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Keep an Eye and an Airway on New Oral Anticoagulants- Spontaneous Retropharyngeal Hematoma in a Patient with Chronic Renal Failure

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Authors' contributions

This work was carried out in collaboration between all authors. Author AK performed the literature review and wrote the initial draft of the manuscript. Author AYW reviewed and updated the draft manuscript. Author GPR reviewed, edited and approved the manuscript for publication. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Spontaneous retropharyngeal hemorrhage can be rapidly fatal, potentially leading to airway obstruction and significant blood loss if not identified and managed promptly. We report a unique case of patient with chronic renal failure presenting with spontaneous retropharyngeal hemorrhage on a new agent anticoagulant as well as providing a current review of the literature. This case aims to increase awareness of this potentially fatal condition. We question the commonly held view by clinicians that minimal monitoring and reduced risk of hemorrhage is a key advantage of new oral agent anticoagulants.

Keywords: Retropharyngeal space; haemorrhage; hematoma; oral anticoagulant; rivaroxaban.

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1. INTRODUCTION

Oral anticoagulation is widely used and bleeding is the most common complication. The usage of new oral agent anticoagulants (NOAC) has been rising in Australia since they were listed on the Pharmaceutical Benefits Scheme. We describe a unique case of spontaneous retropharyngeal hemorrhage (SPRH) in a patient on NOAC with chronic renal failure. Literature pertaining to SPRH is solely based on case reports and it has been described too infrequently to determine its incidence. Whilst the retropharyngeal space is an uncommon bleeding site, it is clinically important as it can lead to life threatening upper airway obstruction. We highlight the need for monitoring patients on NOACs, review the existing literature and discuss management of SPRH.

2. CASE REPORT

89 year old male presented with oropharyngeal discomfort, dysphonia and dysphagia to both solids and liquids that developed acutely over a 4 hour period. Medical history included atrial fibrillation, chronic renal failure (baseline glomerular filtration rate 30), right heart failure, gout and hypertension. The patient was commenced on 15mg of rivaroxaban after an episode of atrial fibrillation 9 months ago. Other medications included bisoprolol, ramipril, frusemide, nitro-glycerine patch and allopurinol. Patient denied any neurological symptoms, gastrointestinal symptoms, trauma, foreign body ingestion, recent procedures or previous bleeding episodes.

The patient was afebrile, with respiratory rate 15−18, oxygen saturation > 98% on room air, heart rate 70 (irregular) and blood pressure 120/80 mm Hg. The patient had a hoarse voice and anterior neck bruising extending from thyroid cartilage to suprasternal notch and sternum (Fig. 1). Oral examination revealed sub-mucosal bruising of the oropharynx (Fig. 2). Nasopharyngoscopy revealed that the submucosal bruising extended from oropharynx to the retropharyngeal wall and involved the piriform fossa bilaterally (Fig. 3). The airway was narrowed but patent.

Laboratory studies revealed mild thrombocytopenia with normal hemoglobin and white cell count. Creatinine was 173 (baseline 160, 10 months ago), estimated glomerular filtration rate 30 (calculated 15) and international normalized ratio 1.1. Computed tomography (CT) angiogram of the neck demonstrated retropharyngeal hematoma measuring 51 ×25 × 48 mm and extending from second to the fifth cervical spine (Fig. 4).

Fig. 1. Bruising of skin over the anterior neck extending from thyroid cartilage to suprasternal notch and sternum

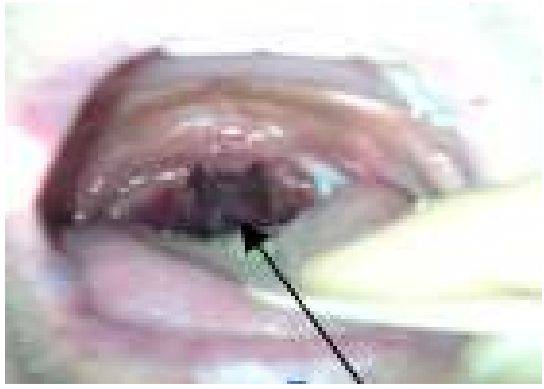

Fig. 2. Oral examination indicating submucosal bruising of oropharynx

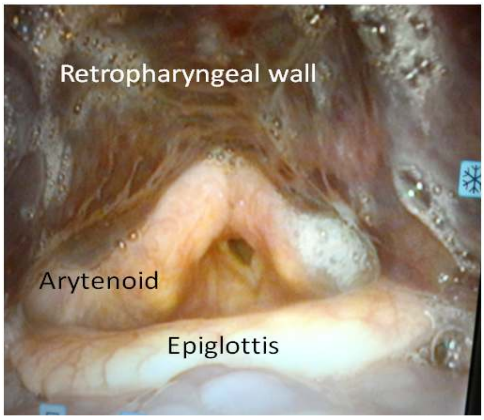

Fig. 3. Nasopharyngscopy: submucosal bruising & swelling of lateral/posterior pharyngeal wall

Fig. 4a.

Fig. 4b.

Fig. 4. CT angiogram of neck in sagittal plane (a) axial plane (b) demonstrating hematoma in retropharyngeal space compressing trachea & oesophagus

SPRH was diagnosed based on clinical and radiological findings. Reduced renal clearance of rivaroxaban due to impaired renal function and nephrotoxic drugs (allopurinol) resulted in increased rivoraxban's therapeutic efficacy and contributed to SPRH.

Intra-venous cefazolin and analgesia were commenced and rivaroxaban was withheld. Pre & post-contrast hydration (1ml/kg/hr) and N-acetyl cysteine was administered to limit the nephrotoxic impact of the contrast. Patient made an uneventful recovery and both voice and swallowing returned to normal. He was discharged 3 days after the initial presentation. The patient was advised to follow up with general practitioner and renal physician to commence on an alternative anticoagulant.

3. DISCUSSION

Retropharangeal space lies between the prevertebral fascia and the posterior wall of the pharynx. SPRH is collection of blood in the retropharangeal space in absence of any clear aetiology. A systemic review in 2015 identified 9 cases of retropharyngeal hematoma in patients on warfarin [1]. There has been no systemic review on *spontaneous* retropharyngeal hematoma and its incidence is not known. Thirty-five articles were found on a thorough search on PubMed for spontaneous retropharyngeal hematoma. 5 of these patients were on anticoagulants and are summarized in the following table (Table 1).

Table 1. Case reports of SPRH in association with anticoagulant

Reference	Precipitating factor	Presenting symptom	Intervention
Al-Fallouji et al. [2]	Case1- Aspirin Case 2 - nil	Case 1 strange neck sensation, dysphagia, dysphonia Case 2 dysphagia,dysphonia	Conservative monitoring
Bloom et al. [3]	Warfarin	Dysphagia, odynophagia	Fresh frozen plasma Vitamin K
Ditkofsky et al. [4]	Warfarin	Throat swelling, difficulty breathing	Fresh frozen plasma
Owens et al. [5]	Warfarin + Violent tussive episode	Dysphagia, sore throat	Tracheostomy, hematoma drainage, Vitamin K
Sinert et al. [6]	Warfarin	Dysphagia, sore throat	Fresh frozen plasma Vitamin K

We were unable to find any previous reports on SPRH in a patient on NOAC with chronic renal failure. SPRH presents with Capp's triad - clinical and imaging findings of tracheal/oesophageal compression, tracheal displacement and bruising over neck and anterior chest [7]. The insertion of pharyngeal muscles that form the boundary of retropharyngeal space can be displaced towards their origin as a result of hemorrhage and can lead to fatal airway obstruction. Retropharyngeal hemorrhage has a reported mortality of up to 20% [8]. CT or magnetic resonance imaging (MRI) can be used to diagnose SPRH. Muñoza et al. [9] emphasize that SPRH can be difficult to diagnose with CT and MRI should be considered to better delineate acute and subacute blood collection.

The patho-physiology of SPRH is not well defined. It has been hypothesised that arteriosclerosis of the small vessels in the retropharangeal space makes them prone to rupture. NOAC selectively inhibit coagulation factors and inhibit clot formation. Most cases of SPRH are thought to be due to bleeding from vessels covering the anterior longitudinal ligament and thyrocervical trunk.

There is no universally agreed guideline on the management of retropharyngeal hemorrhage and the choice between observation, intubation or surgical airway is based on individual clinician preference. Bloom et al. [3] state that airway should be secured when patient develops signs of airway obstruction. This is supported by Duvillard et al. [10] who suggest that medical treatment and close observation are usually sufficient unless there is worsening of dysphagia or dyspnoea. Gurr and Wallis [11] questioned this approach and argued that it is prudent to secure the airway before signs of obstruction occur in order to reduce the complications and the need for drastic measures.

NOACS have different mechanism of action when compared with Warfarin. They are given in fixed doses and do not require routine monitoring. Cardiologists do not monitor patients on NOAC unless there are complicating factors and surveillance with regard to adherence, side effects and complications is left for general practitioners and community pharmacists. Reduced need for monitoring and application of fixed dose is highlighted as a key benefit of NOAC's to general practitioners and community pharmacists leading to patients not being monitored. SPRH in this patient could have been prevented if the NOAC dose was monitored and reduced based on reduction in patient's renal function. Monitoring patients on NOAC is critical as it can lead to conditions like SPRH that develop rapidly, are difficult to diagnose and lead to fatal airway obstruction. Garcia, Barett, Ramacciotti and Weitz summarize the indications for NOAC monitoring [12]. These include monitoring patient adherence, poly-pharmacy, determining bleeding risk (based on body weight, renal function and hepatic impairment), detecting overdose and identifying the mechanism of bleeding. Patient on NOAC have multiple co-morbidities, use multiple prescription medications and are falls risk. As highlighted in Table 1, previous cases of retropharyngeal hemorrhage were managed by reversing the anticoagulation. NOACS do not have an antidote. This makes it critical that patients on NOACs are appropriately educated and carefully monitored to prevent any complications.

NOACs like rivaroxaban have a wide therapeutic index and less intra-subject variability, however, they can cause a wide spectrum of hemorrhagic complications - including rare presentations including bowel hematoma [6] and pulmonary hemorrhage [13]. Kubitza et al. [14] reported that rivaroxaban clearance was reduced with increasing renal impairment, leading to increased plasma exposure and pharmacodynamic effects . Patients on rivaroxaban may be on multiple medications and have renal impairment making titration of drug dosage based on renal function is paramount.

4. CONCLUSION

NOAC use can lead to bleeding complication that can be minor or rapidly fatal. Presence of other medical co-morbidities, renal or cardiac impairment, drug interactions from polypharmacy and risk of bleeding needs to be considered before prescribing anticoagulation therapy. General Practitioners and Pharmacists should evaluate these factors whenever they provide a repeat prescription and dispense a NOAC.

CONSENT

As per international standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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