The Journal of Angioedema

Subcutaneous C1-INH Use in Angiodema With Normal C1-INH Function: A Case Study

Douglas H. Jones, MD, FAAAAI, FACAAI

Rocky Mountain Allergy, Layton, Utah

INTRODUCTION

Despite advances in the diagnosis and treatment of hereditary angioedema (HAE), much is still unknown about this disorder.[1,2] Discussion of the management of patients with bradykinin-mediated angioedema with normal laboratory findings (ie, HAE with normal C1 inhibitor [CI-INH] or idiopathic angioedema) is ongoing,[3-5] as there is still uncertainty about the treatment of these patients. During an acute attack, intravenous access may be difficult in patients with angioedema. A case is presented here in which C1-INH was used subcutaneously in an urgent situation for the treatment of an acute angioedema attack.

CASE SUMMARY

A 16-year-old girl with a history of bradykinin-mediated angioedema and normal laboratory findings presented to the clinic with an acute attack. She had a 3-year history of acute swelling attacks and had been treated successfully with both ecallantide and C1-INH for angioedema. Previous to the use of ecallantide or C1-INH, the patient had extensive trials of high-dose antihistamines and oral steroids, and had been given epinephrine for her swelling attacks. Her symptoms were unresponsive to all of these measures. Repeated C4 levels and C1-INH quantitative and function levels were all normal. There was no family history of swelling. Symptoms first started around menarche, and became more frequent and more severe around her menstrual cycle. She did have improvement in symptoms after starting progesterone; however, it did not control her attacks and she still had them frequently. Subsequently, ecallantide was administered in an acute attack, and it was documented that she had significant improvement within 45 minutes of administration of the drug. Owing to the frequency of symptoms, severity of attacks, and impact of the disease on her quality of life, prophylactic therapy was started with plasma-derived C1-INH. This was effective in reducing the severity and frequency of attacks and improving her quality of life, but she still experienced breakthrough symptoms.

On the occasion reported here, the patient experienced swelling of the arms and feet bilaterally, along with abdominal pain and bloating for the previous 8 hours. Then she developed a fullness in her throat, although she did not have difficulty swallowing or breathing. Ecallantide 30 mg subcutaneously was administered initially. However, her symptoms continued to worsen over the next 30 minutes. C1-INH was attempted multiple times, but intravenous access could not be obtained because of her edema. Each time a flash of blood return was achieved, it would shortly close off because of the edema. The patient was then infused with C1-INH (Berinert) 2000 U at 2 separate sites in the subcutaneous tissue of the right lower abdomen at a rate of 1 mL every 10 seconds. She was monitored for 1 hour and experienced a 50% improvement in her symptoms. Abdominal pain, bloating, and the edema in the extremities were all reduced; the feeling of fullness in the throat subsided as well. Four hours post infusion, she described complete resolution of her symptoms. She did experience local pain with the infusion, but otherwise had no other adverse effects.

This patient successfully infused the same dose on multiple occasions at home, for the treatment of angioedema attacks. She did achieve symptom control; however, the dose needed to maintain this was about 1500 U daily. Owing to the high dose and increased frequency of infusion, she did not continue subcutaneous infusions, but rather went back to routinely infusing IV. She is currently infusing prophylactic C1-INH 1500 U intravenously, 2 to 3 times per week and as needed to maintain control.

DISCUSSION

C1-INH is approved for intravenous use for treatment of both prophylactic (Cinryze) and acute attacks (Berinert). It is only approved for patients with a diagnosis of type 1 or type 2 HAE. However, a growing number of patients, like the one presented here, have bradykinin-mediated angioedema with normal C1-INH function. They need assistance with treatment of their disease as much as do those with type 1 or type 2 HAE, but management of these patients has yet to be clarified. There are many products on the market to treat patients with HAE, but most are only approved for types 1 and 2. This patient was treated with ecallantide and Berinert CI-INH not only because of her age, but also what medication her insurance would approve. Given that she is 16 years old, androgens are not appropriate in her case, and she is too young to receive icatibant. Her insurance would not approve Cinryze, so ecallantide and Berinert CI-INH were administered. Ecallantide alone was often not sufficient to

alleviate her exacerbations and Berinert CI-INH was needed additionally. The combination of the 2 medications treated most exacerbations more quickly and completely than using them individually.

CONCLUSIONS

Until data from randomized controlled studies become available, no firm recommendations regarding treatment of these patients can be made. There has been variable response to approved HAE medications in patients with angioedema and normal laboratory findings. In the present case, the patient responded well to the medications described, but did have breakthrough attacks despite prophylactic therapy. This patient had difficult intravenous access during an acute angioedema attack, and she was given C1-INH successfully via the subcutaneous route, with minimal adverse effects. A higher-than-normal dose was needed, but symptoms resolved within 4 hours. This may provide another option for patients to get needed medication in an acute situation. As there is little experience in treating these patients, further studies are needed.

REFERENCES

1. Lang DM, Werner A, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012;109:395-402.

2. Zuraw BL, Bernstein JA, Lang DM, et al; American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol*. 2013;131:1491-1493.

3. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol Pract*. 2013;1:458-467.

4. Riedl M. Hereditary angioedema with normal C1-INH (HAE type III). *J Allergy Clin Immunol Pract*. 2013;1:427-432.

5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012;33(suppl 1):S145-S156.

DISCLOSURE

The author is a speaker for: Teva, Baxter and Dyax. The author is a consultant for: Sanofi, CSL and Dyax.

ADDRESS CORRESPONDENCE TO:

Douglas H Jones, MD, FAAAAI, FACAAI
1660 W Antelope Dr STE 225
Layton, UT 84041

E-mail: jonesallergy@gmail.com