

CASE REPORT

Oral manifestations of amyloidosis in a multiple myeloma patient: A case report

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The term amyloidosis refers to a wide range of diseases in which amorphous, extracellular, eosinophilic proteinaceous deposits form at various locations. In this article, we describe a case of amyloidosis with multiple myeloma in which the oral symptoms of the disease served as the main diagnostic clues. A male patient in his early 60s who had multiple tongue swellings presented to our department. Following an incisional biopsy, histological analysis revealed the presence of eosinophilic, amorphous hyaline-like material that was positive for Congo red staining and was indicative of amyloidosis. The presence of abnormal plasma cells in the patient's bone marrow aspiration after the biopsy was done was suggestive of multiple myeloma. The patient is currently undergoing the CyBorD (Cyclophosphamide, Bortezomib, and Dexamethasone) treatment for multiple myeloma that has just been diagnosed. We offer this instance to demonstrate that, although uncommon, amyloidosis can initially only manifest as numerous swellings on the tongue.

Keywords: amyloidosis, multiple myeloma, tongue, amyloid

Received 13 March 2023 / Accepted 29 April 2023

Introduction

The term amyloidosis refers to a wide range of diseases with the characteristic of the deposition of amorphous, extracellular, eosinophilic proteinaceous deposits at distinct places. Numerous organs may experience localized or systemic amyloid deposits, which can cause a variety of clinical symptoms. Head and neck amyloidosis is uncommon and frequently indicates underlying plasma cell dyscrasia. The tongue, which develops macroglossia and a firm tongue, is the site of intraoral amyloid deposition that has been most frequently observed [1,2]. Less than 9% of all cases of amyloidosis involve the deposition of amyloid on the tongue, which is an extremely rare occurrence [2].

In this paper, we report a case of amyloidosis with multiple myeloma in which oral manifestations of amyloidosis were the primary indicators leading to the diagnosis.

Case report

A male patient in his early 60s presented to the Department of Oral Medicine and Radiology with a chief complaint of multiple swellings on the tongue for the past one-year duration. The swellings started and progressed to its present size over the period of one year. The patient also had complaints of numbness over bilateral dorsum of

hand associated with pain and swelling over all the fingers. There was altered perception along with altered to cold and heat over the dorsum of the foot. In the past medical history patient was known to be a hypertensive and was on medication for the same for past 2 years. The personal history revealed that the patient had the habit of tobacco chewing for past 20 years. Extra oral examination revealed multiple ill-defined skin-colored cystic swellings on the bilateral thumb, finger tips and near the flexor aspect of the fore arm near the wrist. The palms and soles showed hypertrophy of all the fingers with impaired sensation over the fingertips. Finger nails showed splinter hemorrhage (Figure 1). There were multiple hyperpigmented soft papules present over the bilateral nasal cavity. Intraoral examination revealed multiple soft swellings ranging from 1x1 cm to 3x4 cm over the entire dorsal surface of the tongue. The swellings were pinkish in color with a smooth surfaced and was tender on palpation (Figure 2). Macroglossia was present with crenations/indentations on the lateral border of the tongue.

Based on the history and clinical findings a clinical diagnosis of systemic amyloidosis was given. The radiological examination comprised of a digital orthopantomogram. The orthopantomogram revealed no significant findings.



Fig. 1. Clinical extraoral images (a) Nasal swellings (b) & (d) Swellings at the fingertips; (c) Splinter hemorrhage on the nails

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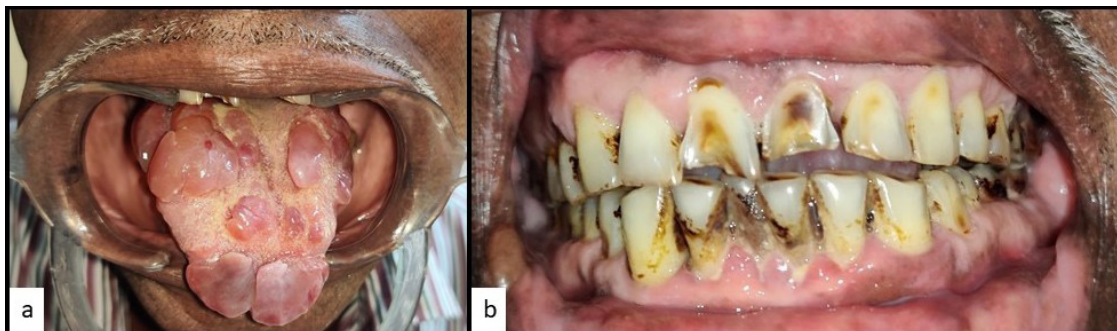


Fig. 2. Intraoral clinical images (a) Tongue (b) Gingiva

The results of the various laboratory investigations carried out are tabulated in Table 1.

An incisional biopsy of one of the tongue swellings and gingival tissue was planned. Patient was explained about the surgical procedure and consent was taken for the same. Local anesthesia was given by infiltration of 2% lignocaine solution with adrenaline around the lesion. For the tongue biopsy a swelling on the right dorsum of the tongue was

removed without mutilation of tissues (Figure 3). The gingival biopsy was performed on the gingival tissue in relation to 33, 34 teeth. After the removal of the biopsy tissues, hemostasis was achieved by application of manual finger pressure at the site (Figure 4). The patient was prescribed Paracetamol 500 mg, Amoxicillin 500 mg, Metronidazole 400mg thrice daily and Ranitidine 150mg twice daily for 3 days.

Table 1. The significant results of lab investigations

<p>Hematology - peripheral smear (edta anticoagulated blood)</p> <p>RBC (Red Blood Cell) - Normochromic normocytic with many macrocytes</p> <ul style="list-style-type: none"> - Mild anisopoikilocytosis, few elliptocytes, tear drop cells, no hemoparasites - Fragmented RBC poikilocytes - WBC (White blood cell) - normal - Platelets adequate; single, seen in clumps
<p>Urine analysis</p> <ul style="list-style-type: none"> - Albumin - +++ - Sugar - Nil - Urine PCR (Protein Creatinine Ratio) - 1.5
<p>Serum protein electrophoresis</p> <ul style="list-style-type: none"> - Normal electrophoretic pattern
<p>Nerve stimulation test</p> <p><i>Motor:</i></p> <ul style="list-style-type: none"> - Increased latency, decreased Compound Muscle Action Potential (CMAP) in left ulnar - Bilateral median nerve not stimuable - F wave absent in Bilateral median and bilateral peroneal nerve <p><i>Sensory:</i></p> <ul style="list-style-type: none"> - Sensory Nerve Action Potential (SNAPs) - not stimuable - Suggestive of sensorimotor axonal polyneuropathy
<p>Ultrasound (USG) Abdomen, pelvis and neck</p> <ul style="list-style-type: none"> - No significant abnormality
<p>Ultrasound (usg) bilateral wrists and hands</p> <ul style="list-style-type: none"> - Evidence of fluid thickening around the flexor tendons of bilateral wrists - Evidence of multiple hyperechoic soft tissue, nodular with increased vascularity along flexor aspect of bilateral palm and fingers (especially thumb) - Largest nodule 3.3 x 2.0 cm in right thumb volar aspect <p><i>Impression:</i></p> <ul style="list-style-type: none"> - Bilateral flexor tenosynovitis - Multiple soft tissue nodules all over flexor aspect of hand and fingers with increased vascularity
<p>Fine Needle aspiration (FNAC) of palmar aspect of thumb (bilateral)</p> <ul style="list-style-type: none"> - Hematoxylin and eosin (H/E) stain - Moderately cellular - Singly scattered and clusters of spindle to polyhedral cells with bland uniform nuclei in a background of fibro collagenous stroma and eosinophilic homogenous material <p><i>Impression:</i> Benign cytology</p>
<p>Magnetic resonance imaging (mri) shoulder</p> <ul style="list-style-type: none"> - Periarticular erosion seen
<p>MRI cervical spine</p> <ul style="list-style-type: none"> - Impression of Cervical spondylosis
<p>Biopsy of nasal mucosa</p> <ul style="list-style-type: none"> - Site: Mucosa from nasal septum - Congo red - negative

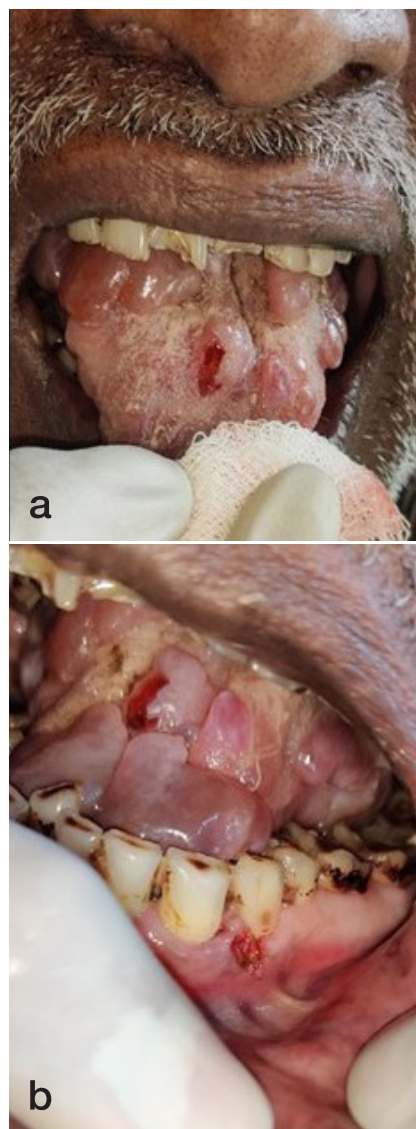


Fig. 3. Intraoperative images during biopsy (a) Tongue (b) Gingiva

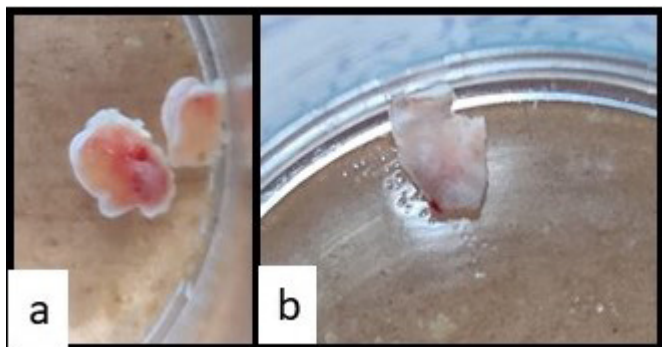


Fig. 4. Biopsy specimen (a) Tongue (b) Gingiva

The excised specimens were sent for histopathologic examination. The histopathologic section of the gingival tissue showed para keratinized stratified squamous epithelium and collagen fibers, diffuse infiltration of chronic inflammatory cells, blood vessels in the connective tissue stroma thereby not correlating with amyloidosis.

The histopathologic section of the tongue tissue showed para keratinized stratified squamous epithelium of varying size, eosinophilic hyaline like material, collagen fibers and blood vessels in the connective tissue stroma under hematoxylin and eosin stain. Stained sections with Congo Red showed the connective tissue exhibiting pinkish red color on light microscopy and apple green birefringence under polarized light microscope. This led to a histopathologic diagnosis of amyloidosis (Figure 5).

On the 7th postoperative day, the biopsy sites showed good healing.

Following the biopsy, the patient's bone marrow aspiration revealed presence of atypical plasma cells – (15%-18% - binucleate forms, plasma blast 1%) which was suggestive of multiple myeloma. The patient is currently under Cyclophosphamide, Bortezomib and Dexamethasone (Cy-BorD) protocol for newly diagnosed case of multiple myeloma. The response to treatment will be checked after four cycles of chemotherapy.

Discussion

Virchow coined the term amyloid to refer to an aberrant extracellular substance discovered in the liver during an

autopsy [3]. There are around 8–12 new cases of systemic amyloidosis worldwide each year [4].

Nodules, papules, plaques, and macroglossia are frequently seen as oral symptoms of amyloidosis [5]. Typically, tongue amyloidosis results in macroglossia, which is characterized by dysphagia, impaired speech, increased tongue volume, and tongue protrusion beyond the alveolar ridge. These features were consistent with the clinical presentation of the present case.

Histology, laboratory testing, clinical signs, such as the presence of apple-green birefringence in the diseased tissues, and other methods are frequently employed to diagnose amyloidosis [6]. A biopsy evaluation of the affected organ or tissue is necessary for a conclusive diagnosis of amyloidosis. These pathological alterations were observed in the tongue tissue that was biopsied.

Amyloidosis and multiple myeloma frequently coexist. Multiple myeloma is a rare form of plasma cell cancer that is characterized by uncontrolled monoclonal plasma cell proliferation that produces a monoclonal paraprotein that causes a variety of complications that finally result in organ malfunction and death.[7]. The paraproteinemia is associated with the excretion of light chains (Bence Jones proteins) in the urine. The example given here is consistent with the median age of presentation, which is in the sixth decade of life. Patients with back pain, bone discomfort, unexplained anemia, renal insufficiency and/or hypercalcemia, recurrent infections, and secondary amyloidosis are suspected of having multiple myeloma [8]. Bone lesions frequently manifest as localized or diffuse osteolytic lesions, or as a punched-out pattern. Mandibular and maxillary bones may be affected by these lesions.

The ultimate goal of treating amyloidosis, which is comparable to treating multiple myeloma, is to eradicate monoclonal plasma cells from the bone marrow and stop the generation of pathogenic immunoglobulin light chains using chemotherapy and stem cell transplantation [9,10].

Recent studies have shown that the effective standard of care for most patients with newly diagnosed amyloidosis is the four-drug combination of subcutaneous daratumumab, bortezomib, cyclophosphamide, and dexamethasone [11].

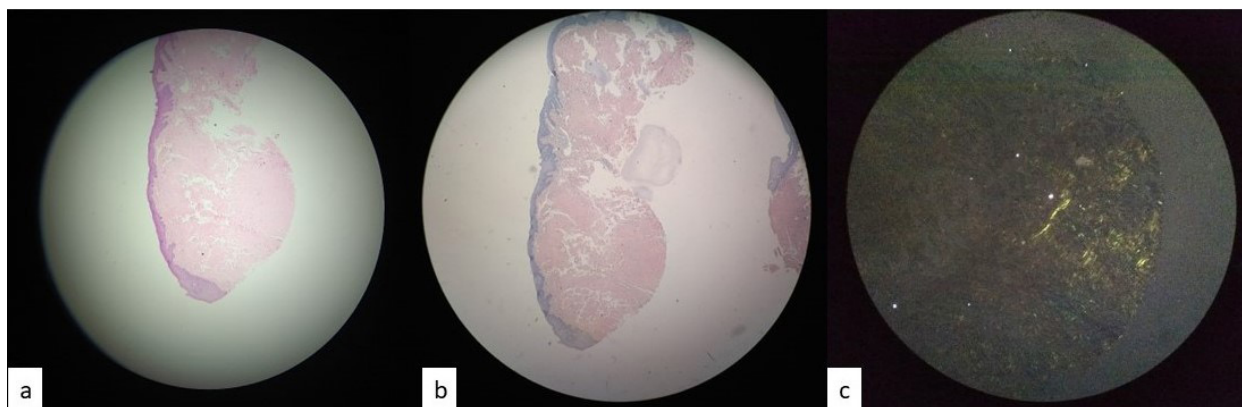


Fig. 5. Histopathologic photomicrograph of tongue specimen. (a) H & E stain (10x magnification); (b) Congo red staining (10x magnification); (c) Apple green birefringence in polarized light (40x magnification)

Amyloidosis can occasionally cause periodontal damage, papules, ulcers, or severe chronic periodontitis. Appropriate periodontal care may reduce amyloidosis-related inflammatory mediators in the body [12].

Learning points/ take home messages

1. We offer this instance to demonstrate that, although uncommon, amyloidosis can initially only manifest as numerous swellings on the tongue.
2. In this case of amyloidosis with multiple myeloma, it was the oral symptoms of the disease that served as the main diagnostic clues.
3. The investigation of multiple tongue swellings should include amyloidosis as a differential diagnosis, and the oral physician and pathologist should be attentive in looking for further systemic involvement and symptoms.

Author's contribution

JS: Manuscript preparation and review, Direct supervision of patient care

SP: Patient care, Manuscript formatting

SS: Manuscript formatting

AM: Patient care, Data collection, Manuscript draft preparation

Conflict of interest

None to declare.

Ethical statement

The patient has given written permission to publish this case report.

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