Jaw Pain in a Pemphigus Patient on Prednisolone, Mycophenolate Mofetil and Denosumab

An 86-year-old Chinese female who was on follow-up with our dermatology service for pemphigus foliaceus presented during her routine review with right-sided jaw pain of 1 week duration. She was edentulous but did not wear dentures and did not recall any preceding dental injury. The patient was known to have other comorbidities including oesophageal cancer (which had been resected more than 10 years ago), glucocorticoid-induced osteoporosis (GIOP), diabetes mellitus, iron deficiency anaemia and stage 3 chronic kidney disease (latest creatinine clearance 22.2 mL/min, eGFR 34 mL/min/1.73 m^2). At the point of presentation, she had been on prednisolone for 4 years (mean dose of 13.2 mg/day) and mycophenolate mofetil for 2 years (at 500 mg daily). She had also received oral alendronic acid 70 mg once a week for 2 years previously for osteoporosis. This had been subsequently changed to subcutaneous injection of denosumab 60 mg every 6 months in view of her worsening renal function and she had received a total of 4 doses prior to this presentation.

Clinical examination revealed an afebrile female who appeared well, apart from an erythematous right cheek swelling and a discharging sinus from the right mandible intraorally. Radiographic examination showed an irregular lucent area at the base of the right coronoid process of the mandible with peripheral sclerosis and a central sclerotic component (Fig. 1). A cone beam computed tomography (CT) showed a moth-eaten appearance of the right angle of the mandible and ramus with areas of osteolysis, sclerosis and bony sequestration (Fig. 2). The patient underwent biopsy, wound debridement and sequestrectomy of the right mandible. Histologic examination showed non-viable bony fragments, mixed inflammatory cell infiltrate and bone culture that grew commensal respiratory flora. The patient had an intact parathyroid hormone of 7.17 pmol/L (normal range, 1.30 pmol/L to 7.60 pmol/L).

What is the likely diagnosis?

A. Bony metastases
B. Osteomyelitis of the jaw
C. Osteonecrosis of the jaw
D. Mandibular fracture
E. Hyperparathyroidism with brown tumour

Discussion

The patient's clinical and histologic findings were consistent with medication-related osteonecrosis of the jaw (MRONJ). Denosumab was ceased and she was given a 1-week course of oral amoxicillin and clavulanic acid. At her latest review 5 months after surgery, the surgical site had completely healed.

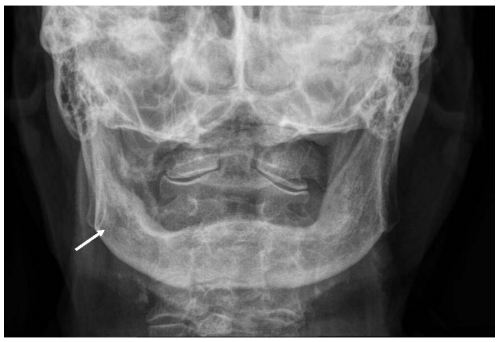

Fig. 1. Mandible radiograph demonstrating irregular lucent area at the base of the right coronoid process of the mandible with peripheral sclerosis and a central sclerotic component (arrow).

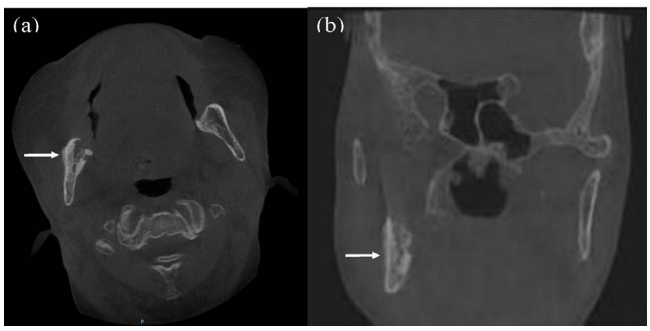

Fig. 2. Cone beam CT showing a moth-eaten appearance of the right angle of the mandible and ramus with areas of osteolysis, sclerosis and bony sequestration in a) transverse view (arrow) and b) in coronal view (arrow).

Answer: C

GIOP is a common issue in patients receiving long-term systemic corticosteroid therapy for inflammatory or autoimmune skin diseases. MRONJ is a serious but uncommon complication of osteoporosis treatment. It is 10-fold more common in oncology patients receiving high doses of intravenous bisphosphonates or denosumab for bony metastases,[1] while the incidence of MRONJ in patients with osteoporosis is between 1/10,000 and 1/100,000.[2,3] It presents with an area of exposed bone in the maxillofacial region that does not heal within 8 weeks. Jaw pain was the most commonly reported early symptom while extra-oral fistula appears later. Invasive dental procedures are a precipitating factor in the majority of cases of MRONJ. However, in a recent case series of 149 patients with MRONJ, 36% were unprovoked.[4]

Prevention of MRONJ involves pre-emptive dental review and treatment of existing dental disease before initiating antiresorptive treatment. Treatment of osteonecrosis of the jaw involves analgesia, oral antimicrobial rinses, systemic antibiotics, and avoidance of further dentoalveolar surgical procedures. In patients with more advanced osteonecrosis (stage 2 or 3 disease), or when non-operative strategies have failed, debridement, sequestrectomy and resection may be required.[5]

Our patient had multiple risk factors for developing MRONJ. This included the use of bisphosphonates and denosumab therapy for osteoporosis for 4 years, a long history of corticosteroid use and her comorbid conditions such as diabetes mellitus and anaemia.[6] Although preventive dental treatment is recommended, unprovoked MRONJ can still occur in edentulous patients such as in this case. Doctors who prescribe oral bisphosphonates routinely for prevention and treatment of GIOP should maintain a high index of suspicion for MRONJ, especially in elderly patients and patients with multiple risk factors.

Options A, B, D and E are possible differential diagnoses for the initial clinical presentation. However, osteomyelitis was ruled out as the patient was not septic and the bone culture grew commensal respiratory flora. Bony metastasis from an occult primary tumour or relapsed oesophageal carcinoma was possible but ruled out by bone histology. The patient did not have an antecedent trauma to the jaw and the radiological appearance was not consistent with that of a fractured mandible, thus ruling out a fracture. Brown tumours are late manifestations of hyperparathyroidism, and jaw bones are commonly affected by brown tumours in primary hyperparathyroidism. The bone histology for brown tumours characteristically consists of giant cells with interstitial haemorrhage, hemosiderin, microfractures and ingrowth of vascularised fibrous tissue with fibroblasts. This was not seen in our case.

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Pei Ming Yeo, [1]*MBBS*, Chia Chun Ang, [1]*MRCP (UK), MMed (Internal Med), FAMS*

[1]Department of Dermatology, Changi General Hospital, Singapore

Address for Correspondence: Dr Yeo Pei Ming, Department of Dermatology, Changi General Hospital, 2 Simei Street 3, Singapore 529889.
Email: feliciayeopm@gmail.com