? Why is there such a short diagnostic window here, and what strategies could we use to diagnose patients?

Dr. Rosenberg:
Certainly. It's important to diagnose it as rapidly as possible, because what happens during an episode of malignant hyperthermia – there's a very significant release of calcium within the muscle cell. And that begins the metabolic process that leads to the hyperthermia and acidosis and muscle membrane breakdown. And this can occur within minutes. It doesn't take hours, it takes minutes. And so it's important to recognize and to treat it as soon as possible, and, to begin treatment with dantrolene, as soon as possible. In the operating room, and sometimes in the emergency room, one of the first signs of malignant hyperthermia is the jaw muscle rigidity when succinylcholine is given. Frequently, succinylcholine is used to intubate a patient, and if the patient's muscles become rigid, particularly around the jaw, that's usually a sign that they may be developing malignant hyperthermia. But the syndrome can occur very, very rapidly, and so it needs to be diagnosed and treated as quickly as possible.

Dr. Turck:
For those just tuning in, you're listening to *The Pulse of Emergency Medicine* on ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Henry Rosenberg, who's sharing some of his most memorable cases in malignant hyperthermia. So Dr. Rosenberg, is there another patient case you'd like to share with our audience?

Dr. Rosenberg:
There are several other cases that I can share. One of them has to do with the association of the changes that are found in malignant hyperthermia with the changes that are found in patients who develop exertional heat stroke. So there was a young man, who was in his 20s, who was in a camp situation, and developed signs of exertional heat stroke. They called the EMTs, and the EMTs came and saw that he was hot and that he was rigid. So what they did, was they gave the patient succinylcholine to intubate him, and when they did that, the muscles of the jaw became very rigid. Although they were able to intubate him, they were bringing the patient to the hospital where he was found to have significant myoglobin in the urine, his CK was extremely high, his liver enzymes were elevated, and they

were very concerned even, that the patient might need a liver transplant. And so he was moved to a hospital that was capable of doing the liver transplant. But instead, what happened is that they just watched what was going on, did not give him any other medications that are known to trigger malignant hyperthermia, and the CK and the liver enzymes slowly decreased, and he did not need a liver transplant, but he did recover eventually, and had some significant muscle weakness. This again was an unusual situation. And I think that the important issue is, if such a case happens, it's important to get a specimen and do an analysis for the genetic changes that are found in malignant hyperthermia, because not only do you make the diagnosis in the patient, but it's important to know in the family, because this is an autosomal dominant syndrome.

Dr. Turck:
Now we know there's a limited diagnostic and treatment window for malignant hyperthermia. So with that being said, Dr. Rosenberg, is it important to utilize a coordinated team response to a malignant hyperthermia crisis?

Dr. Rosenberg:
Well, let me frame this in terms of what our recommendations are in terms of the operating room. In the operating room, malignant hyperthermia is more common, because the inhalation agents are used, and when we have an episode of malignant hyperthermia, we do have a team response. The Association has an outline for what to do in such cases. So you have to have someone who is tasked with bringing the dantrolene in, for drying up the dantrolene, for injecting the dantrolene, for drawing blood gases, for cooling the patient, for alerting the laboratory as to what studies they can expect. And so, once the syndrome is under control, the patient needs to go to the intensive care unit, for at least 24-36 hours, because the syndrome has been known to recrudesce, so that when a patient goes to the intensive care unit, he or she has to be observed fairly closely, to make sure that they don't recrudesce. And if they do, then they have to be treated with dantrolene as well. So yes, a team response is important. Now, let me also point out that after the organization was formed in the early 1970s, one of the first things that was created was a hotline. This is a free hotline for clinicians, so if a person has a patient with malignant hyperthermia, and they have questions, they can call the hotline and be in touch with an expert and ask questions and be guided through the management of the patient. So the Malignant Hyperthermia Association is a team. The Association is a small one, and it's got four paid members who run the organization, but have many volunteers – anesthesiologists, non-anesthesiologists, more experts in this syndrome – who make themselves available to answer questions.

Dr. Turck:
And before we wrap up, Dr. Rosenberg, are there any other takeaways you'd like to leave our audience regarding malignant hyperthermia?

Dr. Rosenberg:
Yes I would. As a result of the genetic studies of malignant hyperthermia and the identification of over 40 DNA variants that predispose the malignant hyperthermia, it becomes possible to do a genetic study of a person who's needing surgery. So prior to the surgery, you can identify in advance, who has one of the genetic traits that predispose to malignant hyperthermia. So this is a form of precision medicine, in the same way that in the obstetrics field that babies are screened for genetic disorders. Now, it hasn't been introduced yet, but there is beginnings of an emphasis on getting genetic studies of patients who are having surgery. The December 2020 issue of Anesthesiology, there's an article about this syndrome and the genetics of malignant hyperthermia. If anybody chooses to, they can read the article, which goes through the genetics and the potential for preventing cases of malignant hyperthermia in advance. And I'd be happy to guide anybody to that article.

Dr. Turck:
Well, that brings us to the end of today's discussion, so with that, I want to thank my guest, Dr. Henry Rosenberg, for joining me to discuss patient cases in malignant hyperthermia. Dr. Rosenberg, it was great having you on the program!

Dr. Rosenberg:
Well, thank you very much. I certainly appreciate the opportunity to talk about this syndrome, which people thought was extremely rare, but now we're finding out that it's not quite as rare as they originally thought, and that if recognized early, you can really save a life.

Announcer:
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