A necrotic orofacial lesion presenting in an immunocompromised patient in the UK: case review with features of noma

Précis: Noma in the 'developed world' is rare. An awareness of the condition is essential for clinicians, as oral hygiene and antibiotics can prevent severe morbidity.

Abstract: Noma is a gangrenous and destructive orofacial disease. It comes from the Greek word *nomein*, meaning 'to devour'. Caused by a rapidly spreading opportunistic infection, noma has a strong affiliation to extreme poverty and is infamously known as the 'face of poverty'. It is predominantly endemic to children between the ages of two and six who are malnourished, and is incited by disease. However, there is rare precedent of this disease emerging in adulthood in more economically developed countries, with noma-like lesions in the UK doubling since 2015. We report on a 90-year-old patient who initially presented to their general medical practitioner for a necrotic lip ulcer, which was originally thought to be a cold sore. The patient was later admitted to hospital due to reduced mobility and severe anaemia, with underlying features of sepsis, malnutrition, immunosuppression, oral necrosis and progressive ulceration over three weeks. Immediate treatment began following admission, including intravenous antibiotics, oral care and nutritional supplementation, before a definitive clinical diagnosis of noma was made after a biopsy, which ruled out malignancy. The rapid treatment response, albeit before a diagnosis was confirmed, allowed for the disease process to halt. This atypical presentation in a UK hospital highlights the need for periodic review of such lesions, so that current knowledge of their presentation and management is maintained.

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Case report

A 90-year-old bed-bound Caucasian man was admitted to hospital due to a mechanical fall and pyrexia of 38.7°C. He also reportedly complained of a three-week history of a sore, swollen tongue, and a non-healing, painful and progressive lip 'ulcer', which was concurrent with his admission (**Figure 1**).

His medical history included: hypertension; previous basal cell carcinoma of the right tragus and squamous cell carcinoma (SCC) of the dorsum of the nose; actinic keratosis; chronic kidney disease (Stage III); and, myelodysplastic syndrome (MDS). He was immunocompromised, having had 84 cycles of chemotherapy with azacitidine (Vidaza) over a period of 11 years. MDS represents a group of cancers that result from ineffective haemopoiesis, leading to blood cytopaenia, and have potential to progress into acute myeloid leukaemia.[1]

The patient visited their general practitioner a week prior to hospital admission, who believed the oral lesion to resemble *Herpes labialis*. The lesion failed to improve with conservative management and increased in size involving the inside and outside of the lip. An urgent cancer referral was raised to the oral and maxillofacial surgery department at Diana, Princess of Wales Hospital, Grimsby, in January 2020.

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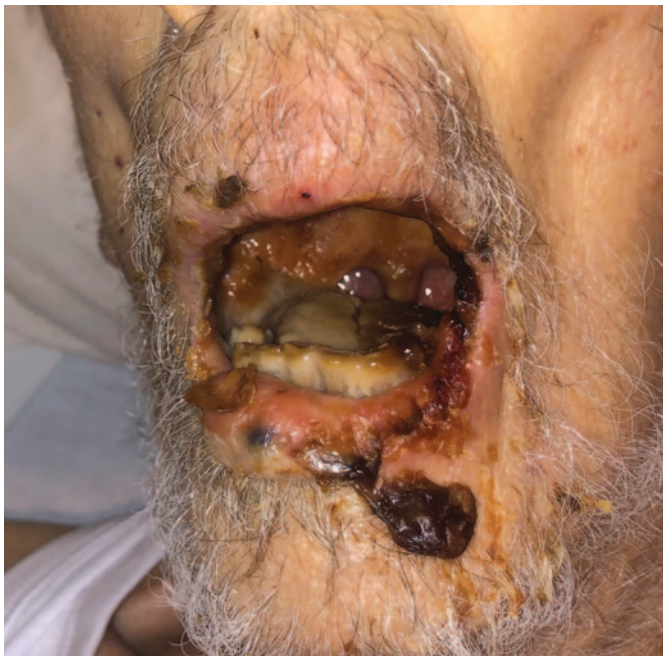

FIGURE 1: Clinical photograph of lower lip lesion. Picture demonstrates ecchymosis and blood-filled blisters surrounded by haemorrhagic crusting. There was also loss of lip competence. Photograph taken after treatment was initiated.

On examination, the patient was febrile and reported difficulty in mouth opening and pain on speaking. There was no history of trauma. The patient appeared to be suffering from an 'SCC-like lesion' on the lower lip, with features of induration, ulceration and non-healing nature. The lesion appeared to devour the left labio-buccal commissure, affecting extra- and intra-oral structures. There was no associated lymphadenopathy. The patient had lost lip competency, with teeth and gingivae easily visible at extraoral examination. Longstanding lack of oral hygiene was characterised by generalised calculus and erythematous mucosa. Features of pseudomembranous candidiasis – wipeable creamy plaques on the dorsum surface of the tongue – were apparent. Trismus of approximately 15mm and a pronounced oral foetor was present. The gingivae were ulcerated and inflamed akin to necrotising ulcerative gingivitis (NUG); however, a full intra-oral examination was not possible due to restricted mouth opening. Cachexia and cutaneous purpura on the neck and arms, secondary to MDS and chemotherapy, were also noted.

Haematological tests on admission revealed that the patient's MDS was refractory with anaemia, thrombocytopaenia and general pancytopaenia (**Table 1**). The patient had clinical signs of dehydration and malnourishment according to a Malnutrition Universal Screen Tool (MUST) score of 2.

Further investigations included blood cultures, which failed to show any growth, and bacteriology swabs, which showed normal flora. An urgent incisional biopsy showed necrosis and acute inflammation with a query of a pyogenic reaction but no malignancy, which was discussed at our local tumour board meeting.

Oral manifestations of MDS are known to cause mucosal ulceration and gingival bleeding with increased susceptibility to oro-infections secondary to immunocompromise.[2] However, the patient's sepsis, malnourishment and enduring immunosuppression, with clinical features of oral necrosis and poor oral hygiene, including foetor oris, allowed a diagnosis of noma to be made.

Table 1: Haematological and biochemical results.

Type of test	Patient's value	Reference levels
Laboratory		
Urea	14.2 ↑	2.5-7.8mmol/L
Creatinine	142 ↑	59-104µmol/L
GFR	37 ↓	90-200mL/min
Haemoglobin	42 ↓	132-170g/L
Platelets	23 x 10^9	150-400 x 10^9/L
WCC	15.1 ↑	4.3-11.2 x 10^9/L
Neutrophils	11.33 ↑	2.1-7.4 x 10^9/L
MCV	112 ↑	81-97fL
C-reactive protein	144 ↑	0-5mg/L
Albumin	25 ↓	35-50g/L
Microbiology		
Culture and sensitivity	Negative	Not applicable

Empirical treatment had begun following admission, before a definitive diagnosis of the lesion was confirmed, for severe symptomatic anaemia and sepsis. Red blood cells and platelets were transfused. Analgesics and antibiotic treatment commenced with intravenous meropenem due to his febrile MDS and then later switched to co-amoxiclav (1.2g every eight hours) for the progressive oral necrosis. Nystatin suspension, benzydamine and chlorhexidine digluconate mouthwashes were also introduced for symptomatic and bacterial control. Due to oro-mucosal pain irritated by oral candidiasis, there had been a marked reduction in oral intake. Dieticians regularly reviewed nutritional uptake with supplementation, and a naso-gastric tube was considered if he failed to improve.

After a period of 15 days (four days after biopsy) involving antimicrobial treatment, fluid resuscitation and re-feeding, the oral necrosis began to improve with features of granulation and healing (**Figure 1**). Local debridement of the necrosis was not required at this time, and the patient was subsequently discharged for palliative care. Sadly, the patient passed away due to longstanding illnesses 39 days after hospital admission.

Discussion

First described in the fifth century by Hippocrates, noma is defined by the World Health Organisation (WHO) International Classification of Diseases (ICD-10) under code A69.0 as "necrotising ulcerative stomatitis".[3] It is a non-communicable necrotising disease that leads to severe tissue necrosis of the face, mouth and other neighbouring structures. Rapid treatment is required to prevent death, and those who survive tend to live with heavy sequelae such as facial disfigurement.[4]

Reported cases largely reside within the 'noma belt', a term used by the WHO to label countries with the highest burden of disease, namely in Burkina Faso, Ethiopia, Mali, Niger, Nigeria and Senegal.[5] Some 90% of global cases develop before the age of ten.[6] It has been effectively eradicated from the 'developed world' due to improvements in healthcare and sanitation. However, there are

increasing reports of noma presenting in adulthood in high-income countries. Since the millennium, the occurrence of noma in the 'developed world' has been reported at least ten times,[7] with cases of noma-like lesions in the UK doubling since 2015.[8,9]

No specific infectious agent or illness has been identified as the single cause of noma due to the rapidity of necrosis and secondary infections.[3] The pathogenesis of noma is believed to be polymicrobial and multifactorial in nature. The role of bacteria has been cited as critical, which is made evident by oral foetor. NUG, a type of periodontal disease characterised by gingival necrosis, pain, bleeding and halitosis, is a known precursor to noma.[10-12] If left untreated, NUG can progress to necrotising periodontitis (NP) that involves the periodontal attachment apparatus. Beyond this, necrotising stomatitis (NS) can follow with or without the presence of NUG/NP, which affects the buccal/labial/lingual/palatal mucosa.[13] In turn, NS without rapid antimicrobial therapy may cause obliteration of the soft and hard tissues. This demarcated lesion is known as noma.[14]

Referral for medical/dental consultation may be indicated for a finding of NUG in primary care, which is nonresponsive to treatment for possible underlying conditions such as leukaemia and malignancy.[15] There is an important acknowledgement for the role of the dentist to prescribe antibiotics (metronidazole 400mg three times a day for three days in adults) in those who are immunocompromised or feature signs of systemic involvement such as fever, malaise and lymphadenopathy.[16] This would be adjunct to local measures (oral hygiene care and debridement) and to assessment of treatment outcomes in 24 hours.[15] Patients with underlying health conditions and sudden deterioration should be referred for urgent medical care, with sustained close monitoring. If the patient was initially seen at a primary dental care setting, intra-oral examination may have likely identified gingival necrosis and thus oral hygiene and possible antimicrobial therapy may have been initiated earlier. Regular general dental input may have prevented this advanced presentation altogether.

One factor or theory for this patient's presentation was sepsis with signs of malnutrition, which acted synergistically with MDS to permit an immunosuppressive state and provide opportunity for a 'superinfection'.[17,18] Systemic infections such as malaria and measles are common precursors to noma in low-income countries, whereas in the high-income countries, sporadic cases of noma and precursor lesions (in adults) have been largely associated with, but not limited to, other concomitant illnesses such as HIV/AIDS, leukaemia and hepatitis B.[7]

As with the current case, a 68-year-old male in 2006 was identified to have NS with underlying lack of oral hygiene, malnourishment and occult hypothyroidism. The patient also had cutaneous purpura, as did our patient. As treatment began early, noma failed to develop.[19] In 2015, researchers in Denmark published a case of noma in a 38-year-old male with a history of alcoholism-induced malnutrition and acute pancreatitis.[7]

Although scarce, there are haematological malignancies reported in the literature concerning patients with noma or noma-like lesions.[20,21] In 2017, a 70-year-old patient with MDS was suspected of having noma following trauma to the corner of their mouth.[9] Both vermillion borders were reportedly destroyed to the level of the labiomental fold. Lip commissures were obliterated, with necrosis to underlying muscle. Similarly to the current case, haematological tests showed anaemia as well as histopathology identifying chronic inflammation with no evidence of malignancy. Cultures, however, showed heavy growth of *Staphylococcus aureus*. Candida species were identified in both the 2017 and the current case.

Cases of noma in high-income countries are associated with poor oral hygiene, malnourishment and immunosuppression. As the latter is often difficult to manage, oral hygiene and nutrition are the key controllable factors to help prevent and delay the threat to life and morbidity associated with noma. A multidisciplinary approach involving dentist, maxillofacial surgeon and medical practitioner is needed.[22]

The classical symptoms of noma include severe pain, fever, oral ulceration, trismus, mucosal oedema, purulent discharge and extreme halitosis. Noma is generally diagnosed on clinical presentation rather than microbiological findings.[7] It has been noted that speed of noma and its precursor lesions in high-income countries appears to be somewhat slower than its poorer counterparts.[21]

The differential diagnoses of noma included SCC, necrotising fasciitis and acute herpetic gingivostomatitis. Other possible diagnoses include streptococcal gangrene, syphilitic yaws, mucormycosis and midfacial lymphoma (Stewart's granuloma).[17] Favourable management requires early diagnosis and immediate treatment with broad-spectrum antibiotics, oral hygiene instruction, rehydration, and correction of haematological and nutritional imbalances.

Conclusion

This case highlights that noma and its precursor lesions, despite its unequivocal rarity in high-income countries, can develop in patients who are immunocompromised, lack oral hygiene and are malnourished. Misdiagnosing noma can lead to high morbidity and mortality due to its rapidly progressing nature and effect on bodily function. The relevance of noma, particularly to primary care service providers, is due to the likelihood of initial lesions being identified by dentists or general practitioners. An appreciation of noma and a periodic reminder of the disease, its signs, symptoms and treatment among clinicians, dentists and medical colleagues working in high-income countries is needed and should permit its inclusion as a differential diagnosis.

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CPD questions

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CPD

1. What drug is the mainstay of treatment for myeloid dysplastic syndrome?

- ○ A: Rivaroxaban
- ○ B: Metformin
- ○ C: Azacytidine
- ○ D: Losartan

2. The classical symptoms of Noma include:

- ○ A: Severe pain, fever, oral ulceration, trismus, mucosal oedema, purulent discharge and extreme halitosis
- ○ B: Pain, bleeding, rapidly growing lesion
- ○ C: Red pulsatile lesion, asymptomatic, expansile and found in the upper lip
- ○ D: Erosive lesion of the lip with a mass found in the neck

3. Management of Noma consists of:

- ○ A: Wide local excision and neck dissection
- ○ B: Biopsy to rule out cancer, meticulous oral hygiene and antibiotics
- ○ C: Disease is self-limiting and there is no treatment
- ○ D: Dental clearance