CASE REPORT

Curious case of muscle spasm

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Introduction

“So you are admitting today? I have a difficult patient for you,” the emergency room attending said. I noticed his relief. “I want you to see the patient in bed two. He is always asking for more pain medication. Today, he is complaining of pain in the medial side of his left thigh. I have ordered an ultrasound.” A cursory chart review showed that 2 years ago, his pain was controlled on hydromorphone. He is now on Morphine as well without relief.

Firm in my resolve, I walked to bed two. Mr. XY, a 67-year-old white male was lying on his side. Within a few minutes, he started having muscle spasms starting in his feet, progressing to his legs, trunk, and arms. His hands and feet were clawed. He was in severe pain. I quickly looked at my watch. The spasm lasted 5 min. As his body relaxed, he became comfortable. He simply said, “Morphine does not affect it.”

For more than 6 months he had these muscle spasms, which came every 20–30 min and lasted 5–12 min, without any relieving or aggravating factors. They persisted even in his sleep. He had also experienced difficulty chewing and swallowing, extreme fatigue, and frequent headaches during the same period. The Emergency Department attending took a deep breath as he approached me, “Doppler is positive for a blood clot. He will need admission.” He shook his head as he walked back.

Key Clinical Message

If no improvement is seen with ongoing treatment for current diagnosis, then diagnosis should be questioned. History taking and physical examination remain essential tools in care of the patient in addition to the current technological advancement.

Keywords

Clinical diagnosis, chronic pain, difficult patient, Isaac syndrome, muscle spasm, shared decision making.

He was diagnosed with Muir-Torre syndrome as he had sebaceous adenomas, sebaceous epithelioma, colon cancer, bladder cancer, hypertension, hyperlipidemia, a history of myocardial infarction, and most recently, renal cancer. All childhood illnesses had resolved without complications. There was no family history of muscle spasms but his father died of colon cancer in 1995.

On examination, his vitals were normal, and so were his higher brain and cranial nerve functions. Kyphoscoliosis was apparent. He appeared greatly distressed due to pain. Again, frequent spasms were noted. His hands and feet were clawed. He was weak, could hardly get up from the bed without holding onto things, and did not want to walk. When he agreed to walk with assistance, he walked with short-stepped gait without foot drop. Romberg could not be tested due to the patient’s inability to stand with feet together. Intention tremor and past pointing were present. The remaining cerebellar examination was normal. Deep tendon reflexes of his lower extremities were present but difficult to elicit. He was inactive most of the time, but he was able to ambulate with a walker for up to 50 feet in a day, mainly to smoke.

Hemoglobin was low at 11.1 g/dL with low ferritin, while the rest of the anemia work-up was unremarkable. His basic metabolic panel and liver enzymes were normal.

It was obvious that muscle spasms were the reason for his pain. We decided to observe him for a day while...
trying to narrow down the differential diagnosis by repeated physical examination and Computerized Tomography (CT) brain scan. Chronic lacunar infarcts in bilateral anterior limbs of the internal capsule were seen.

The working diagnosis was Isaac syndrome (IS), based on a case description from Dr. Isaac[1]. Ideally, a Magnetic Resonance Imaging (MRI) brain scan, Voltage Gated Potassium Channel antibody (VGKC Ab), and Electromyography (EMG) should have been done to confirm the diagnosis.

Muscle spasms were negatively affecting his quality of life. I decided to discuss the option of enrolling in a therapeutic trial. He was ecstatic to learn that there was a possibility that he would not have to live in continuous threat of muscle spasms. The house staff wanted to do everything else to make him feel better prior to the trial of carbamazepine. The next day, he was started on carbamazepine 200 mg three times per day, without telling him the time of the pill administration. His spasms decreased significantly to the point that he could count the number of spasms in a day. He started getting up from the bed and went for a walk independently. Twitching, spasms, and rippling of muscles, which was evident prior to the treatment, became infrequent. The patient reported less muscle stiffness, which spurred a desire to be more mobile. Muscle aches, which he had rated as more than 10/10 earlier, became a 4/10. He could now sleep without muscle spasms. His reflexes became brisk. Overall, the patient’s condition changed dramatically with the administration of carbamazepine. Clinically, we diagnosed him with IS.

Unfortunately, an EMG could not be done as the patient was on anticoagulant. A MRI could not be done due to the patient’s inability to lie down on his back for significant lengths of time. He also refused VGKC antibody testing. When I discussed this with the patient, he did not want me to do any diagnostic test at the time. He explained his refusal: “It is after a long period of suffering, and I am now feeling much better. I do not want to stop this medication right now.” He further explained that once he had completed the course of anticoagulation, work-up, and treatment of renal cancer, he would follow up with neurology for diagnosis and management.

Muir-Torre syndrome is an autosomal-dominant condition characterized by actinic keratosis, seborrheic keratosis [2], sebaceous tumors, cutaneous keratoacanthomas, and visceral carcinomas [3, 4] including colorectal (80%), endometrial (20–60%), urological (4–5%), stomach cancer (11–19%), hepatobiliary (2–7%), small bowel cancer (1–4%), central nervous system tumors (1–3%), and ovarian cancer (9–12%) [5]. It is a variant of hereditary nonpolyposis colon cancer, or Lynch syndrome, with the difference being the association with skin malignancies. Both syndromes are characterized by defects in DNA mismatch repair genes. Patients with Muir-Torre most commonly exhibit mutations in the DNA mismatch repair genes MLH1 and MSH2 [6].

Isaac syndrome (IS), also known as acquired neuromyotonia, is a rare disorder occurring mostly between the ages of 15 and 60. It is characterized by excessive regular or irregular spontaneous muscle activity, twitching, spasms, myokymia, muscle weakness, potentially reduced or abolished tendon reflexes, and progressive stiffness. This muscle activity persists throughout sleep [7, 8] and under general anesthesia. In extreme cases, the voluntary muscle activity such as handgrip and eye or jaw closure may be delayed or blocked (pseudomyotonia) [8]. Patients usually become symptomatic before the age of 40. Other symptoms include hyperhidrosis, cramping, and weight loss. Symptoms are more pronounced in the hands and feet than upper arms and thigh. Hoarseness and breathing difficulty may be present if pharyngeal and laryngeal muscles are affected. Gait may be stiff and unsteady. One-third of the patients may experience numbness and tingling in their skin, though muscle pain is not a common feature. These symptoms may fluctuate in severity and frequency.

Isaac syndrome (IS) can be classified as acquired or hereditary. Most cases are acquired and associated with peripheral neuropathy, autoimmune conditions, radiation exposure, or exposure to metals like gold or mercury. Autoimmune-mediated IS is typically caused by antibodies that bind to voltage-gated potassium channels in the peripheral nervous system [8, 9]. The genetic form is associated with episodic ataxia type 1 and is caused by a mutation in the potassium channel gene KCNA1 on chromosome 12.

Isaac syndrome (IS) is most commonly associated with malignant and benign neoplasms [8] like small cell carcinoma of lung, thymoma, bladder carcinoma, ovarian cancer, and lymphoma. Apart from its association with paraneoplastic syndromes like paraneoplastic cerebellar degeneration and paraneoplastic limbic encephalitis, IS is associated with a variety of autoimmune disorders such as, Hashimoto’s thyroiditis, myasthenia gravis, GBS, chronic hepatitis B, celiac disease, insulin-dependent diabetes mellitus, rheumatic heart disease, Vitamin B12 deficiency, Addison’s disease, and vitiligo.

This case raises several interesting questions. Is it necessary to confirm the diagnosis by tests or can we go straight to a therapeutic trial in selected cases, given the patient’s knowledge, understanding, and permission? In this case, after the patient had begun to improve on the medication, would we stop carbamazepine even if tests did not confirm the diagnosis? Does history taking and physical examination have the same relevance as labs and imaging? Is the testing even necessary if the test result would not change the management of the patient?
We followed the patient for several months on carbamazepine. He was seen in the neurology clinic where an EMG was scheduled for a later date due to his ongoing anticoagulation therapy for DVT. He succumbed to multiple cancers before the EMG but until his death he was spasm-free on carbamazepine and did not require any further pain medication.

Lessons we learned from the case:
• A clinician can make the diagnosis with history and physical examination. Ancillary tests should be the slaves of clinical management and not the masters.
• In case of uncontrolled chronic pain, the cause should be reevaluated periodically.
• Despite the patient wanting to cooperate, it was his medical condition that resulted in him being labeled as a difficult patient. Difficult medical conditions and difficult patients should be differentiated.

Conflict of Interest
None declared.

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