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Multiple Myeloma Diagnosed from Tongue Amyloidosis: A Case Report

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Abstract

Background: Amyloidosis is a metabolic disease of unknown cause and mainly presents with organ damage due to abnormal amyloid deposition. In the oral cavity, it is characterized by macroglossia with a nodule that frequently develops on the tongue. Moreover amyloidosis is often accompanied by multiple myeloma. Herein, we reported a case of multiple myeloma diagnosed from tongue amyloidosis.

Case presentation: The patient was a 66-year-old woman who presented to our department with a chief complaint of roughness on the tongue in July 2014. Her tongue was huge and had nodules. Biopsy of the nodule on the right tongue confirmed a definitive diagnosis of amyloidosis. She complained of paresis on the fingers, for which neuropathy due to amyloidosis was suspected. Blood test showed anemia, increased erythrocyte sedimentation rate, decreased serum albumin, and increased serum β2 microglobulin. Immunoelectrophoresis detected the presence of λ-type M protein in the urine and serum. Bone marrow aspiration from the iliac bone led to the definitive diagnosis of multiple myeloma (IgA λ-type, International Staging System stage I). Lenalidomide, bortezomib, and dexamethasone therapy and autologous peripheral blood stem cell transplantation were administered for multiple myeloma. The treatment effects were “very good partial response” before transplantation and “stringent complete response” after transplantation. As of July 2018, no new nodular formation was seen in the oral cavity, and the general condition was good.

Conclusion: When multiple nodules and macroglossia in the tongue are confirmed to be amyloidosis, a systemic search for the possibility of multiple myeloma is important.

Keywords: Amyloidosis; Multiple myeloma; Tongue

Abbreviations: HE: Hematoxylin and Eosin; IgA: Immunoglobulin A; IMWG: International Myeloma Working Group

Background

Amyloidosis is a metabolic disease of unknown cause and mainly presents with organ damage due to abnormal amyloid deposition. In the oral cavity, it is characterized by macroglossia with a nodule that frequently develops on the tongue. Moreover amyloidosis is often accompanied by multiple myeloma. Herein, we reported a case of multiple myeloma diagnosed from tongue amyloidosis.

Case Report

The patient was a 66-year-old woman who was admitted to our department with a chief complaint of roughness and pain on the tongue in July 2014. Her medical history was unremarkable, except for Bell’s palsy on her right side at 41 years of age. On physical examination, macroglossia, was noted, and the tongue had multiple nodules and tooth indentation on both sides (Figure 1) [1-5].

For diagnosing the tongue tumor, a biopsy was performed on the raised portion of the right tongue. On hematoxylin and eosin (H-E) staining, weakly eosinophilic homogeneous unstructured substance was noted in the perivascular and subepithelial fibrous tissue. This site was suggested to be amyloid deposition because it stained bright orange red on Congo Red staining. The same site was confirmed to exhibit a green polarized image on polarization microscope (Figure 2).

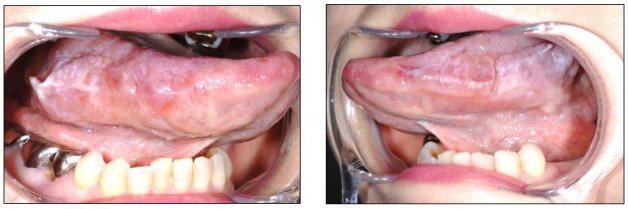
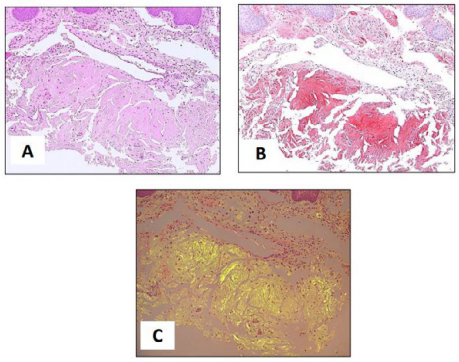


Figure 1: Intraoral finding.



A: H-E staining, ×100
B: Congo Red staining, ×100
C: Polarized microscope image for Congo Red staining, ×100.

Figure 2: Pathological histology.

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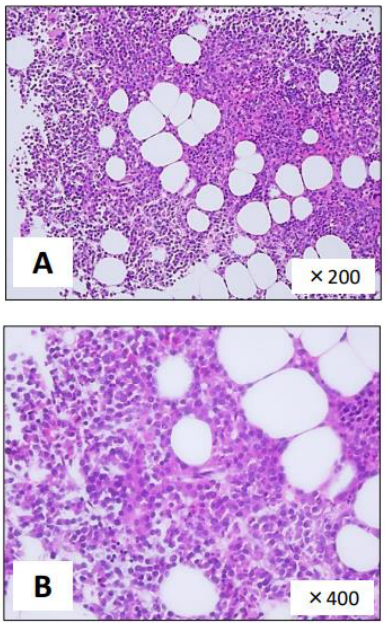
Based on these findings, a definitive diagnosis of tongue amyloidosis was made [6-8].

Further examination of the body revealed paresthesia on the fingers in the preceding 6 months. With a suspicion of neuropathy due to amyloid deposition, we referred the patient to the rheumatology department. Blood test showed anemia, increased red sediment, decreased serum albumin, and increased serum β2 microglobulin (Table 1). Serum examination revealed a tendency for the β fraction of protein to be as high as 19.2%. The high proportion of β fraction suggested that the immunoglobulin A (IgA), which was high, may be an M protein. Immunoelectrophoresis detected the presence of λ-type M-Bow in the urine and serum and IgA-type M-Bow in serum [9,10].

With a suspicion of multiple myeloma, she was referred to the hematology department. Bone marrow aspiration from the iliac bone showed the presence of as high as 63.6% plasma cells with dysplasia. The ratio of adipose marrow to medullary bone cells was 1:1, with normocellularity. There were disseminated small to medium heterotypic plasma cells and nodular proliferation (Figure 3) [11,12].



A: H-E staining, ×200

B: H-E staining, ×400.

Figure 3: Bone marrow smear specimen.

WBC	4500	/μl	TP	6.1 ↓	g/dl
RBC	27.8 × 10^6 ↓	/μl	Alb	3.6 ↓	g/dl
			β2MG	3.01 ↑	mg/l
Hb	9.1 ↓	g/dl	BUN	10	mg/dl
Ht	28.6 ↓	%	CRE	0.73	mg/dl
MCV	102.9 ↑	fl	UA	4.9	mg/dl
MCH	32.7	pg	ALP	284	U/l
MCHC	31.8	g/dl	Na	145	mEq/l
Plt	15.6 × 10^4	/μl	K	4.3	mEq/l
Ret	11	%	Ca	9.2	mg/dl
ESR	93 ↑	mm/hr	CRP	0.04	mg/dl
			IgG	416 ↓	mg/dl
			IgA	508 ↑	mg/dl
			IgM	8 ↓	mg/dl

Table 1: Results of blood test at initial visit of the rheumatology department.

Furthermore, the findings of monoclonal proliferation of λ chains in the region with high CD38 expression on flow cytometry and the absence of chromosomal abnormality on the G-band method indicated a normal female karyotype. Based on these findings, the patient was diagnosed with multiple myeloma (IgA λ type, International Staging System Stage I). X-ray examination did not show any obvious lesions throughout the body.

In November 2014, nine courses of three-drug induction therapy with bortezomib, cyclophosphamide, and dexamethasone were administered for multiple myeloma. In November 2015, autologous peripheral blood stem cell transplantation was performed. After three consecutive consolidation therapies with bortezomib, lenalidomide, and dexamethasone from March 2016, 12 courses of maintenance therapy with bortezomib and lenalidomide were administered in July 2016. The treatment effects were "very good partial response" before transplantation and "stringent complete response" after transplantation. As of July 2018, no new nodular formation was seen in the oral cavity, and the general condition was good (Figure 4).

Discussion

Amyloidosis is a metabolic disease of unknown cause and mainly presents with organ damage due to abnormal amyloid deposition. Moreover, amyloidosis is known to be often complicated with multiple myeloma.

Amyloid deposition on the tongue presents as multiple masses and macroglossia, which may cause dysfunction in articulation and eating disorders. Amyloidosis is diagnosed by histopathologic examination. In this case, biopsy of the tumor on the tongue led to the diagnosis of amyloidosis.

Multiple myeloma is recognized by the presence of monoclonal proliferation of plasma cells, with an increase in its product M protein in the serum and urine. Multiple myeloma has distinctive organ

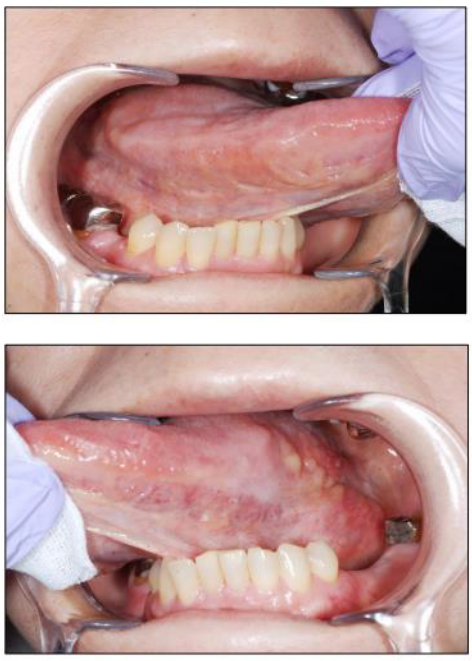


Figure 4: Intraoral finding after autologous peripheral blood stem cell transplantation. There is no new nodular formation in the tongue.

No	Author	Year	Age	Sex	Enlargement	Pain	Bleeding	Dyslalia	Dysphagia	Dysmobility	Macroglossia	Nodule	Mucosal surface	Color	Reference
1	Schwartz	1979	63	F				+			+		Dry, hard		[2]
2	Flick et al.	1980	64	M	+						+	+		White, erythematous, dark purple	[3]
	Kyle	1983	66	M (n=26)		+ (40/47)	+ (11/47)				+ (32/47)		Vascular, bleeding		[4]
3-49				F (n=21)											
50	Salisbury et al.	1983	64	F	+	+	+				+	+	Hemorrhagic-appearing		[5]
51	von Der Wal	1984	67	M	+						+	+	Rubbery, ulcer		[6]
52	von Der Wal	1984	82	F	+			+			+			Pale	[6]
53	von Der Wal	1984	50	F	+							+	Ulcer	Yellow	[6]
54	Babajews et al.	1985	75	F	+			+		+		+	Smooth, non-ulcered	Red, purple	[7]
55	Smith	1985	66	M				+	+		+		Rigidity		[8]
56	Raubenheimer et al.	1986	25	M	+				+	+	+				[9]
57	Jacobs	1988	74	M	+			+	+		+				[10]
58	Loh	1990	55	F	+	+					+	+			[11]
59	Reinish et al.	1994	65	M				+	+		+	+			[12]
60	Hatice et al.	2002	73	M				+	+		+	+	Shiny, ulcer	Red, purple	[13]
61	Ho Lee et al.	2005	68	M	+							+	Waxy	Dark reddish	[14]
62	Went	2008	71	M	+	+					+		Ulcer		[15]
63	Dalampiras et al.	2015	76	M	+	×		+	+		+	+	Normal, petechiae	Bluish	[16]
64	Bunn et al.	2015	57	M	+	+		+	+		+	+	Ulcer		[17]
65	Dawoud	2016	63	F	+	+			+	+	+	+	Smooth		[18]
66	Scheer et al.	2017	68	M	+	+					+	+			[19]
67	Demirkan et al.	2017	54	F	+						+		Teeth indentation		[20]
68	Aluri et al.	2017	61	F	+			+			+				[21]
69	This case		66	F		+					+	+	Teeth indentation	White	
+: Present															

Table 2: Summary of cases presented in the literature of patients with amyloidosis of the tongue as a result of multiple myeloma.

disorders, such as hypercalcemia, renal insufficiency, anemia, and bony lesions. The diagnosis criteria by the International Myeloma Working Group had been widely used for multiple myeloma [1]. Accordingly, this case was diagnosed as multiple myeloma, based on the detection of M protein in serum and urine, increase in clonal plasma cells in the bone marrow (≥ 10%), and the presence of anemia.

To our best knowledge, there are 23 case reports on tongue amyloidosis with multiple myeloma (Table 2). The average age was 64 (range, 25-82), and the ratio of male to female was 1.3:1. The most frequently observed subjective symptoms in the tongue were enlargement, pain, dyslalia, and dysphagia, and the most frequent objective sine was macroglossia, with most of the cases accompanied by nodules. The mucosal surface properties varied from normal to ulcer formation. In our case, the subjective symptom was only tongue pain and the objective finding was macroglossia accompanied with nodules.

In cases diagnosed as amyloidosis, particularly those in the tongue, it is important to search for the possibility of multiple myeloma. Babajews [7] reported a case of tongue amyloidosis that was diagnosed to have multiple myeloma, based on multiple tests for the presence of M protein; in this case, the diagnosis was obtained after two examinations that were performed 3 months apart. Therefore, a negative initial examination does not necessarily rule out multiple myeloma, and performing a repeat examination is important [13-21].

Conclusion

When multiple nodules and macroglossia in the tongue are confirmed to be amyloidosis, a systemic search for the possibility of multiple myeloma is important.

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