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# COMMON ORAL MANIFESTATIONS OF MULTIPLE MYELOMA

## AIM

The aim of this paper is to provide a contemporary review of the orofacial manifestations of multiple myeloma. Recognition of hard tissue and mucosal abnormalities should be followed up by investigation of underlying systemic disease.

## LEARNING OBJECTIVES

- To provide readers with a comprehensive and contemporary description of the orofacial manifestations of multiple myeloma.
- To explain the importance of determining the potential presence of underlying systemic disease when hard or soft tissue abnormalities are observed during routine examination.
- To be aware that systemic disorders may initially present as manifestations in the orofacial tissues.

## LEARNING OUTCOMES

By the end of this article, readers will be able to:

- Demonstrate an enhanced understanding of multiple myeloma.
- Understand the need to investigate the possible presence of underlying disease when abnormalities are detected in the orofacial tissues.
- Be aware that systemic disease may initially present in the orofacial tissues.

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This article aims to identify some common oral signs and symptoms of Multiple Myeloma, (MM) a cancer of the plasma cells. Plasma cells develop from B-lymphocytes (B-cells) found in the bone marrow; their function is to produce antibodies, also known as immunoglobulins (Ig).<sup>1</sup>

## Aetiology

The cause of MM is yet to be identified, although associations with monoclonal gammopathy (MGUS) of undetermined significance have been made.<sup>2</sup> A contributing factor to the development of MM is the presence of one or more plasmacytomas, an accumulation of malignant plasma cells: Solitary Extramedullary Plasmacytomas (SEP)

are usually found in the soft tissues; and Solitary Bone Plasmacytomas (SBP) are located in the bones.<sup>1</sup>

The type of multiple myeloma depends on the immunoglobulins present. Immunoglobulins consist of two types of chains; short protein (light) chains and long protein (heavy) chains. Light chains are often split into two categories; kappa and lambda, and heavy chains are split into five categories; A, D, E, G and M. Other types of myeloma include, 'Bence Jones Myeloma' where an excess number of light chains are produced, and 'Non-secretory Myeloma' where no light chains are produced.<sup>3</sup>

## Risk factors

The most common risk factors for MM are<sup>4</sup>:

- Age – occurrence of MM increases in people around the ages 50-54 and peaks around ages 85-89 years

- Gender – the ratio of males to females with MM in a 2020 Cancer Research UK study was 57:43 respectively
- Family history – having a close relative with MM or MGUS was found to place an individual at a higher risk of developing MM
- Ethnicity – Multiple myeloma has been found to be more common amongst the black community compared to other ethnicities

## Systemic manifestations

Characteristically, patients do not experience any signs or symptoms of MM during the early stages however, if symptoms do occur, they include pain in the bones affected, fractures and compression of the spinal cord, which commonly presents as numbness in the lower body, or 'pins and needles'.<sup>2</sup>

■ **Figures 1 & 2:** This patient presented with discomfort and multiple swellings on his tongue. An incisional biopsy demonstrated the presence of amyloid after staining with Congo Red.

IMAGE COURTESY OF MIKE LEWIS, EMERITUS PROFESSOR, CARDIFF UNIVERSITY



■ **Figure 1**

Patients with multiple myeloma often become anaemic due a decreased number of red blood cells in the body. As the white blood cells are also compromised by the disease, patients can be subject to repeated infections which can last for a prolonged period of time.

The primary investigations for multiple myeloma involve blood tests and diagnostic imaging techniques. Further testing can involve urinalysis, incisional or excisional biopsies and advanced digital imaging techniques, such as CBCT and MRI, to identify the antibodies and proteins present in the body, malignant plasma cells, and any areas affected by the disease.<sup>2</sup>

### Treatment

The appropriate treatment option for MM is decided on a case-by-case basis by a multidisciplinary team (MDT). The least invasive treatment procedure for MM is active monitoring, suitable if the patient is asymptomatic. If the patient is symptomatic, the intensity of the treatment is heavily dependent on how fit and well the patient is.<sup>3</sup> Chemotherapy is common for patients with multiple myeloma, and involves taking medication in the form of a tablet to destroy myeloma cells in the body. Corticosteroids, such as dexamethasone, can supplement chemotherapy by helping target myeloma cells.<sup>2</sup>

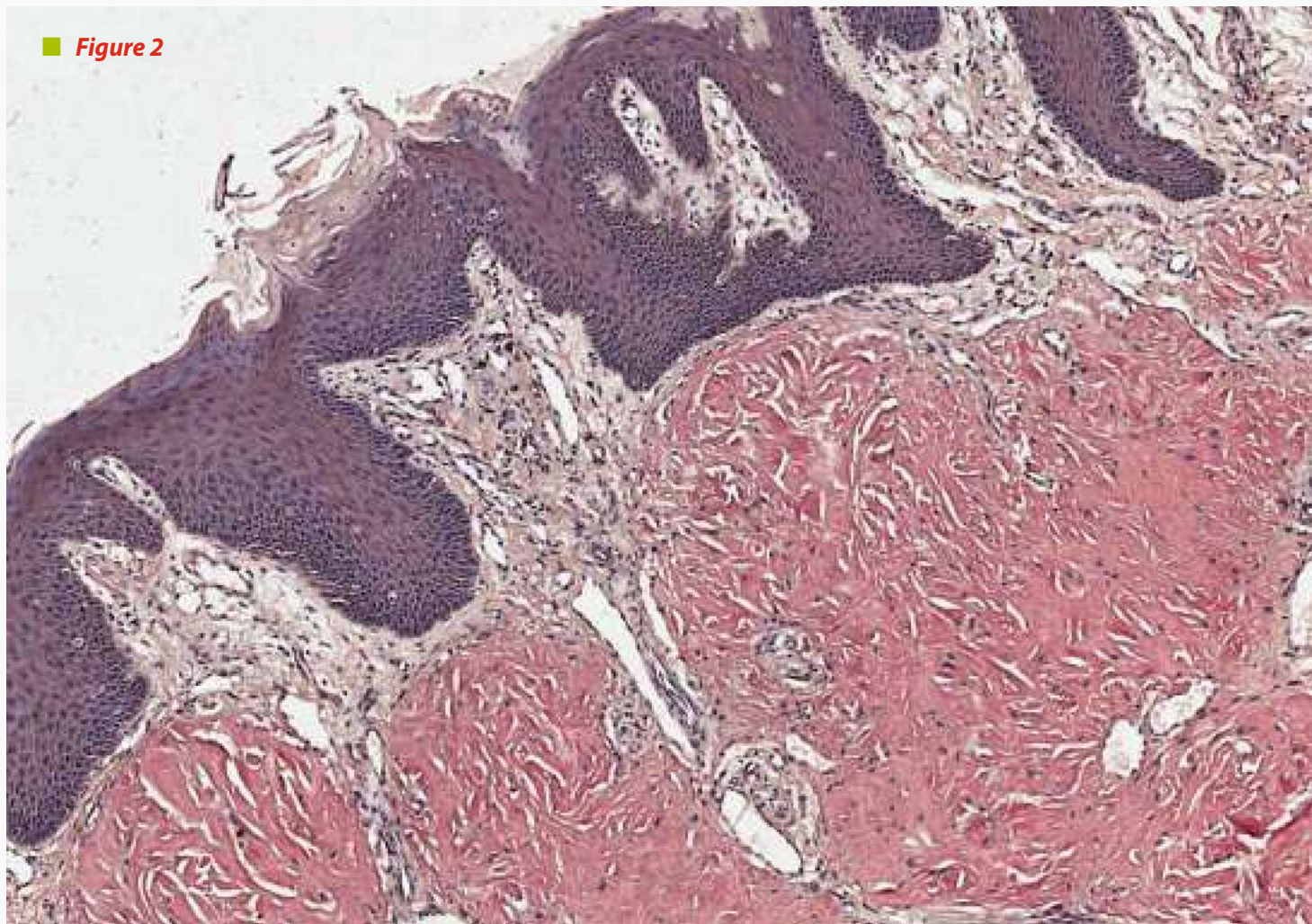
### Prognosis

The prognosis for MM is poor; it can be managed with various treatment options however, it is considered to be a terminal non-curable form of cancer.<sup>1</sup> Even when it is managed effectively, it is common for patients to experience relapses. A study by Cancer Research UK (2014)<sup>5</sup> revealed that the 5-year survival rate for a MM patient is 52.3%, with management of the condition playing a significant role.

### Manifestations of oral hard tissues

A frequently reported manifestation of MM is the presence of osteolytic changes in the mandible and maxilla. Osteolytic changes in bone are characteristic signs of malignancy; they

■ **Figure 2**



identify areas of the bone which have been damaged and are therefore less dense than normal cortical bone.<sup>6</sup> They present visually as ‘punched-out lesions’ on radiographs.<sup>7</sup> Patients often present with a painful mandibular swelling or ‘toothache’, alongside these hard tissue changes.<sup>8,9,10</sup>

Thomas et al. (2015)<sup>11</sup> described a mandibular swelling which was previously interpreted as an infection and treated unsuccessfully with antibiotics. On further examination, the firm swelling was initially suspected to be a parotid gland tumour. Radiographs of the area revealed an osteolytic lesion, later confirmed with CBCT. A differential diagnosis of MM was made, and later confirmed by a bone marrow biopsy.

Shimada et al. (2022)<sup>12</sup> undertook a cross-sectional study investigating 98 patients (55 male, 43 female) ages 43-91, suffering from different stages of MM. Their medical records were assessed prior to undergoing radiographs and CBCT. They revealed that 42.9% of ‘punched out lesions’ (POLs) were found in the skull, and 18.4% were found in the mandible. As the stages of MM progressed, so did the tumour involvement. It was found that the ramus and the angle of the mandible were the most common areas affected in these patients.

Teeth can also be affected by MM; the presence of plasmacytomas can lead to root resorption and tooth mobility.<sup>13</sup>

## Periodontal diseases

Periodontal diseases affect around 743 million people globally.<sup>14</sup> However, bleeding gums can be due to a reduced number of platelets in some forms of cancers.<sup>15</sup> Beaumont et al. (2021a)<sup>10</sup> reported a case of a 57-year-old male with IgA kappa MM, who presented with swelling and pain around his UL56. A radiolucency around a 9-millimetre periodontal pocket was evident on a radiograph. CBCT identified an additional radiolucency palatal to the UL56 and a differential diagnosis of medication related osteonecrosis of the jaw was subsequently made. However, following a biopsy of the area, a plasmacytoma was subsequently diagnosed.

## Oral soft tissues

A frequently reported manifestation is the presence of swellings and soft tissue masses and discolouration in the oral tissues.<sup>10,16,17</sup>

A case report described a 72-year-old male who presented complaining of pain in his mandible on chewing, caused by a soft tissue overgrowth. There had been no evidence of such an abnormality when, previously, he had an extraction in the same area. Intraoral examination revealed an ulcerated pink mass with poorly defined margins. An excisional biopsy detected abnormal plasma cells and bone imaging techniques were used to identify osteolytic lesions, which did not present until three months later. A bone marrow biopsy

identified abnormal plasma cells and aided the diagnosis of stage II MM.<sup>18</sup>

## The tongue

The tongue has been a key area regarding research; studies based on the tongue have investigated the presence of amyloid, a protein that can build up in the body's tissues and impair function (amyloidosis).<sup>10,19</sup> It is closely linked to MM but can also lead to problems such as heart failure and kidney failure.<sup>2</sup> Some symptoms experienced by patients with amyloidosis included pain and stiffness in the tongue (with associated dysphagia), and the presence of yellow or white papules and ulcers. These symptoms can present in immunocompromised<sup>20</sup> or anaemic<sup>21</sup> patients which are both common occurrences in MM.

## Oral candidosis

Candidosis has been observed in patients suffering from burning mouth syndrome (BMS).<sup>22</sup> Some suspected causes for this are psychological factors such as stress and anxiety<sup>23</sup> which should be considered when looking to identify symptoms which are sole manifestations of MM.

Pérusse et al. (1994)<sup>22</sup> described a case of a 63-year-old female with a burning sensation in her mouth. Her hard palate, soft palate and tongue were erythematous on examination and the diagnosis of chronic candidosis was duly made. Due to the unknown cause of the candidal infection, a bone marrow aspirate was subsequently undertaken and a diagnosis of MM was made.

Vučičević-Boras et al. (2004)<sup>24</sup> investigated the case of a 79-year-old female with burning mouth symptoms. Her oral tissues appeared healthy however, radiographs revealed a radiolucency at the apex of the UL2. A microbial swab was positive for candida and, despite the patient being treated with antifungals, the burning sensation remained. Subsequent blood tests revealed an abnormal red blood count. A bone marrow biopsy identified a plasmacytoma, which progressed into MM one year later.

## Altered nerve function

The presence of a plasmacytomas can cause nerve compression, leading to neurological problems.<sup>25</sup> Patients may present complaining of a numb sensation in the lower lip.<sup>26,27</sup> In one such case, a malignant mass in the maxillary premolar region has been found. In another case,<sup>26</sup> the causative malignancy was in the parotid gland, involving the mandibular ramus. Pati et al. (2022)<sup>28</sup> identified a causative mass to be in the patient's parotid gland, which had presented as facial palsy.

Cardoso et al. (2014)<sup>27</sup> described a case where the patient experienced numbness in the mandible with the malignant mass in the gingivobuccal sulcus. The patient had been diagnosed with MM years prior to the diagnosis of this plasmacytoma.

## Diagnostic techniques

Oral manifestations of MM can include pain, swelling and the presence of candida. Some common digital imaging techniques include radiographs, CT scans, MRI and PET scans. A CT scan is a more detailed version of a traditional radiograph, and allows medical professionals to view an area from an alternative angle – they are best used for detecting cancer.<sup>29</sup> MRIs are predominantly used for diagnosing injuries; however, they have an advantage over other methods as they do not involve the use of radiation. A PET scan is the most current digital imaging technique and tends to focus on organs rather than bones.

Other techniques used to aid the diagnosis of MM include urinalysis, haematological investigations and incisional and excisional biopsies – the use of these techniques will depend on the availability of services at the time of diagnosis.

## In summary

There are a number of oral manifestations associated with MM that commonly present in patients and generally affect the mandible, maxilla, teeth, soft tissues and tongue. Diagnostic imaging techniques and incisional biopsies are vital in the diagnosis of oral pathology,

and are often supplemented with haematological testing and urinalysis.

Dental hygienists and dental therapists routinely undertake careful examination of their patients' mouths. It is essential that we are vigilant to any abnormality and take a patient's concerns seriously. It is also important that as clinicians we feel confident to refer on appropriately. It is therefore important that the referral pathway is clear and easily accessible.

### Author

Laura graduated from Cardiff University with a BSc in Dental Hygiene and Dental Therapy in July 2023. She currently practises in North Wales.

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## General Dental Council (GDC) publishes new stats reports and EDI strategy

The General Dental Council (GDC) has published its annual Registration and Fitness to Practise statistical reports for 2023.

The **Registration Statistical Report 2023** showed that the GDC processed 11,476 registration applications from the UK and overseas in 2023, marking a significant increase from the previous peak of 8,979 applications in 2015.

The **Fitness to Practise Statistical Report** revealed a 15% drop in the number of cases referred to a Practice Committee for hearings – 132 in 2023 compared to 156 in 2022.

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