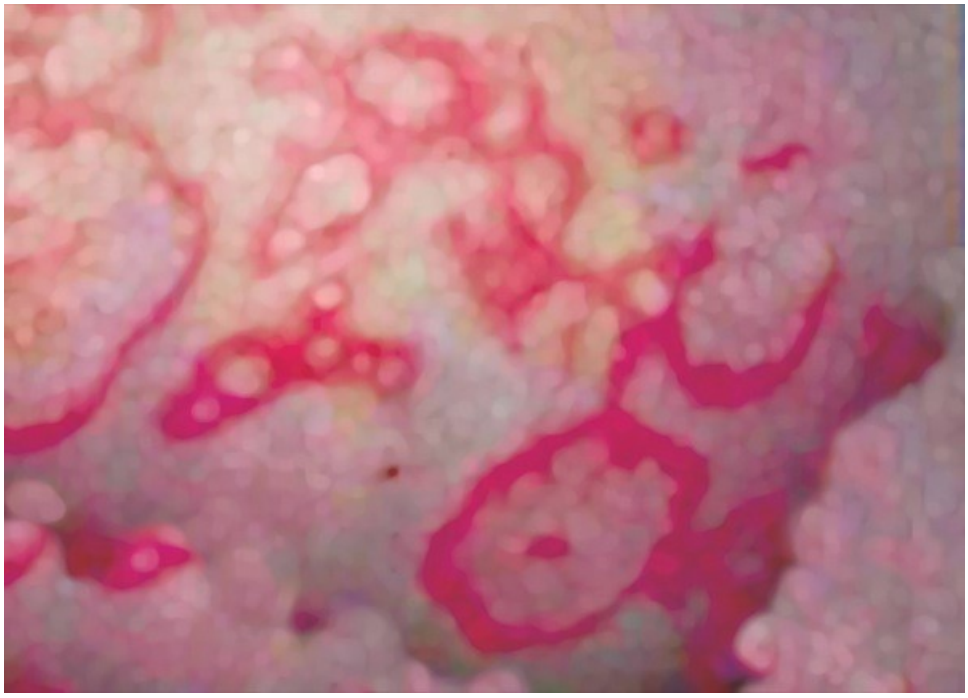
PAINMEDICINE NEWS

Clinical Pain Medicine

SEPTEMBER 25, 2017

# Some Patients With Erythromelalgia Respond Well To Corticosteroids



Orlando, Fla.—Patients with the rare disease erythromelalgia who responded favorably to corticosteroid treatment have been found to have specific characteristics: They reached maximum pain intensity within 21 days of onset, described a clear trigger to their disease (typically surgery or trauma), and were treated more promptly with steroids after diagnosis.

The study's principal investigator, Gabriel Pagani-Estévez, MD, a senior neurology resident at Mayo Clinic, in Rochester, Minn., said that prior to the study, there had been an anecdotal observation

among the co-investigators that certain forms of erythromelalgia may have a beneficial pain response to oral or IV corticosteroids.

“Although erythromelalgia is a rare disease, it confers significant suffering and is linked to a higher suicide rate in these patients than for the general public,” Dr. Pagani-Estévez said. “Erythromelalgia is also a notoriously difficult disease to treat and often refractory to conventional pain treatment.”

Erythromelalgia is an ion channel disorder that affects blood vessels, which become blocked and hyperemic, and causes burning pain. The episodic disorder mostly affects the lower extremities and hands.

**For Rare Disease, a Large Study**

The study, which was presented at the 2017 annual meeting of the American Academy of Pain Medicine, consisted of a 31-patient cohort. “This is a sizable group of patients, considering the rarity of erythromelalgia, which affects about one in 1 million individuals,” Dr. Pagani-Estévez said.

The median patient age was 47 years; 71% were women. All patients received corticosteroids and 45% were nonresponders. Of the 55% of patients who improved on corticosteroid treatment, 29% were complete responders and 26% were partial responders.

A subacute temporal profile to disease reached a zenith in less than 21 days in 48% of patients, of whom 87% were corticosteroid responders.

In addition, 67% of complete corticosteroid responders reported a disease trigger (i.e., surgery, trauma or infection). Both groups of responders also received corticosteroids earlier than nonresponders, at an average of three months after onset versus 24 months.

“Perhaps any erythromelalgia patient could benefit from a trial of oral or intravenous corticosteroids. However, high doses may be required for efficacy,” Dr. Pagani-Estévez said. “Those who received at least 200 mg prednisone cumulatively tended to respond better.

The highest doses were in the range of 1,000 mg over five days, and the majority of the patients who had complete pain elimination were on this highest-dose regimen."

A high-dose corticosteroids trial of at least 200 mg of prednisone cumulatively was administered to 55% of patients, of whom 76% were corticosteroid responders.

Dr. Pagani-Estévez acknowledged that more study patients might have responded to corticosteroids if their dose had been higher.

Patients also often develop a secondary skin injury, simply from submerging their affected limbs in ice water for an extended period of time, according to Dr. Pagani-Estévez. In addition, about two-thirds of erythromelalgia patients will have a coincident small-fiber neuropathy, "which tends to travel with the disease."

As to why some patients respond to corticosteroids and others do not, "erythromelalgia may not be simply one disease, but rather a clinical syndrome or manifestation of different disease states," he said.

Known causes of erythromelalgia include myelodysplastic syndromes like polycythemia vera, and genetic disorders like mutations in the *SCN9A* gene.

"The subset of study patients that responded to the steroids appears to have a more inflammatory or dysimmune etiology," Dr. Pagani-Estévez said. "Patients also peaked quickly with disease intensity, which suggests a prominent inflammatory component." Steroids, which are relatively potent anti-inflammatory medications, are an obvious choice to treat the disorder.

Despite confirming the authors' hypothesis retrospectively, neither markers of autoimmunity nor diagnostic testing results differed between responders and nonresponders. "The inability to discriminate these patients based on the extensive testing available for diagnosing came somewhat as a surprise," Dr. Pagani-Estévez said.

Furthermore, he said it can be difficult to measure a steroid

response objectively. “If you put someone on steroids, and you do not have a clear idea in your mind what you are going to measure or how long the trial will last, that patient might end up on steroids [for the] long term and not need them. Therefore, I recommend you have clear objective parameters, including validated pain scales, and perhaps even using photography to capture the appearance of the skin changes.”

Dr. Pagani-Estévez believes that corticosteroids are another potentially powerful tool in the armamentarium of pain treatments available for erythromelalgia.

Left untreated, patients may have permanent peripheral nociceptive fiber loss, leading to a chronic pain state with central sensitization. “At this point, the disease may be much more difficult to treat,” Dr. Pagani-Estévez said. “Therefore, if you are going to do a steroid trial, hit these patients hard with steroids and hit them early.”

*—Bob Kronemyer*

---

*Dr. Pagani-Estévez reported no relevant financial disclosures.*