CASE REPORT

Rivaroxaban and retropharyngeal haemorrhage

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SUMMARY

Haemorrhage is a well-known and accepted complication of anticoagulation. A retropharyngeal haemorrhage (RH) is a rare condition that without prompt recognition and management may result in fatal complications. We report a case of RH in a 67-year-old man anticoagulated with rivaroxaban for atrial fibrillation. The patient presented to the emergency department, with a two-day history of atraumatic right-sided neck swelling and associated progressive odynophagia, dysphagia and dysphonia. Rivaroxaban is a potent new oral anticoagulant that has been approved for use by National Institute for Health and Care Excellence (NICE) but still has no approved reversal agent. Despite its rarity, an RH is a potentially life threatening complication of anticoagulation that must be carefully considered. This is especially true for a drug that cannot be easily reversed. We present a discussion of this case presentation with possible differential diagnoses and a review of the literature, and recommend the use of Capp's triad as a diagnostic criterion.

BACKGROUND

A retropharyngeal haemorrhage (RH) is a rare condition that without prompt recognition and management may result in fatal complications. Owing to the nature of the condition and the close proximity of overlying structures, complications can involve upper airway obstruction and progressive blood loss¹—depending on severity, these may require immediate surgical intervention.

As this is a rare condition for which immediate management may be necessary, a quick and easy screening tool would be extremely useful. The Capp triad, a screening tool for RH, is not widely known. In order to improve recognition of this life threatening condition, knowledge of Capp's triad is a useful learning point.

CASE PRESENTATION

A 67-year-old man presented to the emergency department (ED), with a 2-day history of neck swelling with odynophagia, dysphagia and mild dysphonia. He had no signs of airway compromise or stridor. He had no history of trauma, foreign body impaction or vomiting, and had not undergone any significant strain. He was non-feverish and appeared systemically well.

On inspection, he had fullness in his neck with maximal swelling and tenderness on the right side inferior to the submandibular region, and a small area of bruising over his thyroid cartilage² (figures 1–3). Examination of his oropharynx was normal.

He had a history of glaucoma, and an extensive cardiac history. This included ischaemic heart

Figure 1 Right lateral view of the neck.

disease with stenting in 2001, impaired left ventricular function, dilated cardiomyopathy and atrial fibrillation (AF) with a permanent pacemaker. Eight days prior to presentation, he had been reviewed by a consultant cardiologist who switched him from warfarin to rivaroxaban (international normalised ratio (INR) 1.1 prior to switch).

He was a non-smoker and did not consume alcohol, and he had no significant family history.

INVESTIGATIONS

Blood tests were completed and showed a C reactive protein (CRP) of 10 mg/L and white cell count (WCC) of $10.2 \times 10^9/L$, making a diagnosis of a large deep neck abscess unlikely. Haemoglobin was 140 g/L and platelet count $207 \times 10^9/L$. Bone profile, magnesium and liver function were all normal. A coagulation profile was not completed on admission and was only considered once haemorrhage was suggested by CT. At this point, the patient was due for transfer to another hospital and, unfortunately, the coagulation profile was not

Figure 2 Midline view of the neck.

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Figure 3 Left lateral view of the neck.

completed until the following day. When completed, the profile results were normal.

Plain chest X-ray showed a widened mediastinum; however, the significance of this was only noted retrospectively (figure 4).

Flexible laryngoscopy showed a right lateral posterior pharyngeal wall haemorrhage and swelling (figure 5).

Urgent CT of the neck and chest showed extensive swelling, which extended from the retropharyngeal space to the diaphragm involving the danger space, with features consistent with haemorrhage (figure 6). Bleeding is thought to have originated from his right inferior thyroid artery.

A fine needle aspiration showed evidence of a simple haematoma, confirming the differential from CT.

DIFFERENTIAL DIAGNOSIS

After initial examination, one of the differential diagnoses was of a deep neck abscess, and, as such, the patient was treated with intravenous antibiotics and steroids, and booked for an urgent CT of the neck. After reviewing blood results along with the clinical picture, our differential of abscess did not fit; the

Figure 5 Image of the larynx obtained from flexible laryngoscopy.

patient's CRP and WCC were normal, he appeared clinically well and was non-feverish.

The area of ecchymosis spread anteriorly over his thyroid cartilage and the diagnosis was changed to haemorrhage secondary to rivaroxaban use. Diagnosis was supported by the results of an urgent CT of the neck and chest—showing features consistent with haemorrhage. Ear, nose and throat department in a tertiary centre with a cardiothoracic surgery unit was contacted and the patient was accepted for transfer.

Diagnosis of a retropharyngeal haematoma was finally confirmed on fine needle aspiration.

TREATMENT

The patient was managed conservatively with intravenous augmentin, intravenous dexamethasone, analgesia and intravenous fluids. His rivaroxaban was stopped on admission and, after consultation with the patient and cardiology specialists over

Figure 4 Chest X-ray.

Figure 6 CT of the laryngeal swelling.

risks versus benefits of further anticoagulation, he was prescribed enoxaparin 1 mg/kg once daily subcutaneously. It was felt that as the bleeding had stopped spontaneously, the risk of further bleeding was less than the risk of further cardiac compromise or stroke secondary to AF. Therefore continued anticoagulation was appropriate.

A number of factors affected the decision to continue with conservative treatment. The patient appeared clinically well, he had no respiratory compromise, the bleeding had stopped spontaneously and the haematoma was not infected. If any of these conditions were different, treatment may have required prompt airway management ± surgical intervention.

Our patient was followed up as an outpatient to ensure resolution of symptoms. On discharge, he continued to take enoxaparin, and was urgently referred back to his cardiologist to further review the risks versus benefits and options for ongoing anticoagulation. This resulted in him being restarted back on warfarin, with a target INR of 2.0–2.5. Warfarin was chosen because of the ability to easily monitor its effect in the community, using INR testing, and due to the ability to pharmacologically reverse its effect in an emergency, with vitamin K and prothrombin complex concentrate (unlike rivaroxaban).² The decision was also influenced by the fact that the patient had previously been on the drug for a number of years without complication, and was keen to continue taking it.

OUTCOME AND FOLLOW-UP

The patient showed significant improvement with conservative management and was discharged home 4 days after admission.

Two days following discharge he re-presented to ED with mild non-specific chest pain and had a repeat CT of the chest and neck. This showed significant reduction of haematoma and small bilateral pleural effusions. He was reassured and discharged home the following day.

At a clinic review (11 days after initial presentation), he showed significant clinical improvement, in keeping with radiological findings.

DISCUSSION

The insidious nature of onset and the rarity of the condition combine to make diagnosis of RH extremely difficult.

A PubMed literature search was undertaken with the terms 'spontaneous' and 'haemorrhage' and 'pharyngeal' as the search criteria. This resulted in 82 papers, which were included or discarded after abstract review. In total, there have been 33 reported cases of RH between 1975 and 2015. Of these cases, 7 were due to anticoagulation with warfarin, 4 due to intra-thyroid or parathyroid bleeding, 3 due to trauma and 7 were due to 'other'; 12 were deemed spontaneous. The 'other' column consisted of aortic dissection, Epstein-Barr infection, haemodialysis, hypertension, polycythaemia rubra vera, haemophilia and thorium dioxide poisoning.

None of the 33 reported cases over the last 40 years have been due to use of rivaroxaban or any of the new oral anticoagulants (NOACs). This case aims to highlight the dangers of anticoagulant use, and the potentially fatal consequences of neck-space haemorrhage.

Owing to the rarity of the condition, diagnosis is likely to be missed or delayed—resulting in a substantial increase in morbidity and mortality. Capp's triad is a useful screening tool that can be used for the classical manifestations of spontaneous RH and all cervicomedistinal haematomas. It consists of superior tracheal and oesophageal obstruction, anterior tracheal displacement and neck bruising.³ In the case discussed above, all three criteria were fulfilled: dysphagia and hoarseness, tracheal displacement, demonstrated on CT and anterior neck ecchymosis.

Retropharyngeal swellings are particularly serious due to the nature of the anatomy of the deep cervical fascial planes. The retropharyngeal space is bound anteriorly by the middle layer of the deep cervical fascia and posteriorly by the alar layer of the prevertebral cervical fascia, and is situated behind the hypopharynx and oesophagus.⁴ The pharyngeal muscles have insertions that move towards their origins, and offer no resistance to expansion of a haematoma. As the haematoma expands it can compress the hypopharynx and cause life threatening upper airway obstruction.

Clinical diagnosis of RH can be difficult without a specific history of coagulopathy, trauma or foreign body ingestion. Inspection of the larynx and hypopharynx with a flexible laryngoscope usually shows signs of pharyngolaryngeal swelling with no obvious bleeding source. A diagnosis of infection or tumour is usually made on this basis. In order to make a final diagnosis,

the clinical picture, blood results, radiological findings and biopsy results must all be considered.

The choice of treatment in this situation can be very difficult. Besides removing any precipitating factors (such as anticoagulation), choosing between simple observation, conservative treatment, intubation and active surgical intervention can prove challenging. The clinician must rely on knowledge of the various neck spaces and their connections, as well as the high rate of airway occlusion and life threatening complications of a retropharyngeal haematoma. If symptoms of airway compromise develop, the airway must be secured as a matter of urgency before complete obstruction occurs.⁵ As in this case, treatment of these patients requires a multidisciplinary approach.

Depending on severity, early involvement of otolaryngology, radiology, vascular surgery, cardiothoracic surgery and anaesthetic specialists may be essential for the successful management of these patients.

NOACs, such as edoxaban, dabigatran, rivaroxaban and apixaban, are used as an alternative to warfarin for stroke prevention

in AF and in anticoagulation for thrombolysis in myocardial infarction.⁶ These drugs are becoming increasingly prevalent in clinical use due to their rapid onset, reduced interaction with other drugs and predictable effects allowing fixed dosing schedules.⁷ Unfortunately, at present there is no reliable reversal agent for these agents and as a result significant difficulties can be encountered when trying to arrest any haemorrhage associated with them. This is the first case of a parapharyngeal haemorrhage associated with NOAC that our department has encountered and, certainly, no reports were found in the literature at the time of writing. This case illustrates not only the insidious presentation and high degree of suspicion required to diagnose an RH, but also highlights the caution that must be exercised when contemplating changing anticoagulation medications in patients.

Contributors JAM was the doctor who admitted the patient and initially managed the case, performed the literature search and drafted the case report. PRB was the registrar on-call who helped manage the acute admission and was involved in editing the case report. CS was the on-call consultant involved in the case, and gave approval of the final draft. LM was the on-call registrar in the tertiary centre and was involved in the patient's care post transfer.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Learning points

- ▶ Airway management is the priority when dealing with patients having a deep neck space swelling, and early involvement of senior support is essential.
- ▶ Clinicians should have a high index of suspicion for potential haemorrhage in patients presenting with dysphagia who are on anticoagulation.
- ▶ If haemorrhage is suspected, a coagulation profile should always be checked.
- ▶ Appearance of new or unexplained widening of the mediastinum demonstrated on chest X-ray should always be noted and investigated further.
- ▶ The Capp triad is a useful screening tool for spontaneous retropharyngeal haemorrhage.

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