Managing the transitioning HAE adolescent

Adolescence: More than just hormones

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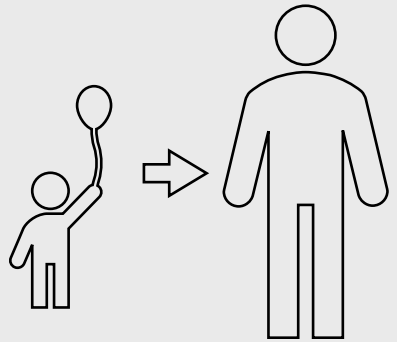

Disclosures

- Speaker and/or consultancy fees received from CSL Behring

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- The views, information or opinions expressed herein are those of the speaker; they do not necessarily reflect those of CSL Behring

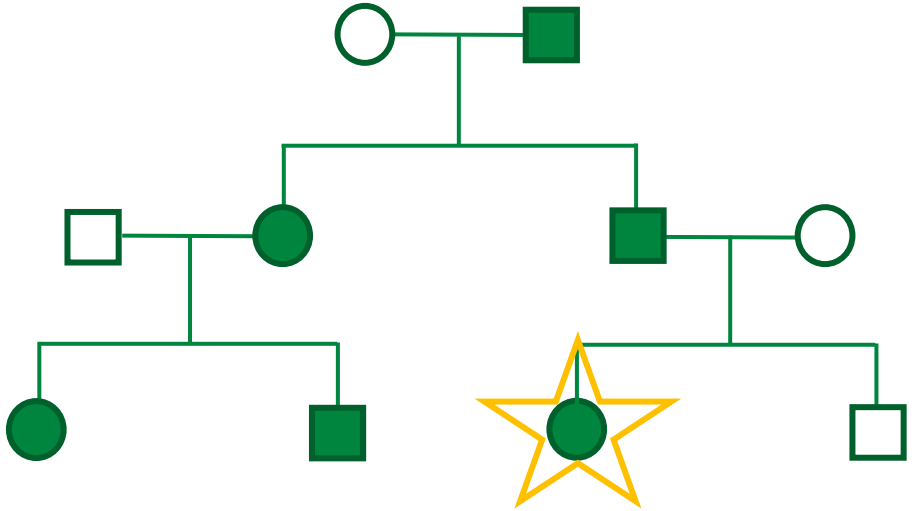
- Slides may contain off-label content

Patient description

- 15-year-old female (born in 2006)
- Family history of angioedema (father)
- Diagnosed at screening
  - C1-INH: 6.17 mg/dL (normal range 12.00–25.00 mg/dL)
  - Functional C1-INH: 26.84% (normal range ≥38%)

Action plan:

- On-demand treatment in case of acute attack with IV pdC1-INH 20 IU/kg
- Pre-procedural prophylaxis with IV pdC1-INH 20 IU/kg



C1-INH, C1-esterase inhibitor; IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor

Case history of attacks

2013

- Age 7
  - Angioedema of the right hand lasting 2 days, accompanied by abdominal pain ➡ Emergency room
  - Treated with IV pdC1-INH resulting in improvement within 1 hour

2014–2015

- Patient suffered 5–7 attacks per year

Action plan:

- On-demand in case of acute attack with IV pdC1-INH 20 IU/kg
- Pre-procedural prophylaxis with IV pdC1-INH 20 IU/kg

IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor

Case history of attacks

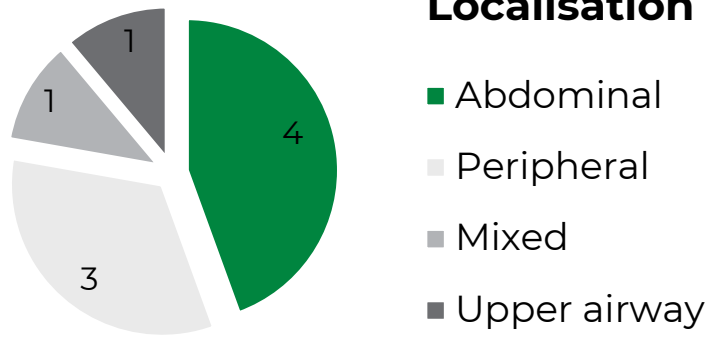
2016

- Age 10
- Patient suffered 9 attacks within a 6-month period

Action plan:

- Long-term prophylactic treatment with tranexamic acid 40 mg/kg/day
- Pre-procedural prophylaxis with IV pdC1-INH 20 IU/kg

- *Helicobacter pylori* was ruled out
- Abdominal ultrasound showed a fatty liver



IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor

Treatment options for children and adolescents in Europe

On-demand	Administration
Plasma-derived C1-INH	IV*
Recombinant C1-INH (≥2 years)	IV
Icatibant (≥2 years)	SC
Pre-procedural prophylaxis	**Administration**
Plasma-derived C1-INH	IV*
Long-term prophylaxis	**Administration**
Plasma-derived C1-INH (≥6 years)	IV†
Plasma-derived C1-INH (≥12 years)	SC
Lanadelumab (≥12 years)	SC
Berotralstat (≥12 years)	Oral
Tranexamic acid	Oral

Due to adverse effects, attenuated androgens are no longer recommended for long-term prophylaxis in children or adolescents prior to Tanner Stage 5 with HAE[1]

*Indications for each product are according to European Prescribing Information. *Indicated for all ages, depending on manufacturer. †Depending on manufacturer.*

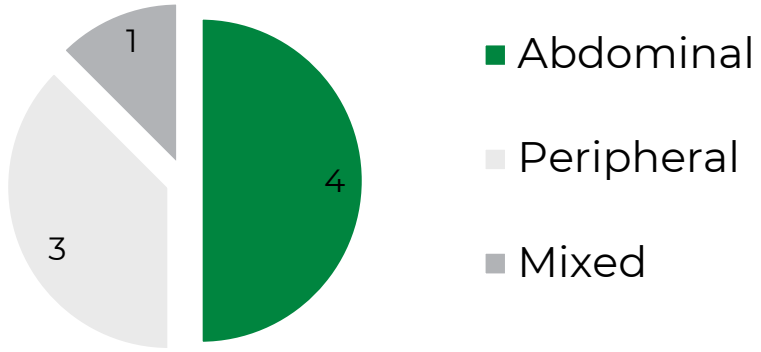
C1-INH, C1-esterase inhibitor; HAE, hereditary angioedema; IV, intravenous; SC, subcutaneous

1. Maurer M. *et al. World Allergy Organ J*. 2018; 73(8):1575–1596.

Treatment with tranexamic acid

Mid 2016–mid 2017

- Age 10
- 8 attacks
- Tranexamic acid was suspended
  - Not effective
- Progestins were evaluated but finally discarded as per consensus with endocrinology



Action plan:

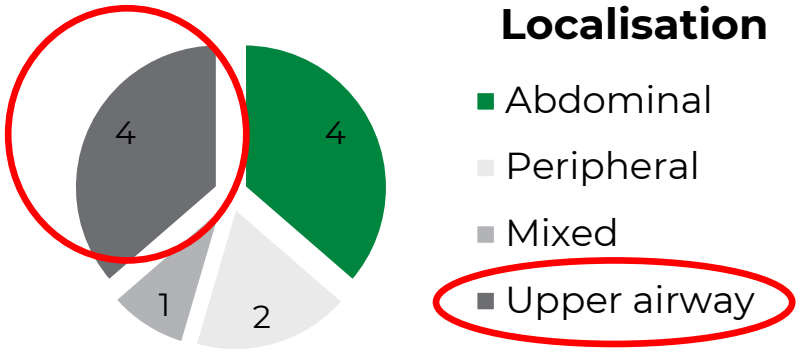
- On-demand in case of acute attack with IV pdC1-INH 20 IU/kg or icatibant acetate
- Pre-procedural prophylaxis with IV pdC1-INH 20 IU/kg

IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor

On-demand treatment

Mid 2017–mid 2018

- Age 11
- Patient suffered 11 attacks
- Self-administration with IV pdC1-INH
- SC icatibant acetate
  - Patient prefers not to use, influenced by her father's experience
- Does not treat peripheral attacks
  - Does not want to administer at school
  - Does not want to go home for treatment and miss out at school



IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor; SC, subcutaneous

Considerations for school children

- It is important that teachers and school nurses are aware of symptoms and the treatment of HAE
- However, there are issues surrounding teachers' willingness to treat
  - Liability
  - Do not want to take the risk of administering treatment in case the outcome is not desirable

Poll: Which factor do you think is the most important when selecting a treatment/developing a treatment plan for adolescents?

A. Current frequency and severity of attacks

B. Quality of life

C. Patient preference

D. Patient lifestyle and activity

Triggers

- Age 12
- Exam period increased attack frequency:
  - Missed some exams
  - Poor academic results
- Psychological stress
  - Felt different from friends
  - Self-excluded from activities
  - Social isolation

Action plan:

- Short-term prophylactic treatment with IV pdC1-INH 20 IU/kg twice weekly during the exam period*

**Berinert® 500/1500 (C1-INH IV) is approved for the treatment and pre-procedure prevention of acute episodes of HAE. CSL Behring does not suggest or recommend the use of C1-INH (IV) in any way other than as described in the Summary of Product Characteristics.*

C1-INH, C1-esterase inhibitor; IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor

Impact on quality of life

- Quality of life impairment:
  - Anxiety
  - Fear of attacks (unpredictability)
  - Avoided after-school activities
  - Avoided travelling without parents' supervision

Action plan:

- Short-term prophylactic treatment with IV pdC1-INH 20 IU/kg before school trips or visiting grandparents on her own*

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C1-INH, C1-esterase inhibitor; IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor.

Long-term prophylaxis

- Despite STP, the patient suffered 17 attacks in 6 months

- Therefore, at age 13 when SC LTP became available, the patient switched to SC pdC1-INH 40 IU/kg twice weekly*
  - Asymptomatic for 9 months
  - Improvement in quality of life

- Patient decided to suspend LTP
  - Fewer triggers during lockdown (2020) – no school etc. ?
  - Uses on-demand therapy to treat attacks (1 attack every 2–3 months)
  - Patient is now more efficient at treating on demand

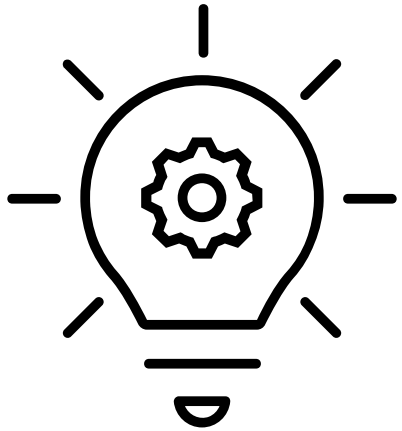
**The approved dosing of C1-INH (SC) is 60 IU/kg twice weekly. CSL Behring does not suggest or recommend the use of C1-INH (SC) in any way other than as described in the Summary of Product Characteristics.*

C1-INH, C1-esterase inhibitor; IU, international units; IV, intravenous; pdC1-INH, plasma-derived C1-esterase inhibitor; SC, subcutaneous; STP, short-term prophylaxis; LTP, long-term prophylaxis

Take-home messages

Older children may hide their symptoms due to anxiety or fear of social isolation

HAE is dynamic during adolescence and the psychological impact of the disease should be proactively assessed



Impact of HAE attacks on school attendance/performance may prevent future career or education opportunities

Treatment plans should be continually re-assessed

Self-administration in young adolescence is feasible

As the disease is constantly changing in adolescence, the indication of LTP should be carefully evaluated

HAE, hereditary angioedema; LTP, long-term prophylaxis