

Jaw Osteomyelitis as a Complication of Sickle Cell Anaemia in Three Omani Patients

Case reports and literature review

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التهاب عظم الفك والنقي كمضاعفة لمرض فقر الدم المنجلي في ثلاثة مرضى عمانيين

تقرير حالات ومراجعته للأدبيات الطبية

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ABSTRACT: Sickle cell anaemia (SCA) is a common haemoglobinopathy among people from the Middle East, the Afro-Caribbean region, the Mediterranean and East India. While osteomyelitis of the long bones is a well-documented complication of SCA, there are few documented cases of SCA patients presenting with jaw osteomyelitis. We report three SCA patients with chronic jaw osteomyelitis who presented to the Department of Oral Health, Sultan Qaboos University Hospital, Muscat, Oman, between 2009 and 2013. Two of the patients had osteomyelitis of the mandible and the third had osteomyelitis of the *maxilla*. In addition, a brief review of the literature is presented focusing on the clinical presentation, diagnosis and management of jaw osteomyelitis among patients with SCA.

Keywords: Sickle Cell Anemia; Osteomyelitis; Jaw; Mandible; Maxilla; Case Report; Oman.

الملخص: يعتبر فقر الدم المنجلي من أمراض إعتلال الدم الهيموغلوبيني المنتشرة في منطقة الشرق الأوسط ومنطقة الكاريبي وحوض البحر الأبيض المتوسط وشرق الهند. في حين يعتبر التهاب العظام الطويلة والنقي من المضاعفات الموثقة في مرضى فقر الدم المنجلي، يوجد عدد قليل من الحالات الموثقة لمرضى فقر الدم المنجلي المصابين بالتهاب عظم الفك والنقي. نعرض هنا تقارير ثلاثة حالات لمرضى فقر الدم المنجلي مصابين بالتهاب عظم الفك والنقي المزمن والذين تقدموا للعلاج في قسم صحة الفم بمستشفى جامعة السلطان قابوس، مسقط، عمان بين عامي 2009 و 2013. إثنان من المرضى كان لديهم التهاب عظم الفك والنقي السفلي، والثالث كان لديه التهاب عظم الفك العلوي. إضافة إلى ذلك، نعرض مراجعة موجزة للأدبيات الطبية مع التركيز على العرض السريري والتشخيص وعلاج حالات التهاب عظم الفك والنقي في مرضى فقر الدم المنجلي.

الكلمات المفتاحية: فقر الدم المنجلي؛ التهاب العظم والنقي؛ الفك؛ الفك السفلي؛ الفك العلوي؛ تقرير الحالة؛ عمان.

SICKLE CELL ANAEMIA (SCA) IS AN AUTOSOMAL recessive haemoglobin disorder. The defective gene coded is *haemoglobin S*, which causes a deformation of the red blood cells (RBCs), making them sickle-shaped.¹ In particular, SCA commonly affects people originating from the Middle East, the Afro-Caribbean region, the Mediterranean and East India; in Oman, the prevalence of SCA is 0.2%.^{1,2} Patients with SCA have a wide spectrum of complications, of which vaso-occlusive crises (VOC) are the most common.¹ Osteomyelitis is an infection of the bone and bone marrow and is a well-documented musculoskeletal complication of SCA, especially in the long bones; SCA patients have a 29–31% risk of experiencing osteomyelitis at least once in their lifetime.^{3–5} However, jaw osteomyelitis is extremely rare among SCA patients, with a reported incidence of 3–5%.^{6,7} This report describes three cases of chronic jaw osteomyelitis among SCA patients in Oman.

Case 1

A 23-year-old man with SCA presented to the Department of Oral Health, Sultan Qaboos University Hospital (SQUH), Muscat, Oman, in 2009 with pus discharge from the site of a recently extracted lower left third molar. He reported that the discharge had started soon after the extraction and did not abate, despite receiving multiple courses of oral antibiotics over the preceding two months. In addition, the patient reported numbness of the left side of his lower lip continuing throughout this period. The patient was known to have SCA with frequent hospital admissions and was currently receiving hydroxyurea. Three weeks prior to the dental extraction, the patient had been admitted due to a sickle cell crisis. A clinical examination revealed that the socket of tooth 38 was not healing and had pus discharge. Additionally, pus discharge was observed in the interdental area between

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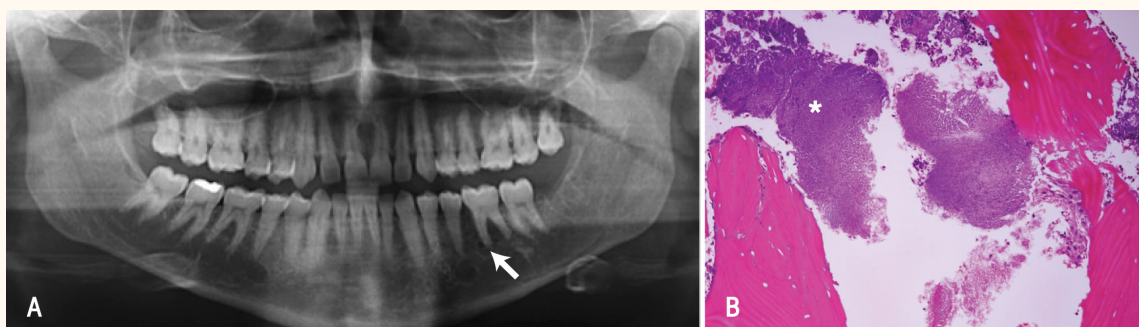


Figure 1: A: An orthopantomogram of a 23-year-old man with sickle cell anaemia showing a periapical radiolucent area related to the mesial root of tooth 36 (arrow) and obliterated pulp spaces in most teeth. B: Haemotoxylin and eosin stain at x60 magnification showing bone necrosis (asterisk) in the left posterior mandible.

teeth 35 and 36. The left submandibular lymph node was palpable and non-tender. An orthopantomogram (OPG) showed an area of radiolucency related to the mesial root of tooth 36 [Figure 1A]. Mandibular osteomyelitis was suspected.

The patient underwent removal of tooth 36, local socket curettage and a biopsy of the alveolar bone under local anaesthesia. Subsequently, he was prescribed a two-week course of oral clindamycin. The biopsy revealed areas of necrotic bone and the presence of *Actinomyces* spp. bacteria, confirming the diagnosis of chronic osteomyelitis [Figure 1B]. A culture of the pus was positive for *Klebsiella pneumoniae* and *Moraxella catarrhalis*, which were sensitive to co-amoxiclav. Following the diagnosis of jaw osteomyelitis, surgical curettage of the left mandible was performed with removal of the involved teeth while the patient was under general anaesthesia. Extensive bone necrosis was observed in the medullary spaces affecting the left mandibular alveolar region around teeth 35 and 37. An extensive cancellous sequestrectomy was carried out to the level of the inferior alveolar nerve and the involved teeth were removed. Following this, the surgical site was packed with bismuth iodine paraffin paste (BIPP). The postoperative period was uneventful. The patient received oral co-amoxiclav for six weeks and the

surgical site was repacked with BIPP every two weeks until it was fully healed. At an eight-month follow-up, the oral wound had healed completely and the patient reported normal lip sensation.

Case 2

A 16-year-old male patient with known SCA presented as an outpatient to the Department of Oral Health at SQUH in 2013 with pus discharge of two months' duration from the lower right posterior alveolus. He reported having had a VOC episode two weeks prior to the start of his symptoms. Initially, he was diagnosed with pericoronitis of the lower right third molar and was treated with multiple courses of oral antibiotics without improvement. A clinical examination indicated pus discharge from the buccal sinus and the gingiva surrounding tooth 46 [Figure 2A]. Tooth 48 was partially erupted and impacted and the patient had numbness on the right side of his lower lip. An OPG revealed an ill-defined radiolucency in the region of tooth 46 [Figure 2B].

A culture of the pus was positive for *Streptococcus anginosus*. Based on the clinical findings, chronic mandibular osteomyelitis was suspected. Accordingly, the patient was admitted and intravenous (IV) co-amoxiclav and metronidazole were administered. He

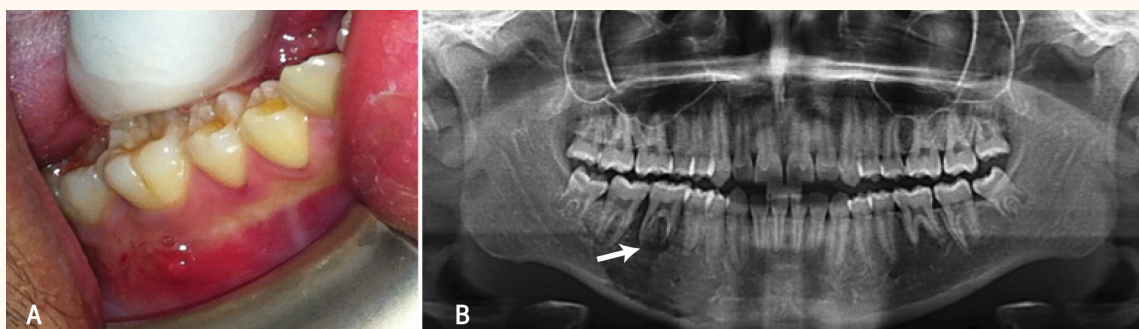


Figure 2: A: Clinical photograph of a 16-year-old male with sickle cell anaemia showing chronic sinus buccal and gingival pus discharge near tooth 46. B: An orthopantomogram showing an ill-defined radiolucent area in the apical region of tooth 46. Note the osteomyelitic appearance of the right body of the mandible (arrow).

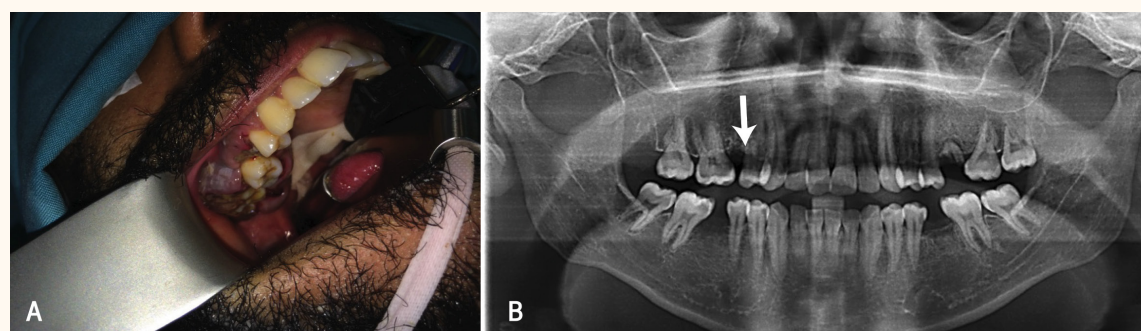


Figure 3: A: Clinical photograph of a 25-year-old male with sickle cell anaemia and swelling in the buccal and palatal aspects of the upper right posterior *alveolus*. B: A postoperative orthopantomogram following the removal of tooth 18 and resolution of the gingival swelling showing bony infarction (arrow) in the region of tooth 15.

subsequently underwent a sequestrectomy of the right mandible with removal of teeth 45 and 46 under general anaesthesia. As tooth 47 was deemed salvageable, a root canal treatment was also performed. Following these procedures, the surgical site was packed with BIPP. The patient had an uneventful postoperative recovery period and was discharged with a prescription for a 30-day course of oral co-amoxiclav. Regular follow-up appointments were scheduled every two weeks to repack the surgical site with BIPP. During these sessions, the patient showed continued improvement with no pus discharge. After six months, the oral wound had healed significantly and the patient noted that sensation to his lower lip had returned.

Case 3

A 25-year-old male patient with SCA was referred to the Department of Oral Health at SQUH in 2013 with severe pain and swelling involving the right posterior *maxilla* following his admission to a local hospital due to a severe VOC. He had a history of frequent hospital admissions, bilateral avascular necrosis of the femoral heads and was currently receiving oral hydroxyurea. A clinical examination showed swelling of the buccal and palatal mucosa with soft tissue buccal necrosis near teeth 17 and 18 [Figure 3A]. However, an OPG did not show any major pathological features other than a small area of bony infarction in the region of tooth 15 [Figure 3B].

The patient underwent removal of tooth 18 with a soft tissue and bone biopsy. Histopathology indicated normal bone and necrotic soft tissue with nonspecific chronic inflammatory cells. The patient was prescribed IV vancomycin and meropenem, with gradual improvement of the maxillary swelling. At a two-month follow-up, the intraoral swelling had subsided completely although the patient reported occasional pain in tooth 17. The tooth was found to be

nonvital and root canal therapy was performed. Two weeks later, the patient presented again with a small area of gingival buccal necrosis near tooth 17 with exposed necrotic bone. A small biopsy taken under local anaesthesia showed chronic inflammatory cells with bone necrosis and large colonies of *Actinomyces* spp. bacteria. A diagnosis of chronic maxillary osteomyelitis was made and the patient underwent a sequestrectomy of the necrotic bone in the posterior *maxilla* up to the floor of the sinus with concurrent removal of teeth 16 and 17. The surgical site was packed with BIPP, which was changed every two weeks. After six weeks, adequate healing was observed and the residual defect was closed using a small buccal advancement flap.

Discussion

Few cases of sickle cell jaw osteomyelitis (SCJO) are reported in the literature [Table 1].^{6–14} According to unpublished hospital data, only the three patients with SCJO described in the present case report were seen at the Department of Oral Health at SQUH over a 14-year period, despite the large number of SCA patients seen at this institution on a regular basis. Additionally, all three patients exhibited severe forms of SCA. It is possible that the low number of SCJO cases may be due to the prevalence of preserved splenic function in Omani patients.¹⁵ In the largest published case series to date, Olaitan *et al.* reported that jaw osteomyelitis occurred predominantly in men (81%) among 16 SCJO patients.⁶ Other reports have also noted a higher prevalence of SCJO among men.^{7–9,11,12,14} Moreover, the majority of SCJO patients reportedly present at a young age, with most patients being between 20–39 years old.^{6–14} Similarly, all three patients in the present case report were male and fell within this age group.

Sickled RBCs have a shorter life span in comparison to normal RBCs (5–15 days versus 120 days).¹⁶

Table 1: Literature review of cases of sickle cell jaw osteomyelitis^{6–14}

Author and year of case report	Number of cases	Age/gender	Site affected	Causative organism
Ryan <i>et al.</i> ⁸ (1971)	1	36/M	Mandible	Normal flora plus <i>Staphylococcus aureus</i>
Girasole <i>et al.</i> ⁹ (1977)	3	22/M	Mandible	<i>Staphylococcus aureus</i>
		34/F	Mandible	<i>Streptococcus viridans</i>
		33/M	Mandible	<i>Pseudomonas</i> spp.
Daramola <i>et al.</i> ⁷ (1982)	1	28/M	Mandible	<i>Salmonella</i> spp.
Iwu ¹⁰ (1989)	3	16/F	Mandible	Negative culture
		20/M	Mandible	N/A
		18/F	Mandible	Negative culture
Patton <i>et al.</i> ¹¹ (1990)	1	34/M	Mandible	Normal flora
Shroyer <i>et al.</i> ¹² (1991)	1	22/M	Mandible	<i>Eikenella corrodens</i> , <i>Bacteroides melaninogenicus</i> , <i>Peptostreptococcus</i> spp., mixed <i>Streptococcus</i> spp. and <i>Staphylococcus</i> spp.
Olaitan <i>et al.</i> ⁶ (1997)	16	12–30/13:3*	Mandible	Mixed (n = 5), <i>Staphylococcus aureus</i> (n = 4), none (n = 4) and others (n = 3)
Borle <i>et al.</i> ¹³ (2001)	1	25/F	Maxilla	<i>Pseudomonas aeruginosa</i>
Araújo <i>et al.</i> ¹⁴ (2015)	1	28/M	Mandible	<i>Streptococcus viridans</i>
Present cases (2009–2013)	3	23/M	Mandible	<i>Actinomyces</i> spp., <i>Klebsiella pneumoniae</i> and <i>Moraxella catarrhalis</i>
		16/M	Mandible	<i>Streptococcus anginosus</i>
		25/M	Maxilla	<i>Actinomyces</i> spp.

F = female; M = male; N/A = not available. *Male-to-female ratio.

At the end of their life, the RBCs are phagocytosed by macrophages. During a VOC episode, the entanglement of sickled cells within the inferior alveolar artery causes blockage, infarction and pulpal necrosis.¹⁶ These ischaemic areas may become necrotic and infected secondarily via either the haematogenous route or by local invasion through the periodontal ligaments.¹⁶ Among reported cases of SCJO, the mandible is the most commonly involved part of the jaw, with the lower molar region being the most common mandibular site.^{6–9,11,12,14} This could be because the mandibular molar region is supplied by the ipsilateral inferior alveolar artery and *periosteum*; due to additional blood supply from the contralateral vessels, the anterior region is less vulnerable to *ischaemia* during a VOC episode when the inferior alveolar artery is involved.⁶ Borle *et al.* reported a single case of maxillary sickle cell osteomyelitis involving the molar region.¹³ To the best of the authors' knowledge, this is the only case of maxillary SCJO reported in the current literature, other than the third case described in the present report.

Shroyer *et al.* proposed two distinct hypotheses to explain the pathophysiology of SCJO.¹² First, a sickling crisis may cause bony infarctions, which become

secondarily colonised by bacteria via haematogenous or local spread from the periodontal region. The second hypothesis suggests that a systemic infection may trigger VOC, resulting in bony infarction.¹² In keeping with the first hypothesis, the first two cases in the current report presented with a history of VOC episodes with subsequent infarction and infection. However, the third case presented with a preceding infection which may have led to a VOC episode and prompted maxillary infarction and osteomyelitis, thus supporting the method of pathogenesis described in the second hypothesis. Patients with SCJO may present with dental pain, pus discharge, necrosis or numbness in the perioral region, the latter of which is predominantly located in the lower lip in cases of inferior alveolar nerve involvement.^{17,18} In the present case report, the two patients with mandibular osteomyelitis presented with pus discharge in the molar region and were initially diagnosed with pericoronitis. Olaitan *et al.* and Shroyer *et al.* also reported pericoronitis to be a common cause of osteomyelitis among SCA patients with mandibular osteomyelitis.^{6,12}

Salmonella has been implicated as the most common causative microorganism of long bone

osteomyelitis among SCA patients.¹⁹ In comparison, *Staphylococcus aureus* is most frequently reported in the literature as the cause of jaw osteomyelitis.^{6–9,12} However, other case reports have attributed the causative agents to be *Streptococcus* spp., *Pseudomonas* spp. and other mixed species.^{6,7,9,12–14} In the current case report, *Actinomyces* spp. were isolated in the first and third cases, organisms which have not been reported previously in the literature in association with jaw osteomyelitis. However, *Streptococcus* spp. and other mixed species were isolated in the second and first cases, respectively.

Early detection and prompt referral to a specialised centre for management with expert care is vital for SCJO patients. As such, dental practitioners and oral and maxillofacial surgeons should have a high index of suspicion regarding this condition when treating SCA patients. The treatment of chronic osteomyelitis involves a sequestrectomy with preservation of the cortices, removal of the involved teeth and the administration of antibiotics.^{7,8,10,14} However, antibiotics should only be used as an adjunct to surgical treatment, since their sole use is not sufficient to manage the condition.^{5,7} This was also evidenced by the first two patients presented in the current report. In order to guide the choice of antibiotics, it is essential to send samples of pus and tissue from the necrotic area for microbiological and histopathological evaluations. In the present cases, general anaesthesia was used to allow adequate access to ensure comprehensive debridement. This is supported by Olaitan *et al.*, although other researchers have recommended use of local anaesthesia instead.^{6,10}

Conclusion

As SCJO is an uncommon condition, it may be underdiagnosed. Dental practitioners and oral and maxillofacial surgeons should be aware of this condition when treating SCA patients. This case report describes three SCA patients with chronic jaw osteomyelitis, in which two patients had osteomyelitis in the mandible and the third had osteomyelitis in the *maxilla*.

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