

Maria attends the Emergency Room

- Maria is a 24 year-old female that has arrived at the Emergency Room
- She states that she is experiencing extreme abdominal pain and vomiting, which started around 2 hours ago
- She has no other relevant diseases or known allergies, and is not taking any medication

Case created by:

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1. What should be the first course of action?

- A. Treat Maria with anti-emetics, analgesics, and fluid replacement therapy
- B. Undertake a physical examination
- C. Send Maria for abdominal imaging
- D. All of the above

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Feedback

- Anti-emetics are used to prevent or reduce nausea and vomiting, analgesics are used to control pain, and fluid replacement therapy is used to correct water and electrolyte deficits
- Patients with gastrointestinal edema may experience nausea, vomiting, diarrhea and abdominal tenderness¹
- Physical examination can reveal tenderness, guarding and rigidity, and Murphy's sign can be tested²
 - Tenderness – abdominal pain
 - Guarding – voluntary or involuntary response of abdominal muscles
 - Rigidity – abdominal firmness
 - Murphy's sign – manoeuvre used to differentiate pain in the right upper quadrant
- Abdominal imaging may reveal the cause of the symptoms

2. Abdominal imaging allows for rapid assessment of angioedema in patients that present with abdominal pain. What imaging manifestations of angioedema can aid diagnosis?

- A. Fluid accumulation in the peritoneum
- B. A thickened bowel wall
- C. Presence of ascites
- D. All of the above

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Feedback

- Abdominal imaging allows us to visualize fluid accumulation in the peritoneum, a thickened bowel wall and ascites in patients, aiding diagnosis of angioedema, including HAE^{1,2}
- Abdominal imaging allows us to rule out different conditions that cause abdominal pain, such as pancreatitis, cholecystitis and diverticulitis³

Diagnosing Maria

- Maria reports that her nausea has abated following anti-emetic treatment
- Maria's abdominal scan reveals edema of the bowel, free fluid in the abdomen, and mild ascites
- From the tests conducted so far, results have indicated angioedema
- Further methods are required to differentiate between mast cell- and bradykinin-mediated angioedema



3. What step(s) would you take next? (select all that apply)

- A. Ask about personal and family history of recurrent swelling / abdominal pain
- B. Treat Maria with IV C1-INH
- C. Treat Maria with antihistamines and corticosteroids
- D. Diagnose Maria with acute gastroenteritis

3. What step(s) would you take next? (select all that apply)

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Feedback

- Abdominal edema most commonly results from allergy and is mast cell-mediated; therefore, the first line of treatment should be antihistamines and corticosteroids, and adrenaline if necessary
- Response to antihistamines and corticosteroids may differentiate between mast cell-mediated angioedema and bradykinin-mediated angioedema¹
- Mast cell-mediated angioedemas respond well to this treatment, whereas bradykinin-mediated angioedemas, such as HAE, do not
- There is a family history of swelling/HAE in 80% of patients with HAE; however, an absence of family history does not exclude HAE as a potential cause²

Prompt treatment

- Maria was treated with antihistamines and corticosteroids; however her symptoms persisted
- Maria confirms that she has no family history of swellings or abdominal pain; however, when asked whether she has had these abdominal symptoms before, Maria states that she experienced a similar episode 1 year ago, which required intensive care
- She was diagnosed at the time with hypovolemic shock due to acute gastroenteritis
- **HAE is suspected**

4. What percentage of patients with HAE experience abdominal attacks?

A. 20%

B. 50%

C. 90%

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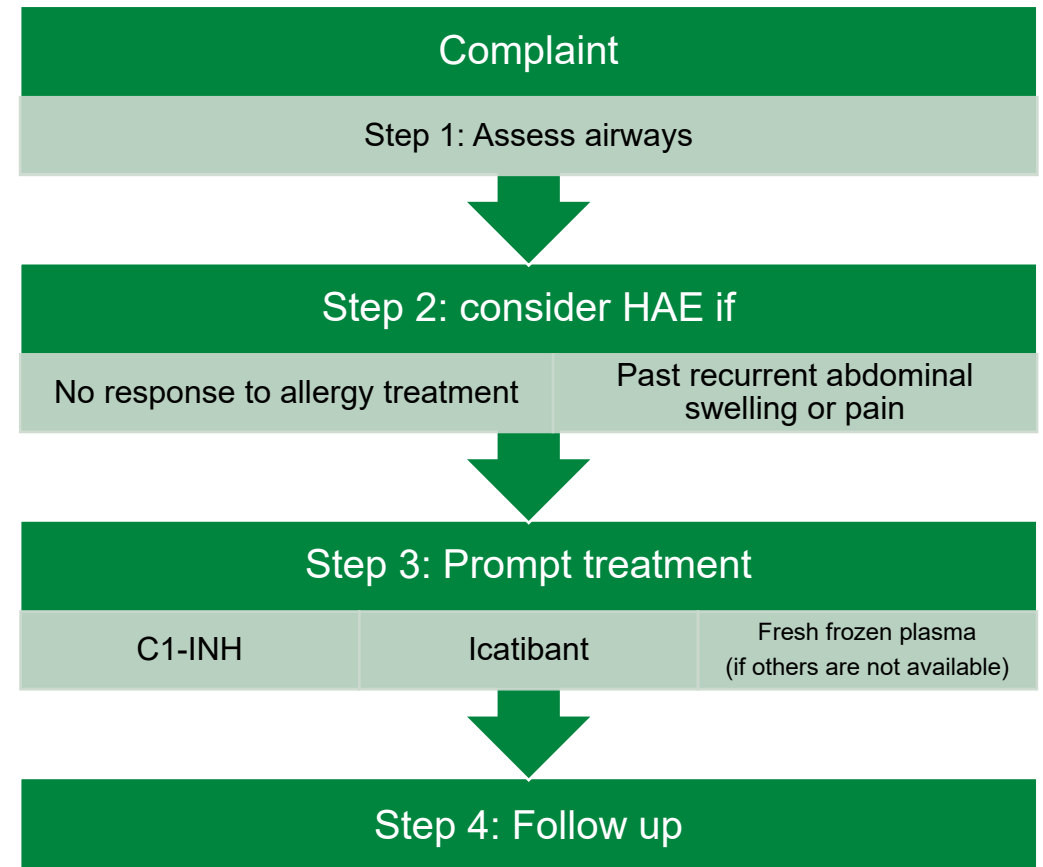
Feedback

- Around 90% of patients diagnosed with HAE have recurrent abdominal attacks,¹ whereas non-hereditary angioedema patients do not²
- It is also important to be aware that, although rare, for some patients, abdominal symptoms may be the only manifestation of HAE

Maria's diagnosis

The Hereditary Angioedema Rapid Triage Tool (described by Betschel et al.) has been implemented to treat the angioedema and differentiate between angioedema types:

- STEP 1:** Maria had no oropharyngeal swelling
- STEP 2:** She has not responded to allergy treatments. She has had past recurrent abdominal swelling/pain
- STEP 3:** Maria is treated with HAE-specific medication
- STEP 4:** Patient follow-up by a specialist experienced in the diagnosis and management of HAE is needed to confirm diagnosis



Treatment and follow up

- Maria was administered intravenous C1-INH and her abdominal pain/swelling resolved over the course of the next two hours
- Further testing to confirm diagnosis should include:
 - Serum C1-INH function and protein concentration
 - Serum C4 testing
 - Genetic testing for *SERPING1* mutations – particularly in patients with no family history of angioedema¹
- Based on Maria's test results, a diagnosis of HAE is confirmed. Maria should be supplied with C1-INH or icatibant to take home and be trained to self-administer in the event of a future attack
- Maria should also be referred to an HAE treatment center where she can receive optimal guidance for the ongoing management of her disease

5. What are the rates of misdiagnosis in patients with HAE?

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Feedback

- A recent observational study has shown that up to 50% of patients with C1-INH-HAE type I or II have been misdiagnosed, most commonly with appendicitis and allergic angioedema¹
- HAE misdiagnosed as appendicitis, for example, can lead to unnecessary surgery and lead to marked delays in appropriate treatment

Summary

- Hereditary angioedema is particularly difficult to diagnose when a patient presents with gastrointestinal symptoms only, as these are similar to those of more common diseases
- If misdiagnosed, patients may undergo unnecessary surgery and prolonged suffering
- The main focus in the Emergency Room should be to quickly differentiate between mast cell-mediated and bradykinin-mediated angioedema, especially in the case of laryngeal edema, which may be life-threatening

Summary

- There are three questions physicians can ask in the event of angioedema that are able to identify the majority of HAE patients:
 - 1. Has the patient experienced recurrent abdominal pain/swelling in the past?**
 - 2. Did the patient's angioedema respond to allergy therapy?**
 - 3. Does the patient have a family history of HAE?**
- By using a 'Hereditary Angioedema Rapid Triage Tool', Maria was efficiently treated and diagnosed with HAE in the Emergency Room, and her condition may now be managed appropriately