# Successful use of a military-grade haemostatic agent for a major head and neck bleed

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#### Abstract

*Background*: Major haemorrhage is a catastrophic complication occurring in 3–4 per cent of head and neck cancer patients. Massive haemorrhage also causes 50 per cent of preventable deaths in combat situations. There has been a surge of interest in the development of effective haemostatic products in the military, with chitosan being one such product.

*Case report*: A 48-year-old lady presented with a life-threatening head and neck bleed. She was known to have a malignant peripheral nerve sheath sarcoma originating from the left parapharyngeal space. Bleeding was successfully controlled with the application of  $\text{Celox}^{\text{TM}}$  granules, a chitosan-based product currently used in the military.

*Conclusion*: This paper describes the first known use of a military haemostatic agent to control a malignant head and neck bleed. Celox granules can be poured directly onto a wound to enhance haemorrhage control. The suggested mechanism of action and reports of current uses of haemostatic agents are described.

Key words: Hemorrhage; Head And Neck Cancer; Hemostatic Techniques; Chitosan; Military Personnel

## Introduction

Major haemorrhage is a catastrophic complication which occurs in 3–4 per cent of head and neck cancer patients.<sup>1,2</sup> Haemorrhage originating from the carotid arteries is usually controlled by direct pressure and arterial ligation; however, this is not always possible and mortality rates are high.<sup>1</sup>

In military combat situations, lethal haemorrhage accounts for approximately 50 per cent of preventable combat deaths.<sup>3</sup> Given recent military operations, there has been a surge of interest in the development of effective haemostatic products, with a number of different agents being studied.<sup>3,4</sup> Chitosan is one such agent currently being supplied to the military for haemorrhage control after combat wounds.<sup>5</sup>

We report the case of a life-threatening bleed in a patient with a malignant peripheral nerve sheath sarcoma originating from the left parapharyngeal space, which was successfully controlled with the application of  $\text{Celox}^{\text{TM}}$  granules (Figure 1), a chitosan-based product currently used in the military.

### **Case report**

Our patient was a 48-year-old lady who had been diagnosed as a child with a neurofibroma originating from below the left mandible. Unfortunately, the neurofibroma later transformed into a malignant peripheral nerve sheath sarcoma, which involved the left parapharyngeal space and base of the skull, and was extending into the left infratemporal region and left mandible. The tumour was noted to be growing very rapidly.

An elective tracheostomy was performed and the tumour was debulked. A course of radical radiotherapy was

completed. However, the mass continued to grow extremely rapidly and was unresectable. Prior to admission, a chronically discharging wound was noted over the left submandibular region which was being dressed by district nurses.

The patient presented to the emergency department with a massive haemorrhage; the bleeding was both external from the wound and internal through her tracheostomy. She was tachycardic and hypotensive, with a haemoglobin of 5.6 g/ dl. She was immediately resuscitated with blood products. Celox granules were inserted into the wound and direct pressure was applied with gauze. Bleeding was controlled prior to transfer to the operating theatre for an emergency exploration of the wound.

Examination in the operating theatre revealed an infected, necrotic neoplasm spreading across the mandible. An arterial bleeding point was identified and transfixed. The infected area was debrided, washed out and closed.

Post-operatively, the patient completed a short course of intravenous antibiotics and was discharged home 3 days later with no further bleeding. On review in clinic six weeks later she reported no further haemorrhage. However, unfortunately scans continued to show progression of the disease and the patient passed away five months later.

# Discussion

Cases of carotid artery rupture are complex. Affected patients have usually undergone extensive surgery and previous irradiation.<sup>1</sup> Healing is impaired due to chronic malnutrition, poor tissue oxygenation and chronic inflammation from

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1032



FIG. 1 Celox granules.

foreign bodies such as a tracheostomy.<sup>1</sup> Infection plays a major role in predisposing the patient to arterial rupture.<sup>1</sup> In our case, several risk factors for a major bleed were present, including recent radiotherapy, wound infection and recurrent tumour.<sup>2</sup>

Bleeding from a junctional zone such as the neck is particularly difficult to control due to the large underlying vascular structures present, the inability to gain proximal surgical control and difficulties in maintaining effective compression.<sup>6</sup> Endovascular approaches such as stenting and embolisation have been successfully used as alternatives to surgery but are not suitable in all cases.<sup>1,2</sup>

We describe the use of Celox, which contains particles of the haemostatic product chitosan in a granular form. This can be poured directly onto a wound and covered with a pressure dressing.<sup>6,7</sup> Several other haemostatic agents have been designed in the form of dressings and granules such as QuikClot<sup>®</sup> and WoundStat<sup>TM</sup>.<sup>6</sup> Due to their use in combat situations, clinical data regarding these products are limited,<sup>6</sup> and use is largely based on efficacy in experimental animal models.<sup>4</sup>

Chitosan itself is a polymer derived from chitin, which is a major component of crustacean shells such as crab and shrimp.<sup>4,8,9</sup> It has long been known to be a powerful haemostatic agent, and it is well tolerated, with no significant toxicity.<sup>5,8</sup>

Chitosan works by causing a direct electrostatic interaction of negatively charged erythrocytes with positively charged side groups on the chitosan polymer, creating an erythrocyte clot at the site of injury that is independent of the classical coagulation cascade.<sup>4,5</sup> There may also be secondary effects on platelet adhesion and aggregation that further add to its haemostatic properties.<sup>5</sup>

Chitosan has been available as a dressing (under the name HemCon<sup>®</sup>) since 2003; initially it was issued just to special operations staff, but more recently it has been issued to all deployed US army personnel. Anecdotal reports of its use in battlefield situations have been encouraging, particularly in treating wounds where tourniquets cannot be applied such as neck wounds.<sup>3,7</sup> A study of combat operations showed that 6 per cent of the reported uses of chitosan dressings were for neck and facial wounds.<sup>3</sup> This use has been supported by *in* 

*vivo* animal model research, which has shown 100 per cent effectiveness in models of lethal haemorrhage.<sup>7</sup>

Chitosan-based products have been successfully used in a variety of non-military emergency situations where conventional measures had failed, including post-partum haemorrhage,<sup>9</sup> post coronary artery bypass graft bleeding and civilian trauma.<sup>3,7</sup> Experiments have also suggested that chitosan can be effective even in the presence of coagulopathy.<sup>4</sup>

An animal model showing improved haemostasis in lingual incisions<sup>10</sup> paved the way for the trial of chitosan in more routine head and neck surgery. Since then, it has been used successfully to improve haemostasis following endoscopic sinus surgery<sup>8</sup> and in recalcitrant epistaxis.<sup>5</sup>

- Major haemorrhage occurs in 3-4 per cent of head and neck cancer patients
- Recent conflicts have fuelled the development of effective haemostatic products in the military
- Chitosan is one such haemostatic product developed by the military
- Chitosan is derived from crustacean shells and works by direct electrostatic interaction with erythrocytes
- This paper reports the first known use of a military haemostatic agent to control a major head and neck bleed

One issue for consideration in the setting of advanced head and neck cancer is the appropriateness of resuscitation and surgical intervention. Ideally, decisions regarding limits to treatment would be discussed with the patient and family prior to an emergency presentation.<sup>1</sup> However, given the non-invasive nature of Celox, this could undoubtedly be useful as a treatment option in an emergency situation, even in a patient for whom more invasive treatment was deemed inappropriate. It is currently recommended that Celox is removed from a wound after application; studies have shown that this is relatively easy to do.<sup>6</sup>

Longer-term effects on tissues and wound healing have not yet been fully established.<sup>6</sup> As the majority of research has been in military settings, it has not been practical or possible to arrange follow up of patients treated with chitosan. Therefore, the long-term stability of the clot formed has also not been fully assessed.<sup>5</sup> However, in the current case there was no further bleeding reported in the short or long term, and the application of chitosan appeared to successfully treat a major bleed.

# Conclusion

Life-threatening haemorrhage is a complication which occurs in 3-4 per cent of head and neck cancer patients.<sup>1,2</sup> This paper reports the successful use of Celox, a military-grade haemostatic agent, which controlled the bleeding in a patient with an advanced malignant peripheral nerve sheath sarcoma of the head and neck, who presented with an acute life-threatening haemorrhage.

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