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A Case of Primary Amyloidosis Complaining of Oral Paresthesia

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A case of amyloidosis and its manifestation are briefly described. A 77-year-old woman who had complained of paresthesia of her oral mucosa and slaver was diagnosed as an amyloidosis by biopsy on tumor originating on her gingiva. Macroglossia, fissula on the tongue, an atrophy of papillae and swelling of the oral floor were seen on oral examination. The serum concentration of IgA extremely high. This suggested that there is some relationship between immunoglobulin and the pathogenesis of amyloidosis. From the viewpoint of safety, a gingival biopsy considered to be preferable to a rectal biopsy when systemic amyloidosis is suspected. (Received December 22, 1982 and accepted December 27, 1982)

Key words: Amyloidosis, Macroglossia, Oral paresthesia

1 Introduction

Amyloidosis is a metabolic disease of unknown origin in which a pathologic proteinaceous substance deposits extracellularly in various tissues and organs of the body. The clinical signs of this disease differ with the site of the amyloid deposits. Other reseachers[1,2,3] have observed that macroglossia may be present if the amyloid substance is deposited in the tongue. But, since there is no specific symptom or sign, the clinical diagnosis of this disease is difficult. Final diagnosis requires a pathological examination. In spite of numerous cases that have recorded, the true nature of amyloidosis is still unknown and the method of therapy has yet to be established.

In this study, we showed a case which was diagnosed at a comparatively early stage by carrying out a biopsy on a mass originating on the upper incisor region of the gingiva. In addition, the patient had also complained of various oral paresthesia.

2 Case Report

A 77-year-old woman was referred to our clinic by her physician on June 26, 1981. The patient had complained of swelling of the tongue, oral floor and bilateral buccal mucose in January 1981. She visited a dental clinic in March, 1981, and at that time was diagnosed as suffering from inadaptation of an upper full denture and a lower partial denture. After insertion of a newly-made denture, her complaints continued. At this time, the serection of her saliva increased and became gluey in consistency, for which reason she could not swallow it. As she felt various other paresthesia on her oral mucosa in April, 1981, she once again visited a medical doctor in June 19, 1981. Clinical examinations indicated that her tongue was slightly enlarged, but that no abnomality existed on her oral mucosa.

On June 26, 1981, a clinical examination was carried out. The patient's constitution was slender, and she weighed 43.0 kg. Her blood pressure was 140/90 mm Hg (drugs were being taken). Her pulse rate was 76/min. and an eye examination revealed no evident icterus or anemia (Fig. 1). The liver and spleen were not enlarged and no abnormal tenderness or masses were noted. The submandibular lymph

Fig. 1 Facial appearance.

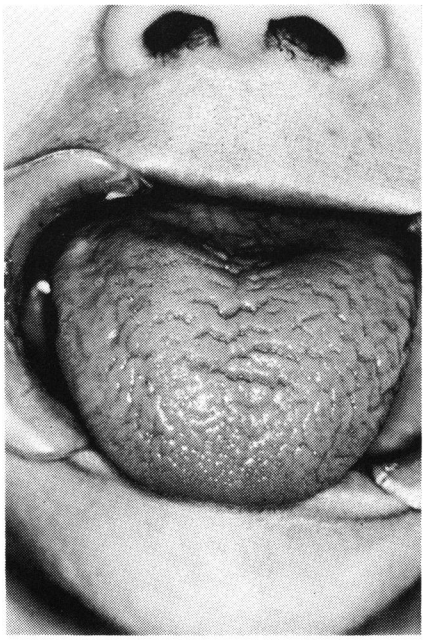

Fig. 2 Macroglossia accompanied by small fissulae and atrophy of papillae.

nodes were bilaterally beam-like in size and not tender. The results of a neurologic examination were within normal limits.

Intra-oral Findings

Her tongue was edematous and red, and the papillae of the tongue were slightly atrophied (Fig. 2). There were many small fissures on the dorsal surface of the tongue. The tongue was swollen and showed macroglossia, but there was no mass or induration by palpation. The oral floor was shallow and wave-like. No abnormality was recognized on her palate, gingiva, and buccal mucosa by inspection and palpation. Dentures were fitted onto the oral mucosa.

Laboratory Findings

A blood cell count and urinalysis were normal values. The Westergren sedimentation rates were 28 mm/h (normal range; 5-20 mm/h) and 47 mm/2 h. The serum concentration of IgG and IgM was 1190 mg/d*l* and 94 mg/d*l*, respectively, which were normal, while the serum IgA concentration was 1.108 mg/d*l* (normal value; 244±81 mg/d*l*) (Table 1). From urinalysis, Bence-Jones protein was negative.

X-P Findings

Radiographic evaluation revealed a slight extension of the heart to the right side (CTR; 0.53) on the chest X-P. An orthopantomographic examination of the upper and lower jaws revealed no abnormalities.

Management and Clinical Course

Although she was treated from the beginning with an antiinframmatory drug, gargle and a minor tranquilizer, her symptoms did not improve. In February, 1982, she consulted us again complaining of denture inadaptation. Oral examinations at that time revealed a mass formation in the upper gingiva. A tumor, a rough-surfaced and irregular-shaped mass, approximately 15×7 mm in diameter, was found. The color of this tumor was dark yellow with surrounding pale red. The gingival mucosa of the tumor circumference showed a slight swelling. The tumor was soft and was fixed to the inner side of the tissue beneath it (Fig. 3). It was removed on March 14, 1982 by surgical operation. The cutting surface of the

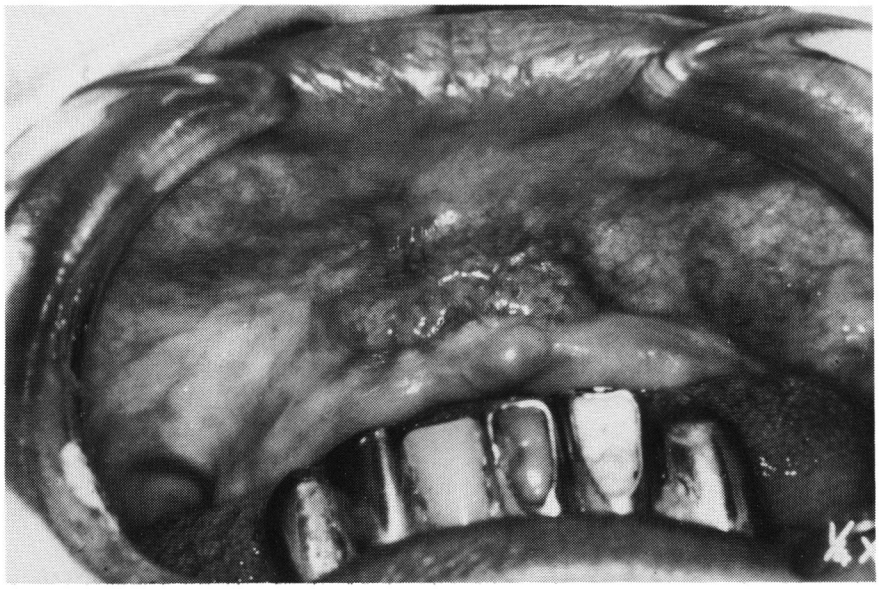

Fig. 3 Mass formation originating from gingiva. (2+2)

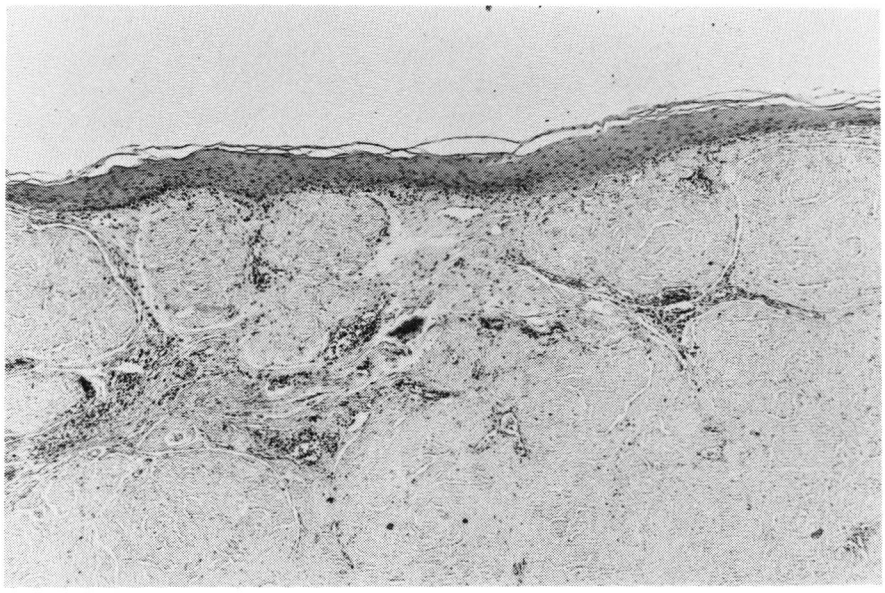

Fig. 4 Histopathological appearance. Massive eosinophilic or hyaline degeneration -like amyloid deposition (Hematoxylin and eosin stain, original magnification ×40).

tumor consisted of a monotonous yellow substance. The postoperative course was good and a full denture was inserted 2 weeks following the operation.

Microscopic Observations

Light microscopically, the amyloid appeared as an amorphous, eosinophilic, hyaline extracellular

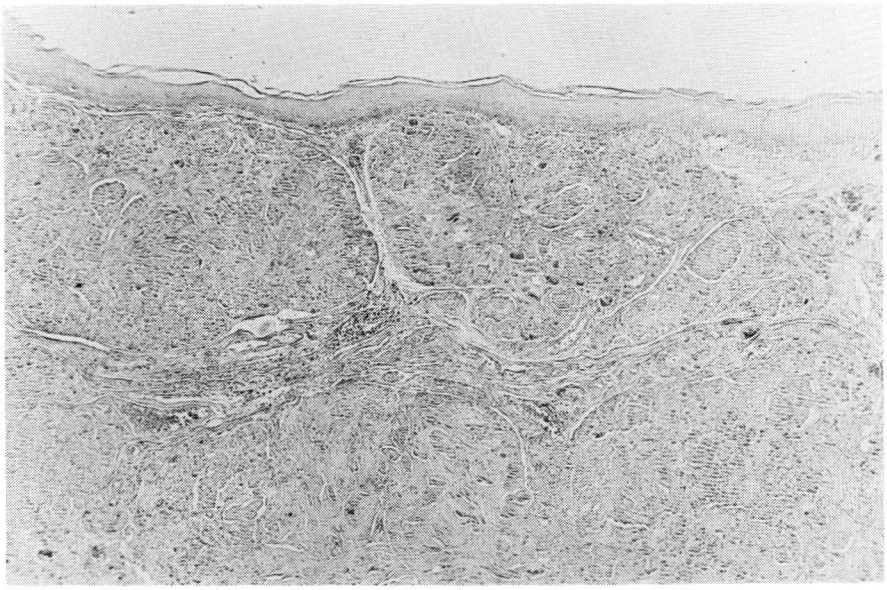

Fig. 5 Histopathological appearance. Amyloid substance appeared yellowish-red. (Congo-red stain, original magnification ×40).

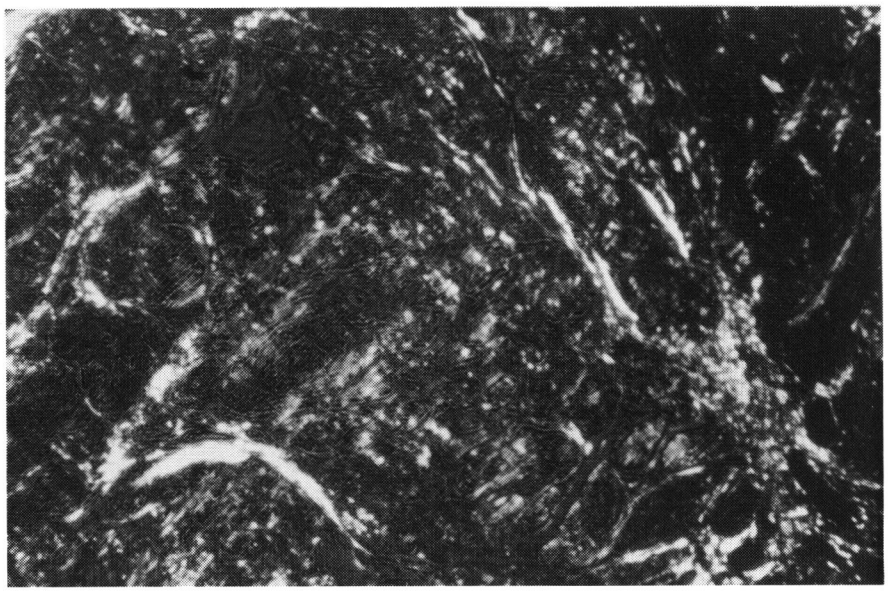

Fig. 6 Histopathological apperrance. Note the green birefringence of the stained amyloid when observed by polarizing microscopy. (Congo-red stain, original magnification ×40).

substances in the hematoxylin-eosin stained tongue tissue (Fig. 4). Some spindle-shaped cells were impacted within the amyloid substance. By microscopic observation of the tumor with Congo-red stain, the amyloid appeared yellowish-red in color (Fig. 5). The green birefringence of the stained amyloid was observed by polarizing microscopy (Fig. 6).

Electromicroscopic Observations

Specimens were obtained by surgery from the gingival tumor. Tissue for ultrastructual examination was fixed over 6 hours in 1 % glutaraldehyde and 4 % formalin. The tissue was cut into blocks of 1 mm^3 and, was rinsed for over 12 hours in 0.1 M cacodyl acid buffer (pH : 7.2–7.4), and was postfixed for 1 hour

Table 1 *Laboratory findings (1982. 6. 15)*

Hematological exam.		β	8.7%	Immunoglobulin	
RBC	$430\times10^4/mm^3$	γ	17.1%	IgA	1108(244±81) mg/dl
Hb	13.3g/dl	GOT	18 IU/*l*	IgG	1190(1417±327) mg/d*l*
Ht	40.0%	GPT	12 IU/*l*	IgM	94(207±76) mg/d*l*
ThC	$18.5\times10^4/mm^3$	Al-P	75 IU/*l*	Urinalysis	
Ret	2‰	LDH	245 IU/*l*	Specific gravity	1.022
WBC	$6100/mm^3$	ZTT	8.5 U	Protein	(−)
Stab	7%	TTT	3.2 U	Sugar	(−)
Seg	62%	T.Til.	0.3 mg/d*l*	Urobilinogen	(−)
Lym	27%	D.Bil.	0.2 mg/d*l*	Bence-Jones P.	(−)
Mono	4%	I.Bil.	0.1 mg/d*l*	Sediment	
Blood Chemistry		Na	142 mEq/*l*	RBC	0-1/GF
T.P.	7.7g/d*l*	K	4.4 mEq/*l*	WBC	0-1/GF
Al.	61.5%	Cl	96 mEq/*l*	Epi.	0-1/GF
Gl.	38.5%	Ca	8.8 mg/*l*	Cylinder	(−)
A/G	1.59	BSR			
α_1	3.1%	1 hour	28 mm		
α_2	9.6%	2 hours	47 mm		

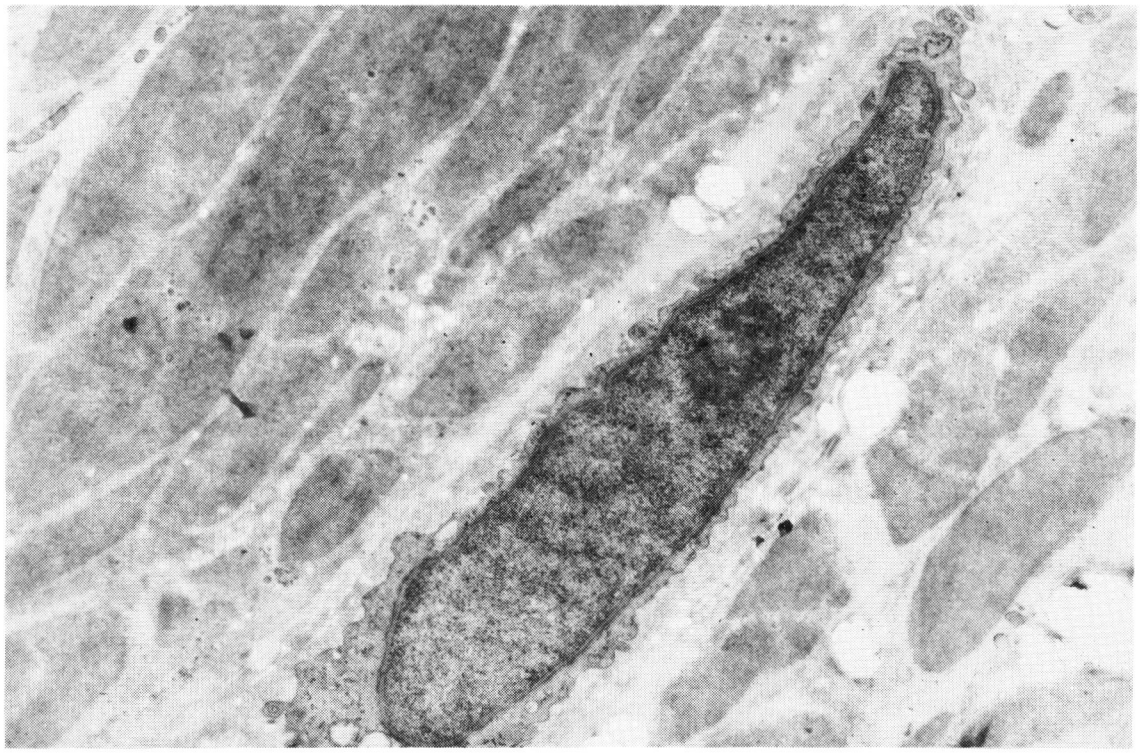

Fig. 7 Electron microscopic appearauce. Deposits of long spindle-shaped amyloid masses with some fibroblast-like cells. (original magnification ×6700)

in 1 % osmium tetroxide at 4℃. Then the tissue blodks were rinsed in 7.5 % sucrose, and after dehydration in ascending concentrations of ethanol, were embedded in Epon 812. Thin sections were stained with uranyl acetate and lead tartarate, and were observed in an electron microscope (JEOL-100 B).

Most of the specimens showed a stromal mass of moderate electron density, with some fibroblast-like cells being scattered (Fig. 7). Deposits of long, spindle-shaped amyloid masses, both large and small, and edematous collagen between these amyloid masses were observed.

3 Discussion

Amyloidosis is a disease characterized by progressive, irreversible deposition of amyloid in the body. Classifications of amyloidosis have been proposed by Reiman *et al.*[4], King[5], Symmers[6], Cohen[7], Isobe and Osserman[8], Kyle and Bayrd[9]. These classifications show slight difference from each other and there is no satisfactory classification of amyloidosis.

However, the following classification, proposed by Reiman *et al.*[4], has been most widely accepted: primary amyloidosis, secondary amyloidosis; amyloidosis associated with myeloma; and tumor forming amyloid deposition. Recently, Isobe and Osserman[8] have suggested a new classification based on the predominant clinical patterns of amyloid distribution. Pattern I comprises principal involvement of the tongue, heart, gastrointestinal tract, skeletal and smooth muscles, carpal ligament, nerves and skin. Pattern II comprises principal involvement of the liver, spleen, kidneys, and adrenal glands. Mixed pattern occurs when amloidosis involves sites of both pattern I and pattern II. The final category is localized amyloidosis; amyloid deposits are limited to a single tissue or organ.

The most common presenting symptoms of amyloidosis are fatigue or weakness, weight loss, dyspnea, paresthesia, and syncope[9]. In our case report, the patient's symptoms were weight loss and oral paresthesia with dysphagia and resultant slaver. Although her weight was 63.0 kg 1 year and 6 months before visiting our clinic, it had fallen to 43.0 kg by the time of her first consultation with us.

Tumor formation was recognized in the gingiva, and this lesion was biopsied. Pathological examination showed amyloid deposition. The oral manifestations may as enlarged, indurated, yellowish nodules at the lateral borders, hemorrhagic bullae and ulcers of aphthous type of her tongue. Macroglossia is the most prominent manifestation in particular, but this has been a feature in only 17 % of cases, according to Kyle and Bayrd[9]. Recurrent hemorrhagic bullae of the oral cavity are seen[10]. Primary amyloidosis present as a swelling in the floor of the mouth[11]. On oral examination, our patient's tongue was enlarged and reddish and the papillae of the tongue were atrophic. There were many small fissures on the dorsal surface of the tongue. It was suggested, without biopsy, that amyloid substance deposition existed in the tongue of our case.

A serum sample examined by electrophoresis showed monoclonal immunoglobulin (M-protein). The serum concentration of IgA was 1,108 mg/d*l*, and the type of light chain was lambda. This finding suggested that there is some relationship between immunoglobulin and the pathogenesis of amyloidosis. Some authors[8,9,12] have also found this high frequency of M-protein in primary amyloidosis. Glenner[12] suggested that these abnormal proteins deposit and change to amyloid substance in the tissue and organs of the body. Since tongue amyloidosis is often classified as primary amyloidosis, it is necessary, especially in the case of elderly persons, to examine the immunological serum proteins.

With the respect to aging, amyloid deposition has been noted to be fairly common in several parts of the body. Yamaguchi *et al.*[13] studied 107 cases obtained from necropsies to determine the frequency of such deposits and their relation to aging, and they found that in cases over age 60, 36.4 % had tongue amyloid. We therefore strongly advocate that the oral surgeon or dentist familiarizes himself with these manifestations and should perform a thorough oral examination, since these findings show that amyloidosis of the

tongue in elderly persons is by no means rare.

Unfortunately, there is no single clinical test that is conclusive for the diagnosis of amyloidosis. At present, a rectal biopsy is most common when systemic amyloidosis is suspected. But, gingival biopsy can be achieved more safely because of their visibility and easy accessibility. From a technical point of view, the gingival biopsy also seems to be preferable.

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口腔異常感覚を主訴とした原発性アミロイドーシスの一症例

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口腔の異常感覚と流涎を主訴として受診した77歳の女性に対し，歯肉腫瘤の切除生検を行ったところアミロイドーシスの診断を得た．本患者の口腔内所見では，巨舌，溝舌，舌乳頭の萎縮および口腔底の腫張などが認められた．血液学的検査では免疫血清蛋白分画でIgAの高値を示し，本症の成因に関与していることが示唆された．

また歯肉の生検は安全で，症例によっては直腸生検より有利であると考えられた．