

Amyloidosis of the Tongue-Report of A Rare Case

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ABSTRACT

Amyloid involvement of the tongue is almost always secondary to systemic amyloidosis. Isolated amyloidosis of the tongue is relatively rare and it accounts for less than 9% of all types of amyloidosis. We are presenting a case of a 54-year-old male patient who complained of an enlarged tongue and bilateral multiple swellings on the lateral borders of the tongue, which had been there since one year. Bilaterally symmetrical, violaceous, purpuric patches interspersed with nodules were seen surrounding the eyes. Histopathologically, the lesion exhibited homogenous eosinophilic amyloid-like material. Special staining with Congo red showed amyloid material as peach red colour under light microscopy and as apple green birefringence under polarized light. Based on these observations, a definitive diagnosis of amyloidosis of tongue was made. Amyloidosis of tongue is uncommon and its features resemble those of a benign tumour. A battery of tests is necessary to differentiate localized amyloidosis from its systemic forms.

Keywords: Amyloidosis, Tongue, Polarized light, Apple green birefringence

CASE REPORT

A 54-year-old man reported with swelling of tongue, which had been seen since one year. On examination, he appeared to be in good general health, but his speech had been slurred ostensibly, due to tongue swelling. On clinical examination, the patient was found to be edentulous, with tongue grossly enlarged, with multiple rubbery nodules and striations on the lateral borders [Table/Fig-1 and 2]. No ulcerations were seen over the surface. Bilaterally symmetrical violaceous purpuric patches which were interspersed with nodules were seen surrounding the eyes. Well circumscribed hyperpigmented plaques were present over the nasal bridge [Table/Fig-3]. Similar small nodules were also seen on the right angle of the mouth and on ala of the nose.

An incisional biopsy was performed on the lateral border of the tongue. Histopathological examination of haematoxylin and eosin (H and E) stained sections revealed extracellular deposition of amorphous, eosinophilic hyaline-like material in the sub-mucosal connective tissue, which appeared to be amyloid [Table/Fig-4]. To confirm the presence of amyloid, a special staining with Congo red was performed, which showed peach red colour on light microscopy [Table/Fig-5] and apple green birefringence on polarized light microscopy [Table/Fig-6].

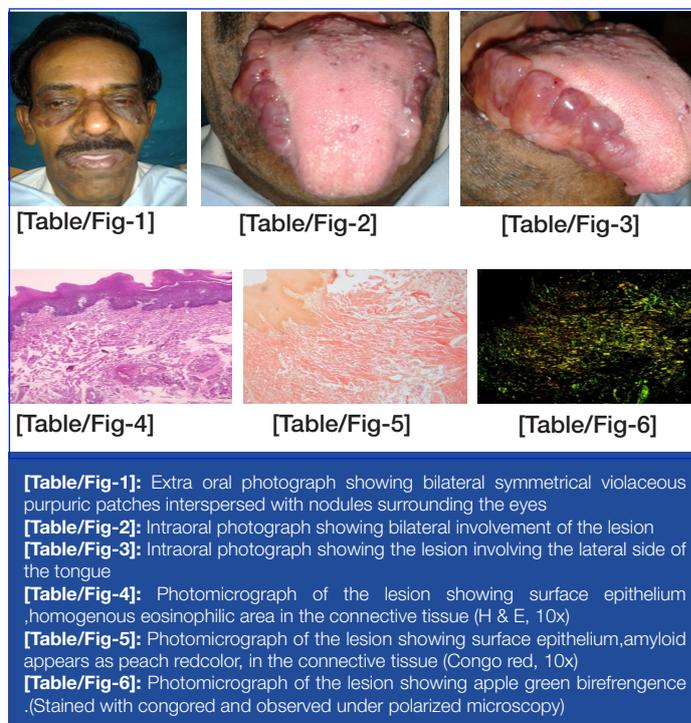
To rule out a systemic involvement, we performed a series of investigations, which included biochemical tests which included urine for Bence-Jones proteins, serum proteins, serum immunoglobulin levels, liver function tests, cardiac and renal evaluation. All these results turned out to be negative. Based on these findings, a definitive diagnosis of amyloidosis of tongue was given.

DISCUSSION

Amyloidosis of the oral cavity is uncommon. The tongue is the most frequent site, followed by the floor of the mouth, buccal mucosa, soft palate, gingiva, hard palate and lower lip region [1]. The head and neck region is affected in 12-90% of the amyloidosis patients [2]. It can also affect pharynx, orbital sinuses, larynx and salivary glands [3].

Amyloid results from an abnormal folding of proteins which are not recyclable or biodegradable and cannot be broken down easily. Therefore, the body finds it difficult to remove these proteins. This leads to the formation of oligomers and fibrils, that are deposited in tissues and organs [4,5].

Amyloidosis can be acquired (it develops over time due to unknown reasons) or hereditary (it occurs due to a faulty gene which is passed



[Table/Fig-1]: Extra oral photograph showing bilateral symmetrical violaceous purpuric patches interspersed with nodules surrounding the eyes
[Table/Fig-2]: Intraoral photograph showing bilateral involvement of the lesion
[Table/Fig-3]: Intraoral photograph showing the lesion involving the lateral side of the tongue
[Table/Fig-4]: Photomicrograph of the lesion showing surface epithelium, homogenous eosinophilic area in the connective tissue (H & E, 10x)
[Table/Fig-5]: Photomicrograph of the lesion showing surface epithelium, amyloid appears as peach red color, in the connective tissue (Congo red, 10x)
[Table/Fig-6]: Photomicrograph of the lesion showing apple green birefringence. (Stained with Congo red and observed under polarized microscopy)

on within families). It can be localized (amyloid protein is produced and deposited only in one small area of the body), or systemic (amyloid protein circulates in the blood and it gets deposited in one or several organs of the body) [4].

Earlier, amyloidosis was typically classified into four major types: primary amyloidosis, secondary amyloidosis, familial or hereditary amyloidosis and localized amyloidosis. Primary amyloidosis includes deposition of fibrillar aggregates of monoclonal immunoglobulin light chain in vital organs like liver, heart, kidney, liver, spleen. Secondary amyloidosis is a serious complication of some primary diseases such as rheumatic arthritis, multiple myeloma, chronic suppuration, Hodgkin's lymphoma, tuberculosis, Syphilis And Ricketts [6,7].

Hereditary or familial amyloidosis occurs when a gene mutation is inherited, leading to the life-long production of an abnormal protein. The most common types of hereditary amyloidosis are ATTR (transthyretin gene mutation) and AFib (fibrinogen alpha chain gene mutation) [4,7].

Localized amyloidosis is a rare type of amyloidosis which is not

associated with either multiple myeloma or systemic amyloidosis and which does not usually progress to systemic amyloidosis [2]. Head and neck involvement of amyloidosis is commonly seen in both localized and systemic forms of this disease. Cases of localized tongue amyloidosis are extremely rare, with not more than 30 cases being reported in the literature so far. Present case was a localized form of disease.

Symptoms vary greatly from patient to patient and between the different types of amyloidosis. Symptoms are often vague, mimicking other medical conditions. The most common symptoms are fatigue, unexplained weight loss, swelling of the ankles and legs due to fluid accumulation (oedema), shortness of breath, loss of appetite, an enlarged tongue (macroglossia), unexplained bruising around the eyes, numbness or tingling in the hands and feet (peripheral neuropathy) [8]. Our patient did not show any of the above features.

Clinically, for generalized macroglossia, besides amyloidosis, one should consider tuberculosis, lymphangioma, hypothyroidism, acromegaly, granular cell tumours, lingual infarction caused by giant cell arteritis, idiopathic muscular hypertrophy and Beckwith-Wiedemann syndrome under differential diagnosis. All these pathologies were ruled out after the biopsy was done, which furnished the final diagnosis as confirmed amyloidosis [2].

Localized amyloidosis of tongue typically presents as macroglossia, tongue protrusion beyond the alveolar ridge, speech impairment and dysphagia [4]. On the lateral borders, they present as yellow or raised white nodules. Kyle and Bayrd, in their review, found only 22 cases (9%) that were localized [10]. Kerner et al., University of California, Los Angeles, reported a similar series. They observed that localized amyloidosis did not evolve to primary or secondary systemic amyloidosis or multiple myeloma [11]. In a review made by Kenji et al., a total number of 5 cases had been reported, which did not have any secondary involvement (Angiero et al., Haraguchi et al., Koren et al.). Our present case also showed similar features as were reported in the above studies [12].

All amyloid deposits share the following physical characteristics, which include (a) appearance of amorphous, eosinophilic deposits under light microscope after haematoxylin and eosin staining (b) a bright, apple green birefringence under polarized light after staining with Congo red, and (c) a β -pleated sheet structure which is demonstrated on x-ray diffraction [13]. An oral involvement is extremely rare, but when it is involved, it presents primarily on the tongue. The present case fulfilled all these criteria.

It is very essential to rule out systemic from localized amyloidosis, since the aetiology, treatment and outcome of both vary. This can be done by carrying out extensive biochemical investigations, which include serum and urine immunofixation, to detect Bence-Jones Proteins and by doing a bone marrow examination for plasma cell dyscrasia [7]. An echocardiogram can be obtained, to rule out a cardiac involvement. Abdominal fat biopsy, which according to Dr

G Gallo's experience had a 94% success rate, shows positivity if systemic amyloidosis is involved [14]. All the above tests were negative in our case.

We can also use ancillary techniques like magnetic resonance imaging, Tc-99m phosphate radionuclide imaging and I serum amyloid P scintigraphy [2]. Surgical excision is usually the treatment of choice. Our patient refused any surgical intervention. Adjuvant therapies like chemotherapy and steroids were not beneficial [13].

There is no cure for amyloidosis. The prognosis is poor in generalized and myeloma associated amyloidosis; those with immunocyte derived amyloidosis have a median survival rate of two years after the diagnosis. Treatment is essential, which is given to suppress the development of the amyloid-forming protein. If amyloidosis is related to another condition, then treatment will include targeting of that underlying condition. Our patient refused to take treatment, because it did not cause any major problem for him.

In summary, amyloidosis of tongue is rare and its features resemble those of a benign tumour. A series of tests are necessary to rule out all the possible known aetiological factors which are cause for secondary amyloidosis. New therapeutic strategies are targeted at correcting protein misfolding and inhibitory fibrillogenesis.

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