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CORRESPONDENCE

Successful management of hereditary angioedema with icatibant during the postpartum period

Hereditary angioedema (HAE) is a rare disease with variable clinical symptoms. Female patients are often more severely affected because estrogen plays a role during angioedema attacks. Despite the urgency of managing HAE during the perinatal period, the safety of using icatibant, a bradykinin-receptor antagonist, has not been established due to a lack of case-based reports.[1]

A Japanese woman was referred to our hospital due to recurrent episodes of dyspnea, abdominal pain, and edema of the fingers and face that started when she was 24 years old (Figure 1A). She was diagnosed with HAE based on family history, decreased C1-INH functional activity (<25%; normal, 70%-130%) and C4 level (5.0 mg/dl; normal, 11-34 mg/dl), and an increased intestinal wall thickness revealed by computed tomography (Figure 1B). She had been treated with occasional on-demand intravenous injection of 1000 IU plasma-derived C1-INH (pdC1-INH) at the emergency department. She became pregnant at 35 years old through artificial fertilization. During the pregnancy, she managed HAE attacks with on-demand injections of pdC1-INH. Upon delivery and other invasive medical procedures, short-term prophylaxis of pdC1-INH was used, which was the only accepted treatment for pregnant patients with HAE in Japan at that time.

At 36 years old, she gave birth and started breastfeeding. Four months after delivery, she started subcutaneous self-administration of icatibant 30 mg as management of HAE attacks during the postpartum period after giving informed consent and being informed of the risks and benefits of icatibant during breastfeeding. Icatibant

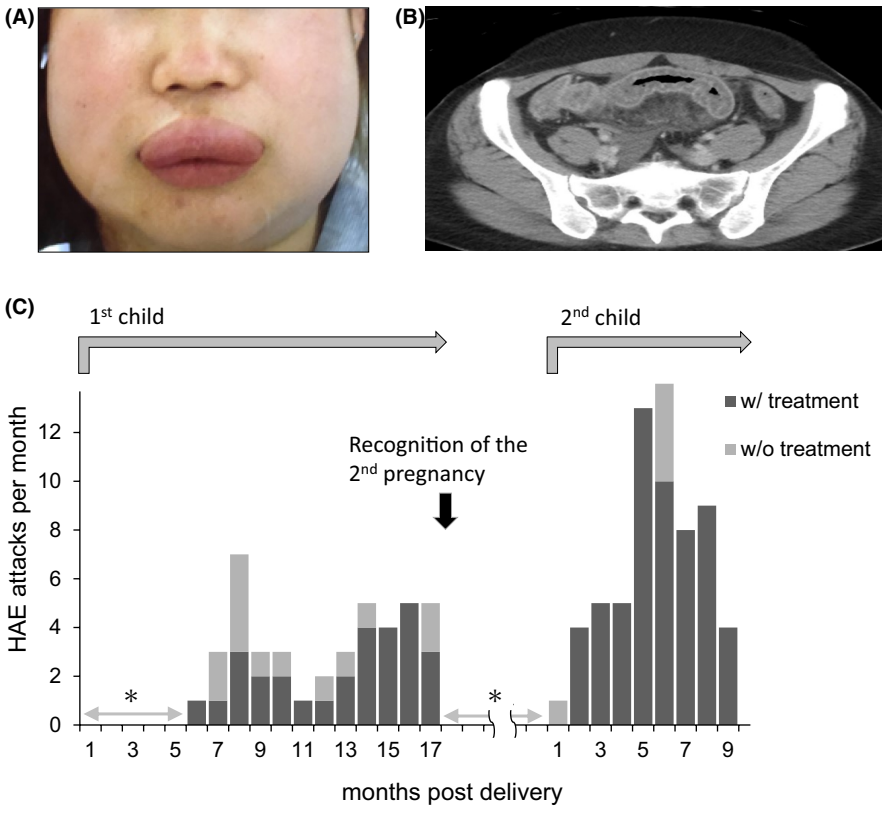

FIGURE 1 (A) Facial swelling during a hereditary angioedema (HAE) attack. (B) Computed tomography image of the abdomen with intestinal edema during an HAE attack. (C) Histogram of the frequency of monthly HAE attacks during self-administration of icatibant. The asterisk indicates when HAE attacks were treated by on-demand injection of plasma-derived C1 inhibitor at the emergency room

administration was based on the following: in cases of severe swelling of the limbs, icatibant was used after the final breastfeeding before the infant's bedtime, and breastfeeding was resumed the following day at intervals of 6 h or more from the last dose of icatibant. In cases of swelling of the face and neck and abdominal pain, icatibant was immediately self-administered, and artificial milk was given instead of breast milk. She continued breastfeeding for 1 year while on on-demand icatibant treatment (Figure 1C). At 38 years old, she became pregnant again and resumed on-demand treatment with pdC1-INH, reverting to on-demand icatibant treatment after delivery and when the infant was 1 month old (Figure 1C). When the frequency of attacks is high, it is impractical to visit the emergency department for pdC1-INH treatment during each attack. Thus, icatibant was immediately self-administered during angioedema attacks, which at its peak occurred almost every other day. She has been satisfied with the improvement of symptoms after icatibant administration, which has also significantly improved her quality of life.

Although breastfeeding has long-term benefits for both a mother and her infant, postpartum patients with HAE tend to give up breastfeeding, instead prioritizing on-demand icatibant treatment. Some literature reports the safety of icatibant use during the perinatal period,[2,3] while no report in the lactating period. According to the manufacturer's instructions, the risk of exposing breastfeeding infants to icatibant is relatively low because systemic absorption through breastmilk is not expected.[4] Based on the blood pharmacokinetics of icatibant, it is rapidly and almost completely absorbed after subcutaneous injection, and the maximum serum concentration is reached within 30 min. Its plasma half-life is 1-2 h, and it is not detected in the serum after 6 h.[5,6] In the present case, icatibant was safely used in a lactating patient with HAE. Further evaluation is needed to establish the safety of icatibant for lactating patients with HAE.

AUTHOR CONTRIBUTIONS

YK contributed to conceptualization and writing; AY and NA contributed to resources, data collection, and manuscript editing.

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DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: Oral informed consent was obtained from the patient.

Registry and Registration No. of the study/trial: N/A.

Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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