Laryngeal amyloidosis in patients with apolipoprotein AI mutations L174S and L178P

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INTRODUCTION

Hoarseness associated with laryngeal amyloid deposits is one of the characteristic clinical presentations of localized AL amyloidosis. We report two patients with laryngeal amyloid who atypically were found to have associated systemic amyloid deposits on further investigation. No plasma cell dyscrasia was identified, but DNA analysis identified mutations in the apoAI gene respectively encoding the variants Leu174Ser, previously associated with amyloidosis, and Leu178Pro which has previously been associated with accelerated atherosclerosis.

OBJECTIVE

To study the clinical and pathological characteristics of the two patients with laryngeal amyloidosis in whom these apoAI mutations were detected.

METHODS

The larynx was examined by videolaryngostroboscopy. The voice was analyzed with the GRBAS-system (perceptual voice evaluation; G-overall, R-roughness, B-breathiness, A-asthenicity, S-strained quality; ranging from 0-normal to 3-highest score), phonation times and phonetography. Biopsies were stained with HE, congo red, and analyzed immunohistochemically. Organ function was assessed and tissue involvement by amyloid further determined by rectal biopsy, abdominal fat tissue aspirate, and serum amyloid P component (^{123}I-SAP) scintigraphy.

RESULTS

The laryngeal localization of amyloid was remarkably similar in the two patients, occurring as small, irregular floppy proliferations affecting the borders of both vocal cords and hampering epithelial movement. The picture contrasted with the firm bulky proliferations typically seen in localized laryngeal AL amyloidosis (1). In both cases laryngeal biopsies stained equivocally with antibodies to apoAI, but not with those to immunoglobulin light chains. No giant cells, monoclonal plasma cells or microcalcifications were seen.

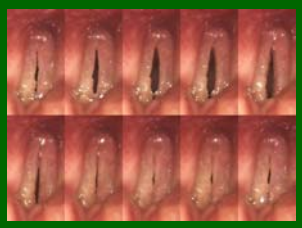
The 45-year-old woman with apoAI L174S had joint pain, bilateral CTS, polyneuropathy and ventricular tachycardias without increased thickness of the ventricular walls. Abdominal fat and rectum did not show amyloid. ^{123}I-SAP-scintigraphy showed increased uptake in the shoulders. Her phonetogram decreased to 24 semitones, dynamic range 20-30 dB.
The 67-year-old man with apoAI L178P had signs of autonomic neuropathy; serum NT-proBNP value was slightly elevated (400, N<330 ng/l), but echocardiography and ^{123}I-SAP-scintigraphy were unremarkable. Amyloid was detected in his abdominal fat aspirate. Rectal biopsy did not show amyloid. His phonetogram was normal with 33 semitones, dynamic range 30-40 dB.

Follow-up of both patients is underway to determine whether they will develop clinically significant systemic amyloidosis.

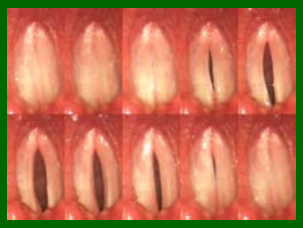
	G	R	B	A	S
L174S	1	0	1	0	0
L178P	2	1	2	0	2

Videolaryngostroboscopy: Vocal cords

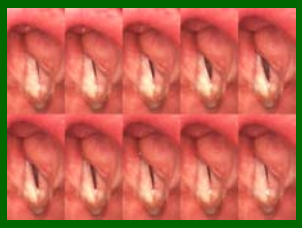
ApoAI L174S



ApoAI L178P



Healthy control



Localized AL amyloid

CONCLUSIONS

- **The findings in these patients, including the simple macroscopic appearences, suggest that their laryngeal amyloid deposits may be the first manifestation of hereditary systemic AApoAI amyloidosis**
- **It is important to detect AApoAI amyloidosis because that disease may severely affect nerves, kidney, stomach, liver, and heart**
- **Comprehensive investigation including apoAI genotyping should be considered in patients who present with apparently localized amyloidosis**

1. Bartels et al. Laryngeal amyloidosis: localized versus systemic disease and update on diagnosis and therapy. Ann Otol Rhinol Laryngol 2004; 113:741-8.