Case report of a life-threatening bleed from oral hereditary haemorrhagic telangiectasia

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Case description

A 76-year-old female patient presented to the Waikato Hospital emergency department with a three-day history of profuse intraoral bleeding. She reported approximately 1.5 L of blood loss over the preceding three days. At presentation, she was haemodynamically stable and denied having any syncopal episodes or bleeding from other sites.

The patient had a history of hereditary haemorrhagic telangiectasia (HHT), which was initially diagnosed in her 30s. She had ongoing epistaxis three to four times daily even after intranasal laser (yttrium aluminium garnet) cauterisation for nasal telangiectasias in 2010. A chest computed tomography (CT) scan, magnetic resonance imaging (MRI) of the brain and upper gastrointestinal endoscopy showed no evidence of arteriovenous malformations (AVMs). Genetic testing in 2020 confirmed a pathogenic variant in the *ACVRL1* gene, which is associated with HHT. She has a strong family history with her mother, elder sister and younger brother diagnosed with HHT. She had multiple cutaneous telangiectasias (***Figure 1A***).

Other significant medical history included atrial fibrillation, osteoarthritis (right knee replacement), bariatric surgery, hypertension and anaemia. Her regular medications included dabigatran, digoxin, fluoxetine, frusemide, bisoprolol and iron supplementation, and she had had an adverse reaction to penicillin.

On examination there were multiple telangiectatic lesions over her anterior dorsum of the tongue that were non-pulsatile (***Figure 1B***). There was no blood in the nose or external auditory meatus. She was admitted under the care of the oral and maxillofacial surgery department. Initially she was managed with 1 g intravenous tranexamic acid every 6 hours as recommended by haematology, and her dabigatran was withheld. Otolaryngology performed flexible nasoendoscopy and found a small telangiectasia on the tip of the epiglottis but no active nasopharyngeal bleeding. On day two of her admission her haemoglobin level dropped from 99 to 84 g/L. She received one unit of red blood cells (235 mL) and 1 g of ferrinject (ferric carboxymaltose) in 250 mL NaCl.

ABSTRACT

Hereditary haemorrhagic telangiectasia (HHT) is a vascular disorder that results in the formation of multiple mucocutaneous arteriovenous malformations (AVMs). Clinically, it manifests as telangiectasias resulting in epistaxis, gastrointestinal bleeds and subsequent iron deficiency anaemia, along with visceral AVMs involving the lungs, liver and brain. HHT rarely presents in the oral cavity. It is inherited in an autosomal dominant pattern and commonly presents in the second decade of life with episodes of recurrent epistaxis. This case report outlines a rare presentation of a severe tongue bleed in an individual with HHT in the oral cavity and its management. With oral HHT being uncommon, treatment protocols have not been established.

A computed tomography angiogram (CTA), carotid angiogram and MRI scan of the neck found multiple enlarged abnormal appearing vessels bilaterally in the anterior third of the tongue (***Figure 2A*** and ***Figure 2B***). The imagery noted distention and prominent vessels of the facial veins, right parapharyngeal fat, bilateral soft palate and submucosa of the upper and lower lips.

Following initial conservative treatment with tranexamic acid-soaked gauze, applied with pressure, bleeding restarted. Discussion with interventional radiology concluded that embolisation of the vessels carried significant risk of ischaemic necrosis of the tongue. Further management options discussed with the patient included laser ablation to telangiectasias with intralesional bevacizumab injections, or formal surgical management. She opted for a more definitive solution and underwent a partial glossectomy, excising the telangiectasic lesions. This was performed by excising a wedge of 25 mm × 27 mm × 8 mm of tissue from the anterior aspect of the tongue with monopolar diathermy, and the underlying muscle was ablated with CO_2 laser (***Figure 3A***). On the posterior aspect of the tongue, the deeper vessels were cauterised with laser followed by bipolar diathermy, then mattress-sutured with 4/0 Vicryl Rapide (Ethicon). Closure was with 4/0 Vicryl Rapide with layered mattress and interrupted sutures. Post-operatively, she was immediately extubated and transferred to the ward. She was commenced on a

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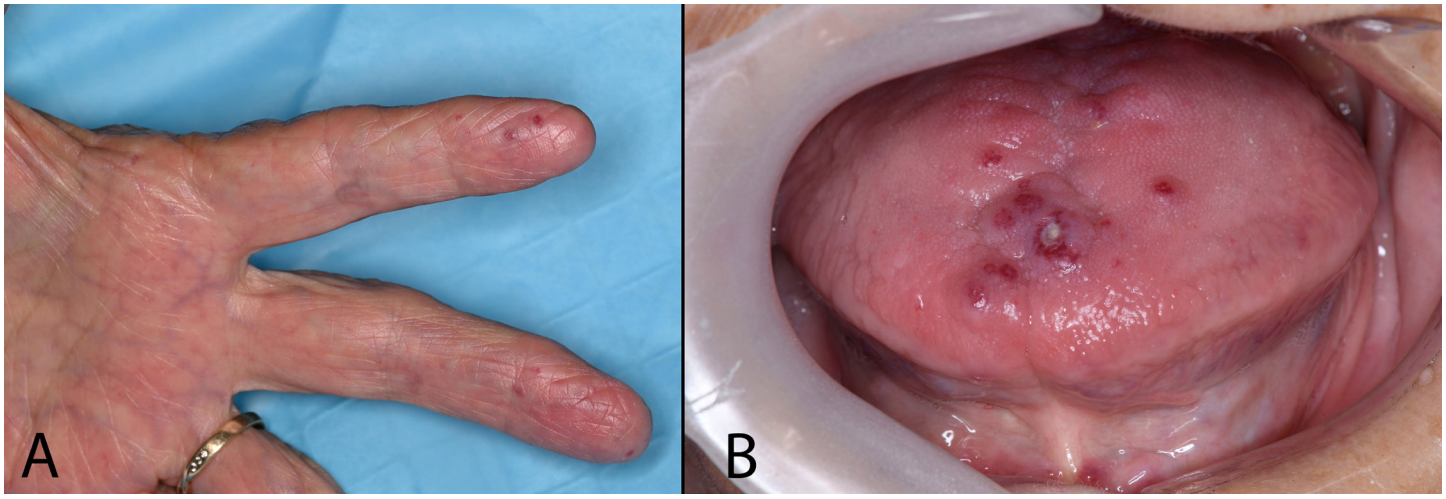

Figure 1. Clinical photographs demonstrating mucocutaneous telangiectasias. (A) Multiple telangiectatic lesions are evident on the distal aspects of the patient's fingertips. (B) Prominent telangiectasias are observed on the ventral surface of the tongue.

clear fluid diet, which was well tolerated and gradually upgraded as tolerated. The specimen was sent for histopathological examination, which showed large dilated vascular channels lined by flattened endothelial cells, features in keeping with a vascular malformation and the clinical diagnosis of HHT.

Post-operatively, she recovered well in hospital over the following five days. There were no further episodes of bleeding from her tongue and the surgical sites healed unremarkably. Her dabigatran was recommenced four days post-operatively. Unfortunately, her recovery was complicated by acquiring COVID-19. She was discharged on non-steroidal anti-inflammatory mouthwash and antibiotics.

The patient was reviewed in the outpatient clinic at one- and six-months post-operatively (***Figure 3B***). She had reported no further bleeding and had good tongue function, including speech and swallow with no dietary restrictions.

Discussion

Hereditary haemorrhagic telangiectasia is a disorder of the vascular endothelium. It was first discovered by pathologist Henry Gawen Sutton in 1864; however, it would be another 32 years until it was distinguished from haemophilia by Henri Jules Louis Marie Rendu.[1,2] It is an autosomal-dominant inherited disorder with a prevalence of 1 in 5000 to 8000.[3]

HHT1 has a mutation in the *ENG* gene (chromosome 9q33-34), HHT2 has a mutation in the *ACVRL1* gene and HHT associated with juvenile polyposis has a mutation in the gene *MADH4*.[4-6] The vessels in HHT have compromised cytoskeleton and dysfunctional remodelling of the endothelium. This results in chronically dilated vessels with poor elasticity that are susceptible to bleeding.[4,7] Acute haemorrhage can be life-threatening if it occurs in a closed space (eg, cerebral AVMs), leading to organ dysfunction. Acute bleeds into open spaces such as the nasal cavity and gastrointestinal tract are better tolerated.

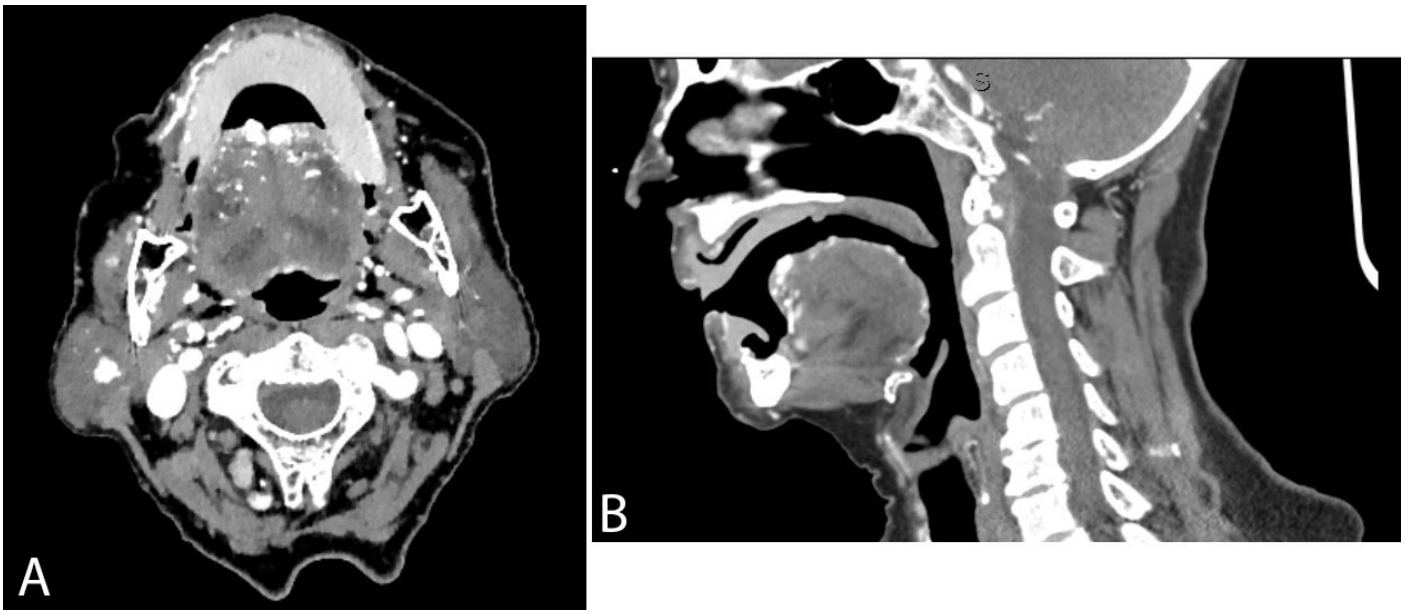

Figure 2. Computed tomography angiogram of the tongue. (A) Axial and (B) sagittal views demonstrating multiple enlarged, abnormal vessels bilaterally in the anterior third of the tongue.

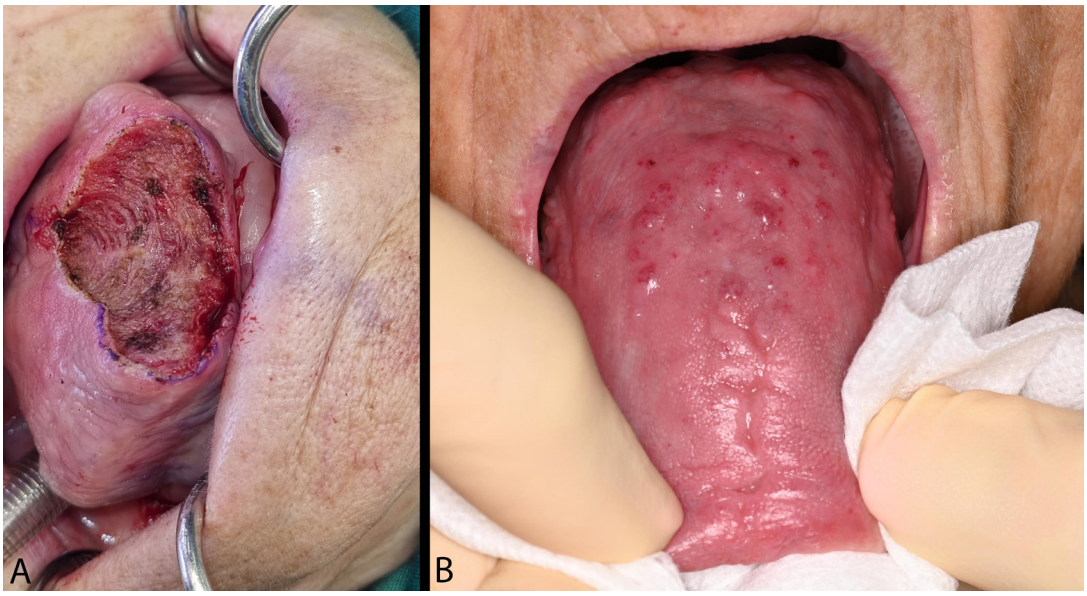

Figure 3. Clinical photographs of the tongue following surgical excision. (A) Intraoperative view post–wedge excision. (B) Six-month follow-up showing healed surgical site.

Anaemia occurs in approximately 50% of individuals with HHT, primarily due to chronic bleeding and depletion of iron stores.[8]

Telangiectasias in HHT normally develop between the ages of 20 and 30 years and increase in occurrence with age.[9] Recurrent bleeding from AVMs and telangiectasias increase in severity and frequency with age.[9,10] Over 93% of patients with HHT experience epistaxis with an average frequency of 18 times a month for 7.5 minutes.[11] The mean age of onset is 12 years.[11] The telangiectasias will blanch to pressure and promptly refill as they often present superficially on the mucosal surface. Intraoral trauma from mastication can result in bleeding for these patients.

Investigations include a carotid angiogram and MRI scan of the neck. Other investigations can include chest CT scan, brain MRI and upper gastrointestinal endoscopy to assess for other AVMs.

The Curacao diagnostic criteria for HHT were developed in 2000.[12] An individual meeting three of the criteria of spontaneous epistaxis, cutaneous and mucosal telangiectasias, visceral lesions and positive family history is identified as a "definite case". Visceral AVMs are abnormal capillary-free communications between the pulmonary and systemic circulations, which is associated with arterial hypoxaemia caused by right-to-left shunts.[13]

Treatment options for individuals with HHT are dependent on the location of vascular malformations and severity of bleeds and range from medical to surgical. The combination of oestrogen and progesterone helps stimulate metaplasia and increases thickness of nasal mucosa; however, this has restricted use due to hormonal therapy side effects. Tranexamic acid has been shown to reduce the duration of epistaxis.[12,14] Bevacizumab is a recombinant humanised antibody that inhibits circulating vascular endothelial growth factor (VEGF), which down-regulates angiogenesis. In mouse models, increased VEGF was shown to drive telangiectasia and AVMs. Normalisation of these levels shows a decrease in formation of the AVMs in type 2 HHT.[15] Thalidomide is an immunomodulatory drug that down-regulates VEGF and improves the vascular wall; however, due to its side effects such as neuropathy it has lost popularity.[16,17] A recent systematic review by Thiele and colleagues found that sclerotherapy reduced the frequency and severity of epistaxis.[18]

Niklasson and colleagues[19] conducted a literature review of 103 articles related to oral manifestations of HHT. The overall conclusion was a clear need for higher quality research examining larger populations to establish a more robust evidence-based treatment guide for clinicians. Additionally, HHT patients with known pulmonary AVMs should be given antibiotic prophylaxis before dental procedures to minimise the risk of bacteraemia.[20]

Dentists and other health professionals who examine the oral cavity can aid in the early diagnosis of HHT as most telangiectasias will present in the mucosa, gingiva, palate, tongue and lips.[19] Nasal telangiectasias will more often present in children; however, they may go on to develop oral telangiectasias. Oral bleeds, especially significant ones, are rare, and knowledge of treatment options is limited. Thus, documentation of the management of oral bleeds is important, particularly where the outcome has been successful.

Author contributions

van Kuijk M: Conceptualization, methodology, formal analysis, visualization, original draft.
Singleton C: Conceptualization, data curation, reviewing and editing, consultation.
Ke L: Methodology, formal analysis, original draft.
Singh T: Conceptualization, investigation, data curation, visualization, reviewing and editing, consultation.

Patient consent

The patient provided written consent for publication.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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