Meta-Analysis Article

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 butpotentially 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

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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

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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.

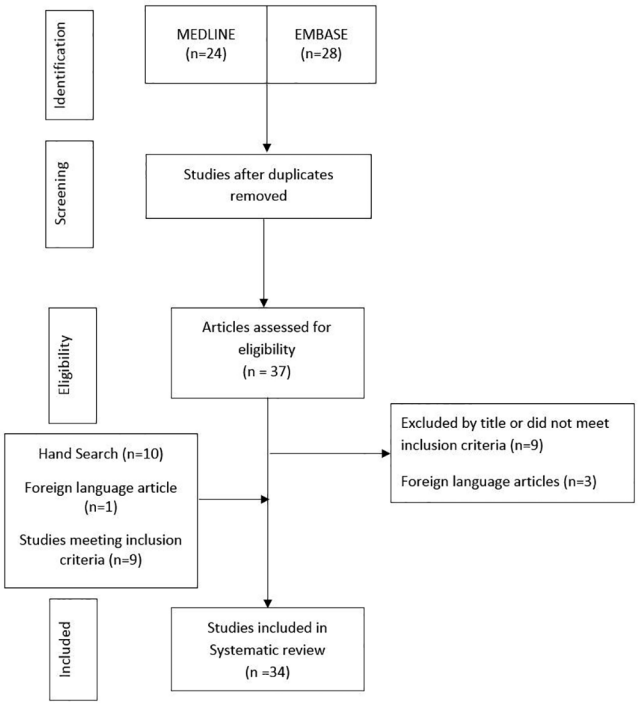

Figure 1: Flowchart describing a systematic search and study selection process

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 we 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%), bleeding from another site (*n* = 9, 24.32%), drooling (*n* = 5, 13.51%), 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 (6.71days 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		Respiratory compromise
						Dose (mg/d)	Indication	
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	…	Retropharyngeal	5	Paroxysmal AF	
Boster*et al.*, 1983	58	F	…	…	Submandibular, supraglottic	7.5	DVT, TIA	Y
Brooks *et al.*, 1981	65	F	No	Bactrim-warfarin interaction	Retropharyngeal	6	AF	N
Brown *et al.*, 2002	81	M	Clopidogrel, aspirin, heparin	Airway manipulation during intubation	Retropharyngeal, epiglottic	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	3.75	DVT	Y
Cohen *et al.*, 1989	63	F	…	Vigorous coughing for 4 days	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	
Gonzalez-Garcia *et al.*, 2005	60	M	No	None	Sublingual	7.5	DVT, Chronic AF	Y
Gooder*et al.*, 1980	21	F	No	None	Sublingual	…	DVT	Y
Gupta *et al.*, 2003	56	F	No	Alcohol and warfarin interaction	Sublingual, pharyngeal, laryngeal	2	AF	N
Hatzakorzian *et al.*, 2005	75	F	…	Airway manipulation during intubation	Epiglottic	3.5	AF	N
Jandreau *et al.*, 1997	69	M	…	H/o bronchitis 6 days ago	Laryngeal (B/L aryepiglottic)	…	Mechanical mitral valve, paroxysmal AF	N
Kara *et al.*, 2012	72	F	NSAIDs, antiplatelet agent (not specified)	Mandibular denture use	Sublingual	5	CABG	N
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		Respiratory compromise
						Dose (mg/d)	Indication	
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 ± 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%),[3,12-20] 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 ± 4.04, hemoglobin (Hb) 12.35 ± 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
Gooder *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

(PCC) was instituted in 18 (48.65%)[2,3,6,8,9,11-15,17-20,27,32] cases [Table 2]. Cricothyrotomy was performed in two (5.41%) cases,[21,23] tracheotomy in 12 (32.43%) cases,[1,4,5,11,21-26,31,33] endotracheal intubation in five (13.51%) cases,[1,4,10,22,28] nasotracheal intubation in four (10.81%) cases,[5,7,16,29] and surgical evacuation of hematoma in two (5.41%) cases.[4,7]

Most of the cases had a good outcome with the mean duration to resolution being 7.69 ± 5.44 days. The complications included respiratory compromise in 18 cases (48.65%), pulmonary edema,[21] aspiration pneumonia,[22] and mild pneumonitis[23] in one case each. One patient died due to anoxic brain injury.[11]There was no significant difference between the mean age (58.94 vs 61.17, $P = 0.607$), warfarin dose (6.03 mg vs 4.67 mg, $P = 0.282$), time to resolution (8.20 vs 6.53, $P = 0.412$), and INR (6.59 vs 8.86, $P = 0.194$) between the patients undergoing conservative and nonconservative management. Similarly, there was no significant correlation between time to resolution and age (Pearson's $r = 0.044$, $P = 0.832$) or INR (Pearson's $r = -0.427$, $P = 0.113$).

Most cases did not mention whether warfarin was restarted or not during the follow-up period. It was switched to aspirin in five cases[17,18,22,24,26] and restarted immediately after resolution of the symptoms in three cases;[8,11,27] however, the dose at which it was restarted was not clear.

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.[3,31] 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.

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,[23] 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.

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.[1,13,18] 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.[1] 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.[11]

Prophylactic antibiotics were used in six cases; however, they are not usually indicated as abscess formation does not occur.[1]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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