Successful Use of Lanadelumab in an Older Patient With Type II Hereditary Angioedema

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BACKGROUND: Type II hereditary angioedema (HAE) is a rare, genetic disorder characterized by recurring subcutaneous and/or submucosal edema throughout the body and causes significant morbidity and mortality. Lanadelumab is a novel, long-term prophylactic treatment option for HAE and has proven to be an effective treatment option. However, data are limited in patients with type II HAE or aged ≥ 65 years. We present a case of HAE treated with lanadelumab in a patient of an underrepresented population.

CASE PRESENTATION: An 81-year-old male patient was diagnosed with type II HAE at the age of 75 years. Initially, he described having attacks of abdominal pain weekly that could last up to several days. At age 77 years, he began an on-demand treatment, icatibant, which diminished pain. However, after increasing frequency of attacks, the patient started receiving lanadelumab 300 mg subcutaneously every 2 weeks. He went from requiring on-demand treatment 2 to 3 times per month to once in 6 months.

CONCLUSIONS: Long-term prophylaxis is critical for managing HAE patients, but data are limited for patients with type II HAE and aged ≥ 65 years. Our case supports the use of lanadelumab in these populations.
levels (24 mg/dL), and low levels of C1 esterase inhibitor activity (28% of normal).

Initially, he described having weekly attacks of abdominal pain that could last 1 to several days. At worst, these attacks would last up to a month, causing a decrease in appetite and weight loss. At age 77 years, he began an on-demand treatment, icatibant, a bradykinin receptor blocker. After initiating icatibant during an acute attack, the pain would diminish within 1 to 2 hours, and within several hours, he would be pain free. Previously, pain relief would take several days to weeks. He continued to use icatibant on-demand, typically requiring treatment every 1 to 2 months for only the more severe attacks.

After an increasing frequency of abdominal pain attacks, prophylactic medication was recommended. Therefore, subcutaneous lanadelumab 300 mg every 2 weeks was initiated for long-term prophylaxis. The patient went from requiring on-demand treatment 2 to 3 times per month to once in 6 months after starting lanadelumab. In addition, he tolerated the medication well without any AEs.

**DISCUSSION**

According to the international WAO/EAACI 2021 guidelines, HAE treatment goals are “to achieve complete control of the disease and to normalize patients’ lives.” On-demand treatment options include C1 esterase inhibitor, icatibant, or ecallantide (a kallikrein inhibitor). Long-term prophylaxis in HAE should be considered, accounting for disease activity, burden, control, and patient preference. Five medications have been used for long-term prophylaxis: antifibrinolytic agents (not recommended), attenuated androgens (considered second-line), C1 esterase inhibitor, berotralstat, and lanadelumab.

Antifibrinolytics are no longer recommended for long-term prophylactic treatment as their efficacy is poor and was not considered for our patient. Attenuated androgens, such as danazol, have a history of prophylactic use in patients with HAE due to their good efficacy but are suboptimal due to their significant AE profile and many drug-drug interactions. In addition, androgens have many contraindications, including hypertension and hypertriglyceridemia, which were both present in our patient. Consequently, danazol was not an advised treatment for our patient. C1 esterase inhibitor is often used to prevent HAE attacks and can be given intravenously or subcutaneously, typically administered biweekly. A potential AE of C1 esterase inhibitor is thrombosis. Therefore, C1 esterase inhibitor was not a preferred choice in our older patient with a history of hypercoagulability. Berotralstat, a plasma kallikrein inhibitor, is an oral treatment option that also has shown efficacy in long-term prophylaxis. The most common AEs of berotralstat tend to be gastrointestinal symptoms, and the medication requires dose adjustment for patients with hepatic impairment. Berotralstat was not considered because it was not an approved treatment option at the time of this patient’s treatment. Lanadelumab is a human monoclonal antibody against plasma kallikrein, which decreases bradykinin production in patients with HAE, thus preventing angioedema attacks. Data regarding the use of lanadelumab in patients with type II HAE are limited, but because HAE with normal C1 esterase inhibitor levels involves the production of bradykinin via kallikrein, lanadelumab should still be effective. Lanadelumab was chosen for our patient because of its minimal AEs and is not known to increase the risk of thrombosis.

Lanadelumab is a novel medication, recently approved in 2018 by the US Food and Drug Administration for the treatment of type I and type 2 HAE in patients aged ≥ 12 years. The phase 3 Hereditary Angioedema Long-term Prophylaxis (HELP) study concluded that treatment with subcutaneous lanadelumab for 26 weeks significantly decreased the frequency of angioedema attacks compared with placebo. However, 113 (90.4%) of patients in the phase III HELP study had type I HAE. Of the 125 patients that completed this randomized, double-blind study, only 12 had type II HAE. In addition, this study only included 5 patients aged ≥ 65 years. Also, no patients aged ≥ 65 years were part of the treatment arms that included a lanadelumab dose of 300 mg. In a case series of 12 patients in Canada, treatment with lanadelumab decreased angioedema attacks by
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However, the series only included 1 patient with type II HAE who was aged 36 years. Therefore, our case demonstrates the efficacy of lanadelumab in a patient aged ≥ 65 years with type II HAE.

CONCLUSIONS
HAE is a rare and potentially fatal disease characterized by recurrent, unpredictable attacks of edema throughout the body. The disease burden adversely affects a patient’s quality of life. Therefore, long-term prophylaxis is critical to managing patients with HAE. Lanadelumab has been proven as an effective long-term prophylactic treatment option for HAE attacks. This case supports the use of lanadelumab in patients with type II HAE and patients aged ≥ 65 years.

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Ethics and consent
No informed consent was obtained from the patient; patient identifiers were removed to protect the patient’s identity.

References