# Airway Obstruction Caused by Hemorrhage: Managing a Life-Threatening Complication in Patients With Acquired Hemophilia A: A Case Report

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A 60-year-old woman presented with extensive swelling in the throat and impending airway obstruction. Following a well-established 2-step flexible bronchoscopic intubation procedure, a computed tomography scan identified a large hematoma compromising the airway. Laboratory testing confirmed the diagnosis of acquired hemophilia A (AHA), a rare condition that can potentially be life-threatening, particularly when it results in airway obstruction. The risk of fatal bleeding is substantial when difficult airway management guidelines call for a surgical airway. This case report describes the essentials of hemostatic treatment of AHA and our approach to the management of a difficult airway. (A&A Practice. 2020;14:83–6.)

## GLOSSARY

**AHA** = acquired hemophilia A; **aPTT** = activated partial thromboplastin time; **BMI** = body mass index; **bsa** = body surface area; **CT** = computed tomography; **ICU** = intensive care unit; **INR** = international normalized ratio; **INTEM** = rotational thromboelastometry of the intrinsic coagulation pathway; **ROTEM** = rotational thromboelastometry; **rpFVIII** = recombinant porcine factor VIII

Acquired hemophilia A (AHA) is a rare disorder occurring in 1 to 1.5 persons per million per year. It is triggered by a reaction of autoantibodies, most commonly against coagulation factor VIII. AHA is associated with bleeding that occurs spontaneously or after minor trauma and that generally develops in soft and subcutaneous tissue or muscle. Bleeding can be fatal in 5%–10% of patients, depending on severity or location.[1,2]

Treatment of AHA generally includes management of the acute bleeding, eradication of the inhibiting autoantibodies, and treatment of any underlying disease.[1–3] The management of a compromised airway has to be guided by a difficult airway algorithm.[4–7] However, airway compromise caused and complicated by AHA presents a unique condition. Uncontrolled bleeding can further obstruct the airway in the necessity of a surgical airway. This is particularly true if AHA is undiagnosed or is inadequately treated.[8,9] Therefore, early diagnosis and correct hemostatic management are critical, and the involvement of experienced hematologists is necessary to ensure appropriate therapy when managing the airway.[1,2]

This case report describes the management of a patient who was admitted to the hospital with a life-threatening airway obstruction related to preexisting but undiagnosed AHA.

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Written consent was obtained from the patient for the publication of this case report.

## CASE DESCRIPTION

Several months before admission to the hospital, a 60-year-old woman without previous comorbidities apart from obesity (body mass index [BMI] = 32, height = 160 cm, weight = 82 kg) visited her general practitioner because of a swollen lower leg. Deep vein thrombosis was ruled out. An ultrasound, performed a few days later, revealed a hematoma in the gastrocnemius muscle, but no specific treatment was started and standard coagulation parameters were not obtained. Over the following weeks, the patient noticed the development of additional hematomas after minor trauma.

Five months after appearance of the first symptoms, the patient developed swelling in the neck, which led to massive respiratory distress. The patient was admitted to the emergency department with imminent airway obstruction, presenting with tachycardia (120 bpm), hypertension (192/85 mm Hg), and decreased oxygen saturation (92%). Twenty minutes after admission, her airway was secured via flexible bronchoscopic intubation performed with the patient in semisitting position in accordance with our institution's difficult airway algorithm. However, in contrast to our usual procedure, 1% lidocaine was administered through the bronchoscope for topical anesthesia instead of transcricoidal local anesthesia, due to the massive swelling of the neck.

After placement of the bronchoscope into the trachea, an intravenous general anesthetic (etomidate, 20 mg) was administered, and after loss of consciousness, the tube was advanced over the bronchoscope. Throughout the intubation procedure, the patient's vital signs remained stable, without a drop in oxygen saturation, and heart rate and blood pressure returned to normal after the procedure was completed. This procedure was performed in the presence

of an ear, nose, and throat specialist who was prepared to perform a surgical airway, taking into consideration the anatomical changes arising from the swelling (Figure 1).

After the airway was secured, a computed tomography (CT) scan revealed massive soft tissue swelling in the retro- and parapharyngeal space, consistent with a hematoma, but no evidence of active bleeding was found (Figures 2 and 3). Laboratory results revealed anemia (hemoglobin 61 g/L), an elevated platelet count (739 × $10^9$/L), and a normal international normalized ratio (INR), but a prolonged activated partial thromboplastin time (aPTT; 107 seconds) and coagulation time (333 seconds) were observed in the rotational thromboelastometry of the intrinsic coagulation pathway (INTEM) assay of the rotational thromboelastometry (ROTEM; TEM International, Munich, Germany) analysis. The results of a mixing test ordered by the treating hematologists to evaluate possible reasons for aPTT prolongation suggested the presence of an inhibitor. Further laboratory testing revealed a marginally traceable factor VIII (0.0004%) and a high inhibitor titer (522 U/L), typical of AHA.

To avoid further increase in the hematoma and to start treating AHA, recombinant factor $VII_a$ (90 µg/kg every 6 hours) and tranexamic acid (500 mg every 8 hours) were administered to the patient. Corticosteroids (2 mg/kg) and later rituximab (375 mg/$m^2$) were administered to eradicate factor VIII inhibitors.

The patient was admitted to the intensive care unit (ICU) under the assumption that the airway would remain obstructed for several days. A surgical tracheostomy performed 2 days after admission under continued administration of recombinant factor $VII_a$ proved uneventful. Thereafter, a change in hemostatic treatment to recombinant porcine factor VIII (rpFVIII) (200 E/kg every 8 hours) allowed laboratory monitoring of factor VIII. Factor VIII levels increased only gradually, suggesting the presence of cross-reactive antibodies. Therefore, we added reduced doses of factor $VII_a$ (2 mg) to control oozing episodes at puncture sites. The Table provides an overview of the pharmacological treatments administered during the ICU stay.

One week after admission, a CT scan revealed a shrinking of the hematoma. After another week, the patient was decannulated and transferred from the ICU to ward. No additional major bleeding events occurred during the subsequent hospital stay. While AHA treatment includes medication with highly procoagulatory effects, no thromboembolic complications occurred. No underlying cause of AHA could be identified.

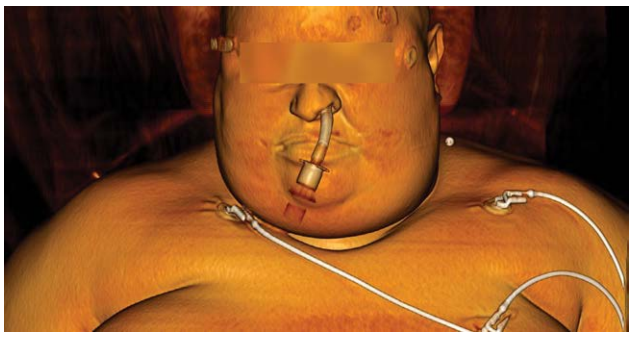

**Figure 1.** CT scan on day of admission showing a reconstruction of the difficult surface anatomy of the neck. CT indicates computed tomography.

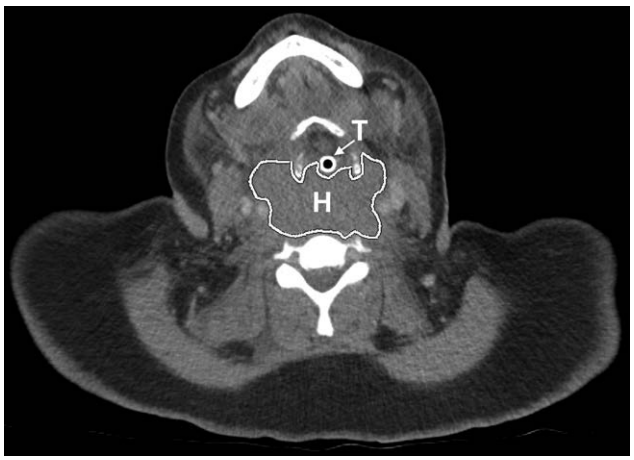


**Figure 2.** CT scan (transversal axis) on the day of admission revealing expansion of the hematoma in the pharyngeal space. CT indicates computed tomography; H, hematoma; T, tube.

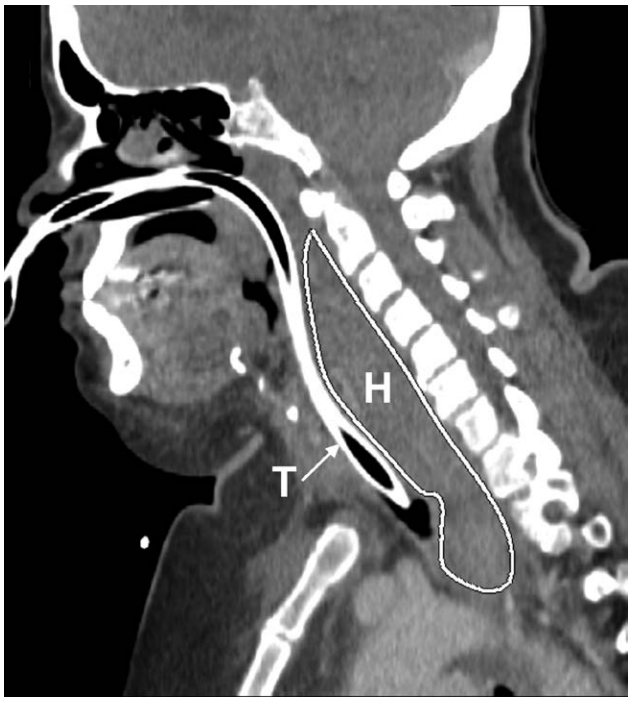


**Figure 3.** CT scan (sagittal axis) on the day of admission revealing expansion of the hematoma. CT indicates computed tomography; H, hematoma; T, tube.

## DISCUSSION

AHA is a rare condition with a bleeding pattern different from hereditary hemophilia. While hemarthrosis commonly occurs in patients with congenital hemophilia, bleeding in the muscles and mucous membranes is typical for AHA. Both the severity and location of the bleeding can contribute to a life-threatening situation, as in our case, in which bleeding led to an obstructed airway. AHA can be associated with comorbidities such as malignancies and autoimmune diseases or can be drug induced or related to pregnancy. In half of all cases, no underlying disorder can be identified.[1–3]

**Table. Drug Treatment**

| Therapy | Agent | Initial Dose; Initial Interval | Remarks |
|---|---|---|---|
| Hemostatic | Recombinant factor $VII_a$ | 90 µg/kg; 6 h | Fixed dose stopped when factor VIII began |
| | Recombinant porcine factor VIII | 200 U/kg; 8 h | Available; started on day 3 |
| | Tranexamic acid | 500 U; 6 h | Stopped on day 16 |
| Immunosuppressive | Methylprednisolone | 2 mg/kg; 24 h | Tapered slowly |
| | Rituximab | 375 $mg/m^2$ bsa; (remarks) | Total: 4 doses |

Abbreviation: bsa, body surface area.

AHA should be suspected in patients with abnormal bleeding independent of associated trauma, in addition to laboratory results including prolonged aPTT in the presence of a normal INR and normal platelet count.[1–3] Timely recognition of this rare disorder can be challenging, and diagnostic delays are well described in the literature.[8,9] This also applies to our patient, who was diagnosed months after her initial symptoms appeared.

Treatment focuses on management of acute bleeding, eradication of inhibitors, and treatment of any underlying disease. The first-line strategy to control bleeding involves the administration of bypassing agents, including recombinant factor $VII_a$ and activated prothrombin complex concentrates.[1–3] However, these agents can cause severe thromboembolic complications, and effectiveness on hemostatic response can only be monitored by clinical assessment. In 2016, rpFVIII was approved as a treatment for AHA by the regulatory authorities in Switzerland. In contrast to human factor VIII, rpFVIII causes little or no cross-reactivity to the antibodies and, therefore, application of rpFVIII allows continued measurement of endogenous factor VIII levels. This may guide hemostatic therapy in addition to clinical monitoring.[10,11] To enable laboratory monitoring, we switched to rpFVIII once it was available.

Corticosteroids used alone or in combination with cytostatic agents may eradicate factor VIII inhibitors. In about 30% of cases, the inhibitor disappears spontaneously.[1,2] In any case, immediate involvement by a hematologist is of utmost importance for early diagnosis of AHA and appropriate treatment with nonstandard medications.[1,2,9]

In our patient, airway obstruction required emergency airway management. There are various algorithms for the management of a difficult airway,[4–6] and our institution uses a well-established standard operating procedure.[6,7,12] In case of an anticipated difficult airway with maintained spontaneous breathing, we perform flexible bronchoscopic intubation in 2 steps.

First, for awake bronchoscopy, we perform local anesthesia with application of lidocaine (1%, 2 mL) transcricoidally or through the bronchoscope. The latter appeared to be the safer option in our case, because identification of the cricothyroid membrane was not possible due to the huge amount of swelling. In addition, we attempted to avoid further bleeding, although we were not aware of the diagnosis of AHA at the time of intubation.

Second, after placing the bronchoscope into the trachea, we thereafter administer etomidate (0.2–0.3 mg/kg) that induces a short-lasting general anesthesia and allows for secure passage of the endotracheal tube through the vocal cords but avoids coughing.[6,7,12] This approach can be criticized as losing the way of "awake" fiberoptic intubation. However, interruption of spontaneous breathing by etomidate lasts for a very short time period only.[13] In contrast, as recently shown, many "awake" strategies include administration of hypnotics (eg, midazolam, propofol) and/or opioids (eg, fentanyl, remifentanil)[14] producing unpredictable effects on consciousness and spontaneous breathing. Standardization of the approach (as thought and performed at our institution) makes action and effect predictable for every team member irrespective of the individual provider and, in consequence, increases safety.

Few case reports describe airway compromise related to AHA that requires an immediate or delayed surgical airway.[8,9] Any surgical intervention entails the risk of additional bleeding. However, flexible bronchoscopic intubation was successful in the case of our patient. In the next step, after the airway is secured, the persistence of the underlying airway problem has to be considered. If the obstruction is expected to last for a short time period, timely extubation can be attempted. However, if obstruction is expected to last for several days or weeks, a tracheostomy has to be performed.[15] Therefore, hemostatic treatment in the presence of AHA has to be implemented before any surgical intervention.[1,2,9] Percutaneous dilational tracheostomy, a standard technique in the ICU,[15] was not considered in our patient because of the difficult surface anatomy of the neck.

To summarize, AHA is a rare disorder that can be acutely life-threatening depending on the severity and location of bleeding. Following a well-established airway management algorithm allows for successful management of a difficult airway, irrespective of the underlying cause. As in this case, a timely diagnosis of AHA in close collaboration with a hematologist, anesthetist, and intensivist is of utmost importance to ensure appropriate treatment of acute and persistent airway compromise.

## DISCLOSURES

**Name:** Susann Endermann, MD.
**Contribution**: This author helped care for the patient and write the manuscript.
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