Upper Airway Hematoma Secondary to Warfarin Therapy: A Systematic Review of Reported Cases

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Abstract

Upper airway hematoma (UAH) is a rare but life-threatening complication of oral anticoagulants requiring early recognition. However, no consensus exists regarding the best approach to treatment. We therefore, sought to systematically review the published literature on UAH to elaborate its demographic and clinical characteristics, treatment, complications, and outcomes. A systematic electronic search of PubMed and EMBASE for case reports, case series, and related articles of UAH related to warfarin published from inception (November 1950) to March 2015 was carried out. Categorical variables were expressed as percentage and continuous variables as mean ± standard deviation (SD). Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 20.0. All cases were reported to have UAH as a complication of anticoagulation therapy with warfarin. Demographic and clinical characteristics, treatment, complications and outcomes of UAH were studied. Thirty-eight cases of UAH were identified from 34 reports in the literature. No gender preponderance (male = 52.78%) was seen and the average age of presentation was 60.11 ± 12.50 years. Dysphagia, sore throat, and neck swelling were the most common symptoms and the mean international normalized ratio (INR) at presentation was 8.07 ± 4.04. Most cases had sublingual hematoma (66.57%) followed by retropharyngeal hematoma (27.03%). Of the cases, 48.65% were managed conservatively while the rest underwent either cricothyrotomy or intubation with the time to resolution being 7.69 ± 5.44 days. UAH is a rare but potentially serious complication of warfarin therapy. It is more common in the elderly population with supratherapeutic INR; inciting events were present in many cases. Overall, it has a good prognosis with significant morbidity present only if concomitant respiratory compromise is present. Reversal of anticoagulation with low threshold for artificial airway placement in the event of airway compromise leads to a favorable outcome in most cases.

Keywords: Airway obstruction, hematoma, mouth floor, warfarin

Introduction

Upper airway hematoma (UAH) secondary to warfarin therapy is rare but potentially life-threatening conditions. Hematomas/bleeding at various sites including sublingual, retropharyngeal, submaxillary and the epiglottis have been described. Although a sublingual hematoma can be confused with infectious processes such as Ludwig’s angina, it is frequently obvious on examination. However, the other hematomas described can have more subtle signs until they lead to airway obstruction.
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compromise.[1] UAH may occur due to different inciting events including cervical spinal injury, rheumatoid arthritis, neck surgery, injury to great vessels, and violent head movements. It may also occur spontaneously in patients on anticoagulation therapy or with a bleeding diathesis.[2,3] Although rare, UAH is a very serious event but only case reports exist with no higher level of evidence. Hence, with no consensus in place, the diagnosis and management of this condition remains a challenge. We therefore, sought to systematically review the published literature on UAH to elaborate its demographic and clinical characteristics, treatment, complications, and outcomes.

Materials and Methods

Ethical considerations
As the study did not involve human subjects or hospital chart review, institutional review board (IRB) approval/exemption was not required.

Search strategy and data collection
A systematic electronic search of Medline and EMBASE for case reports, case series, abstracts, and related articles of UAH secondary to warfarin therapy published from inception to March 2015 was performed independently by three authors (PK, RP, and PS) using two broad themes. For upper airway hematoma, the search terms used were “sublingual hematoma,” “sublingual hemorrhage,” “sublingual bleeding,” “epiglottic hematoma,” “supraglottic hematoma,” “neck hematoma,” “submaxillary hematoma,” and “retropharyngeal hematoma.” For the theme warfarin therapy, the search terms used were “warfarin” (mesh), “warfarine,” “warfarin sodium,” “warfant,” “warfarin,” “warfarin potassium,” and “Tedicumar.” The search was limited to human studies. Bibliographies of the reviewed articles were further scanned to identify additional reports. Care was taken to avoid duplication. Thirty-four articles with 38 cases in the English language were identified. The details of the selection process are outlined in Figure 1. The demographic variables, clinical presentations, diagnostic modalities, treatment, outcomes, and complications of UAH were studied. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 20.0 (IBM Corporation, Armonk, NY, USA). A P value of <0.05 was considered to be statistically significant. Categorical variables were expressed as percentages and continuous variables as mean ± standard deviation (SD). Binomial logistic regression analysis was used to identify independent predictors of airway compromise and independent t-test was used to compare the means between the subgroups.

Results

Demographics and clinical presentation
Among the 38 cases of UAH identified, there was no significant gender variation (male vs female, 52.78% vs 47.22%, P = 0.446). The mean age of presentation was 60.11 ± 12.50 years. A majority of the hematomas were sublingual (n = 25, 66.57%) and retropharyngeal (n = 10, 27.03%), with supraglottic, laryngeal, lingual, and submandibular ones being less common [Table 1]. The most common predisposing factors noted were: Violent coughing (n = 6), drug interaction with warfarin (n = 3), airway manipulation during intubation (n = 2), trauma (n = 2), and denture use (n = 2). There were no apparent predisposing factors in the rest of the cases (n = 16, 43.24%). The most common presenting symptom associated with UAH were sore throat (n = 29, 78.38%), dysphagia (n = 24, 64.86%), and neck swelling (n = 22, 59.46%). Respiratory compromise was seen in 18 cases (46.65%). Other less common presenting features were as follows: ecchymosis (n = 14, 37.84%) hoarseness (n = 11, 29.73%), dysphonia (n = 9, 24.32%), and trismus (n = 3, 8.11%). There was no difference in the mean age (63.35 vs 56.50, P = 0.108), warfarin dose (4.31 mg vs 6.31mg, P = 0.119), time to resolution (6.71 days vs 8.60 days, P = 0.417), and international normalized ratio (INR) (8.95 vs 7.12, P = 0.357) between patients with and without respiratory compromise. On binomial logistic regression, there were no significant
Table 1: Demographic and clinical features of the included cases

| Author, year         | Age (years) | Sex | Concurrent antiplatelets/anticoagulants | Predisposing event                                              | Site of bleeding                  | Warfarin Dose (mg/d) | Indication                  | Respiratory compromise |
|----------------------|-------------|-----|----------------------------------------|------------------------------------------------------------------|-----------------------------------|----------------------|--------------------------|------------------------|
| Akoglu et al., 2008  | 48          | M   | No                                     | Massage of the neck and back 3 days ago                        | Retropharyngeal                   | ...                  | Mechanical aortic valve   | N                      |
| Bachmann et al., 1987| 67          | M   | No                                     | None                                                             | Sublingual                        | 2                    | DVT                      | Y                      |
| Bapat et al., 2001   | 53          | F   | No                                     | Blunt trauma to the head and shoulder 36 h ago                  | Retropharyngeal and mediastinal   | ...                  | Mechanical aortic valve   | Y                      |
| Berthelsen et al., 2012| 49        | M   | No                                     | None                                                             | Sublingual                        | ...                  | Prosthetic aortic valve   | N                      |
| Bloom et al., 2002   | 57          | M   | No                                     | None                                                             | Sublingual                        | 5                    | Paroxysmal AF             | Y                      |
| Boster et al., 1983  | 58          | F   | ...                                    | Submandibular, supraglottic                                      | Retropharyngeal                   | 7.5                  | DVT, TIA                 | Y                      |
| Brooks et al., 1981  | 65          | F   | No                                     | Bactrim-warfarin interaction                                     | Airway manipulation during intubation| 6                    | AF                       | N                      |
| Brown et al., 2002   | 81          | M   | Clopidogrel, aspirin, heparin           | None                                                             | ...                               | 2.5                  | CABG, CEA                | Y                      |
| Cashman et al., 2011 | 57          | F   | No                                     | None                                                             | Sublingual, supraglottic          | ...                  | AF                       | Y                      |
| Cohen et al., 1989   | 65          | F   | ...                                    | Sublingual, pharyngeal                                          | Sublingual                        | 3.75                 | DVT                      | Y                      |
| Cohen et al., 1989   | 63          | F   | Vigorous coughing for 4 days           | Sublingual, pharyngeal                                          | Sublingual                        | 7.5                  | CVA                      | Y                      |
| Duong et al., 1986   | 57          | M   | No                                     | None                                                             | Sublingual                        | ...                  | DVT                      | Y                      |
| Frohna et al., 2012  | 73          | F   | No                                     | None                                                             | Lingual and sublingual            | ...                  | Mechanical aortic valve, AF, H/O HIT | Y                      |
| Gonzalez-Garcia et al., 2005 | 60       | M   | No                                     | None                                                             | Sublingual                        | 7.5                  | DVT, Chronic AF           | Y                      |
| Goederet et al., 1980| 21          | F   | No                                     | None                                                             | Sublingual                        | ...                  | DVT                      | Y                      |
| Gupta et al., 2003   | 56          | F   | Alcohol and warfarin interaction       | Sublingual, pharyngeal, laryngeal                               | Epiglottic                        | 3.5                  | AF                       | N                      |
| Hatzakorzian et al., 2005| 75        | F   | ...                                    | Airway manipulation during intubation                            | Laryngeal (B/L aryepiglottic)     | ...                  | Mechanical mitral valve, paroxysmal AF | N                      |
| Jandreau et al., 1997| 69          | M   | H/O bronchitis 6 days ago               | Mandibular denture use                                          | Sublingual                        | 5                    | CABG                     | N                      |
| Kara et al., 2012    | 72          | F   | NSAIDs, antiplatelet agent (not specified) | Mandibular denture use                                          | Sublingual                        | 5                    | Mechanical mitral valve   | Y                      |
| Lee et al., 1980     | 41          | F   | No                                     | Vigorous coughing                                               | Sublingual                        | 7.5                  | Mechanical mitral valve   | Y                      |
| Lepore, 1976         | 58          | M   | No                                     | None                                                             | Sublingual, retropharyngeal       | 12.5                 | Chronic thrombophlebitis  | Y                      |

Continued
Table 1: Continued

| Author, year | Age (years) | Sex | Concurrent antiplatelets/anticoagulants | Predisposing event | Site of bleeding | Warfarin Dose (mg/d) | Warfarin Indication | Respiratory compromise |
|--------------|-------------|-----|----------------------------------------|-------------------|-----------------|---------------------|---------------------|----------------------|
| Lim et al., 2005 | 81          | M   | aspirin                                | None              | Sublingual, laryngeal | ...                | AF                  | Y                    |
| Moftah et al., 2012 | 71          | M   | No                                     | Cough and decreased absorption of vitamin K from diarrhea | Sublingual                | 3                   | AF                  | N                    |
| Murray et al., 1983 | 32          | M   | ...                                    | Phenylbutazone-warfarin interaction | Sublingual                | 6                   | DVT                 | Y                    |
| Moraes et al., 2013 | 54          | F   | No                                     | None              | Sublingual, pharyngeal | 5                   | AF                  | N                    |
| Owens et al., 1975 | 61          | M   | ...                                    | Violent sneezing and coughing | Retropharyngeal           | ...                 | PV                  | N                    |
| Parvizi et al., 2011 | 66          | M   | ...                                    | Violent coughing fit | Sublingual, supraglottic | ...                 | AF                  | N                    |
| Puri et al., 2012 | 73          | F   | ...                                    | Traumatic denture  | Sublingual                | 5                   | Mechanical mitral and aortic valve | Impending |
| Reussi et al., 1968 | 62          | ... | ...                                    | ...               | Retropharyngeal           | ...                 | Thrombophlebitis migrans | Y                    |
| Rosenbaum et al., 1979 | 53          | M   | No                                     | None              | Sublingual, submaxillary | ...                 | Prosthetic mitral valve | Y                    |
| Rosenbaum et al., 1979 | 52          | M   | No                                     | None              | Submaxillary, sublingual | ...                 | Prosthetic aortic valve | Y                    |
| Rosenbaum et al., 1979 | 71          | M   | No                                     | None              | Sublingual and retropharyngeal | ...                 | CABG, prosthetic aortic valve | N                    |
| Thatcher et al., 1987 | 56          | F   | No                                     | Jolt of the neck  | Retropharyngeal           | ...                 | Acute PE/DVT        | Y                    |
| Yaman et al., 2011 | 72          | M   | ...                                    | None              | Sublingual, laryngeal    | ...                 | CVA                 | N                    |
| Yaman et al., 2011 | 55          | F   | No                                     | None              | Supraglottic              | ...                 | Mechanical mitral valve | N                    |
| Buyuklu et al., 2014 | 70          | F   | ...                                    | None              | Lingual, sublingual      | ...                 | AF                  | N                    |
| Pathak et al., 2014 | 50          | F   | No                                     | None              | Sublingual                | ...                 | Acute PE/DVT        | N                    |
| Vaghasia et al., 2014 | 87          | F   | Warfarin                               | None              | Sublingual                | ...                 | SVC thrombosis      | Y                    |

AF = Atrial fibrillation, CABG = Coronary artery bypass grafting, CVA = Cerebrovascular accident, CEA = Carcinoembryonic antigen, DVT = Deep vein thrombosis, HIT = Heparin-induced thrombocytopenia, SVC = Superior vena cava, TIA = Transient ischemic attack

predictors of respiratory compromise (age, $P = 0.112$; INR, $P = 0.396$).

Warfarin dose and indications

The mean dose of warfarin taken by the patients was $5.34 \pm 2.58$ mg. The indications for warfarin were as follows: Mechanical valves (MVs) ($n = 11$, 29.73%),[2,4-11] atrial fibrillation (AF) ($n = 10$, 27.03%),[3,12-28] venous thromboembolism (VTE) ($n = 9$, 24.32%),[1,21-28] chronic thrombophlebitis ($n = 2$, 5.41%),[29,30] and polycythemia vera ($n = 1$, 2.70%).[31] The indication of anticoagulation was unclear in four cases.[8,22,32,33] Three cases received concomitant antiplatelet therapy.[16,32,33] [Table 2].

Laboratory parameters

The laboratory values at the time of presentation were: INR 8.07 $\pm$ 4.04, hemoglobin (Hb) 12.35 $\pm$ 2.04 g/dL, and platelets were within the normal range except for one case where thrombocytosis was noted.[31]

Treatment and prognosis

Conservative management with vitamin K, fresh frozen plasma (FFP), or prothrombin complex concentrate
Table 2: Laboratory parameters, management, and outcomes of the included cases

| Author, year | INR | PTT | Hb  | Plt | Medical therapy                                    | Airway treatment                  | Outcome |
|--------------|-----|-----|-----|-----|---------------------------------------------------|-----------------------------------|---------|
| Akoglu et al., 2008 | 5.9 | …   | 10.4|     | Vitamin K, FFP, blood transfusion, prophylactic antibiotics | Conservative                      | Resolution of hematoma within 2 weeks |
| Bachmann et al., 1987 | …   | 120 | …   |     | FFP, SQ heparin                                     | Cricothyroidotomy, tracheostomy   | Pulmonary edema on relief of airway obstruction, resolution of hematoma |
| Bapat et al., 2001 | 6.9 | …   | …   |     | FFP                                              | Endotracheal intubation, tracheostomy, surgical evacuation of hematoma | Complete recovery |
| Berthelsen et al., 2012 | 10  | …   | …   |     | Vitamin K                                          | Endotracheal intubation            | Resolution of hematoma after 4 days |
| Bloom et al., 2002 | 5.4 | 110 | 11  | 275,000| Vitamin K, FFP, clindamycin, Decadron, blood transfusion | Conservative                      | Resolution of hematoma within 6 days |
| Boster et al., 1983 | …   | 127 | 13.5| Normal| Vitamin K, FFP                                     | Tracheostomy                      | Resolution of hematoma in 5 days, warfarin stopped and aspirin started |
| Brooks et al., 1981 | …   | 180 | 10  | 285,000| Vitamin K, FFP                                    | Conservative                      | Resolution of hematoma within 5 days |
| Brown et al., 2002 | 1.7 | …   | …   |     | …                                                | Tracheostomy                      | Resolution of hematoma within 10 days |
| Cashman et al., 2011 | 9   | …   | 13.5| Normal| Vitamin K, FFP, SQ heparin                        | Conservative                      | Resolution of hematoma |
| Cohen et al., 1989 | …   | 120 | 14  | 302,000| Vitamin K                                          | Tracheostomy                      | Aspiration pneumonia, resolution of hematoma after 9 days, aspirin and dipyridamole given for 5 days mo followed by warfarin 2.5 mg on alternate days |
| Cohen et al., 1989 | …   | …   | 12.3| …    | Penicillin, hydrocortisone, vitamin K, FFP        | Endotracheal intubation            | Resolution of hematoma, warfarin stopped, aspirin started |
| Duong et al., 1986 | …   | 150 | …   | …    | Vitamin K, FFP, SQ heparin                        | Cricothyroidotomy, tracheostomy   | Mild pneumonitis, resolution of hematoma |
| Frohna et al., 2012 | 4   | …   | …   | …    | Vitamin K, FFP                                    | Nasotracheal intubation, tracheostomy on the 5th day | Resolution of hematoma by day 14 |
| Gonzalez-Garcia et al., 2005 | 8   | 120 | 6.2 | …    | FFP                                              | Endotracheal intubation, tracheostomy on the 3rd day | Resolution of hematoma after day 5 |
| Goorder et al., 1980 | …   | …   | 14.2| Normal| Vitamin K, prothrombin complex                   | Tracheostomy                      | Resolution of hematoma, warfarin stopped, aspirin started |
| Gupta et al., 2003 | 10  | …   | 12.5| …    | Vitamin K                                         | Conservative                      | Resolution of hematoma in 2 days |
| Hatzakorzian et al., 2005 | Normal | … | 13.5| Normal | Dexamethasone                                    | Conservative                      | Resolution of hematoma within 4 days |
| Jandreau et al., 1997 | 9   | 76.5| 11.3| 336,000| Cefuroxime, dexamethasone, heparin | Conservative                      | Resolution of hematoma |

Continued
### Table 2: Continued

| Author, year | INR | PTT | Hb | Plt | Medical therapy | Airway treatment | Outcome |
|--------------|-----|-----|----|-----|-----------------|------------------|---------|
| Lee et al., 1980 | ... | 144 | ... | ... | Vitamin K, FFP | Conservative | Resolution of hematoma within 6 days |
| Lepore, 1976 | ... | 106 | ... | ... | FFP, vitamin K, hydrocortisone, ampicillin | Nasotracheal intubation using bronchoscope | Resolution of hematoma within 6 days |
| Lim et al., 2005 | 10 | ... | ... | ... | Prothrombin complex, vitamin K | Nasotracheal intubation | Resolution of hematoma within 24 h, warfarin stopped |
| Moftah et al., 2012 | 6.6 | ... | ... | ... | Vitamin K, hydrocortisone | Conservative | Resolution of hematoma, warfarin stopped, aspirin started |
| Murray et al., 1983 | ... | 126 | 10.2 | ... | ... | Tracheostomy | ... |
| Moraes et al., 2013 | 5.5 | ... | 13.3 | 120,000 | Vitamin K, FFP | Conservative | Resolution of hematoma after 3 days, warfarin stopped and aspirin started |
| Owens et al., 1975 | ... | ... | ... | Thrombocytosis | Vitamin K | Tracheostomy | Evacuation of hematoma after 2 weeks, duodenal ulcer bleeding requiring antrectomy and vagotomy |
| Parvizi et al., 2011 | 7.6 | ... | 15 | ... | Vitamin K, prothrombin complex, dexamethasone, epinephrine nebulizer | Conservative | Resolution of hematoma in 4 days |
| Puri et al., 2012 | 5.5 | ... | ... | ... | Prothrombin complex, vitamin K, hydrocortisone | Nasotracheal intubation, surgical decompression of hematoma | Resolution of hematoma |
| Reussi et al., 1968 | ... | ... | ... | ... | Vitamin K | ... | Resolution of hematoma within 20 days |
| Rosenbaum et al., 1979 | ... | ... | ... | ... | Vitamin K | Tracheostomy | Death due to anoxic brain injury |
| Rosenbaum et al., 1979 | ... | ... | ... | ... | Vitamin K, prothrombin complex | Conservative | Resolution of hematoma within 10 days, warfarin continued |
| Rosenbaum et al., 1979 | ... | 89 | ... | ... | Vitamin K, FFP | Conservative | Resolution of hematoma, aspirin, and dipyridamole given for 3 weeks followed by warfarin |
| Thatcher et al., 1987 | ... | ... | 11.7 | 549,000 | Vitamin K, FFP | Intubation | Resolution of hematoma within 2 wk |
| Yaman et al., 2011 | 15.5 | ... | 13.6 | 235,000 | Vitamin K, FFP, methylprednisolone, cefazolin | Conservative | Resolution of hematoma within 7 days, started LMWH |
| Yaman et al., 2011 | 4.5 | ... | 12.6 | 290,000 | Vitamin K, methylprednisolone | Conservative | Resolution of hematoma within 3 days, warfarin restarted after 7 days |
| Buyuklu et al., 2014 | 19 | ... | 13 | ... | Vitamin K, FFP | Conservative | Resolution of hematoma within 3 days |
| Pathak et al., 2014 | 5.2 | ... | 14.5 | 269,000 | Vitamin K | Conservative | Resolution of hematoma within 3 days, and warfarin restarted after 4 days |
| Vaghasia et al., 2014 | 8 | ... | ... | ... | Vitamin K, FFP | Nasotracheal intubation | Resolution of hematoma |

FPP = Fresh frozen plasma, Hb = Hemoglobin, Plt = Platelets, PTT = Partial thromboplastin time, SQ = Subcutaneous
Clinical features and diagnosis

UAH may be preceded by predisposing factors such as violent coughing and trauma or it may be spontaneous (43.24% of cases in our study). Sore throat, dysphagia, and neck swelling are the most common presenting symptoms of UAH, which were consistent with our study. These are nonspecific findings that may be associated with many common clinical syndromes such as acute respiratory tract infections. Additionally, since our study did not find any difference in age, INR, or dose of warfarin between patients with and without respiratory compromise, a high level of suspicion is required for diagnosis at an earlier stage. This may be one of the reasons why more than half of the patients have respiratory compromise at presentation. Unlike what has been reported previously, our study found that sublingual space (66.57%) was most commonly involved followed by retropharyngeal space (27.03%). Differentiation from acute infectious process such as Ludwig’s angina or retropharyngeal abscess is crucial as they are managed quite differently.

Discussion

Background

In spite of the increasing popularity of the newer anticoagulants, warfarin remains the most commonly prescribed oral anticoagulant in the United States with >25 million warfarin prescriptions in the United States in 2010.[34] Warfarin acts as a vitamin K antagonist by binding with the vitamin K 2, 3-epoxide reductase in the hepatic microsome and blocking the action of vitamin K-dependent factors II, VII, IX, X, protein C, and protein S. It is commonly used for chronic anticoagulation in patients with atrial fibrillation (AF), venous thromboembolism (VTE), and artificial heart valves. Warfarin levels are monitored with regular INR with a target of 2 to 3 in AF and VTE and 2.5 to 3.5 in patients with mechanical heart valves. Interaction with commonly used medications including broad spectrum antibiotics, quinidine, salicylate, and thyroxine as well as with alcohol and diet often make anticoagulation with warfarin challenging.[3] The concurrent usage of platelet inhibiting agents such as aspirin and nonsteroidal anti-inflammatories further increases the risk of bleeding.[3] The risk of bleeding, internal or external, is related to INR in a log linear fashion[3] and is known to be higher with INR levels >4.5,[4] which is consistent with the mean INR of 8 in our study. The incidence of bleeding in patients on warfarin is about 6.8%.[3] Upper airway hematoma is a rare complication. Sublingual, retropharyngeal, submaxillary, and epiglottic hematomas or bleeding have been described. It is important to recognize these early as they can lead to life-threatening complications such as airway compromise.

Management

No definite consensus to treatment exists in the literature. While Hefer et al.[35] reported similar outcomes among all patients with retropharyngeal hematoma up to 1993 with observation versus aggressive early airway management, Cohen and Warman[22] support early tracheotomy in all patients, with observation limited to only mild cases. Similarly, Rosenbaum[11] recommends close intensive care unit (ICU) monitoring. The data of our review was in line with Hefer et al.[35] in that the outcomes (time to resolution) did not differ in the conservative and aggressive approach. Moreover, advanced age and higher INR failed to predict the likelihood of respiratory compromise. Hence, in mild cases with no airway compromise, our study favors medical therapy with reversal of the coagulopathy with vitamin K and FFP or PCC preferably in an ICU setting.[1,12,13] The recommended dose of FFP and PCC is 4 units/kg with INR greater than 1.5 and 50 units/kg with INR greater than 6, respectively.[13] Although surgical drainage has been described,[36] it is not warranted in most cases as it carries the risk of increasing soft tissue edema and airway compromise.[37] Spontaneous resolution usually occurs with normalization of coagulation parameters.[1]
Patients with severe airway compromise should be considered a medical emergency and endotracheal intubation may be indicated as life-threatening hemorrhage can occur into the sublingual space rapidly. Patients should be evaluated by an otolaryngologist (or any other physician capable managing and evaluating a critical airway including performing a flexible laryngoscopy) and those with impending airway obstruction should be managed by a team of experienced anesthesiologists and otolaryngologists. The preferred management should be fiber-optically-guided nasotracheal intubation; cricothyrotomy or awake tracheotomy should be done only in cases where intubation is not possible and orotracheal intubation contraindicated as mask ventilation may be impossible.

Propylactic antibiotics were used in six cases; however, they are not usually indicated as abscess formation does not occur. Although steroids were used in 10 cases, there was no definitive evidence of benefit. The patient may be restarted on warfarin with regular monitoring of INR once the hematoma resolves, provided that he/she is able to maintain an optimum level of INR. None of the reported cases had INR in the desired range; hence, it is unlikely that UAH occurs with a normal INR.

Limitations of the study
Our study had several limitations. This is a retrospective series of reported cases in the current literature and has inherent biases related to such studies including selection and publication biases. Also, we included only articles available in the English language. Due to the small sample size, statistical analysis was limited. Asymptomatic cases of UAH are unlikely to be recognized; hence, the reported cases may not represent the overall patient population with UAH.

Conclusion
UAH is a rare but potentially serious complication of warfarin therapy, which should be differentiated from the more common infectious etiologies. It is more common in the elderly population with supratherapeutic INR and some inciting event present in many cases. Overall, it has a good prognosis with significant morbidity present only if concomitant respiratory compromise is present. Only mild cases should be observed, preferably in an ICU setting and conservative management is possible in these patients but no patient characteristics predict airway compromise or successful conservative management. Reversal of anticoagulation with low threshold for artificial airway placement in the event of airway compromise is the treatment of choice.

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Conflicts of interest
There are no conflicts of interest.

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