CASE REPORT

Localized Nasopharyngeal Amyloidosis

Yen-Sheng Chen[1,3], Wing-Yin Li[2], Ching-Yin Ho[1,3]*

Departments of [1]Otolaryngology and [2]Pathology, Taipei Veterans General Hospital, and [3]National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

A mass in the nasopharynx often implies a malignancy in adults, particularly in the endemic areas of Epstein–Barr virus-associated undifferentiated carcinoma. We report an 86-year-old male patient who presented to our rhinologic outpatient department with postnasal drip for several years, with no other associated nasal symptoms. Physical examination with nasal endoscopy found a prominent bulge in the nasopharynx. Pathological examination of the biopsied specimens identified features consistent with amyloidosis. Magnetic resonance imaging demonstrated an enhanced soft-tissue mass localized to the nasopharyngeal region. We excluded the possibility of a partial representation of a potential systemic amyloidosis. Regular follow-up including nasal endoscopy was undertaken. Over 3 years of observation, the disease process remained silent. Here, the clinical presentation, diagnosis and treatment options of this rare entity are discussed. [*J Chin Med Assoc* 2010;73(10):549–552]

Key Words: amyloid, head and neck amyloidosis, localized amyloidosis, nasopharynx

Introduction

Since Rudolph Virchow's initial description of the term "amyloid" in 1854, amyloidosis has become recognized as a group of disorders resulting from extracellular tissue deposition of fibrils comprised of low-molecular-weight subunits of a variety of proteins.[1] En route to fibrillogenesis, misfolding of proteins occurs, which converts soluble precursor proteins into insoluble polymeric amyloid fibrils. Several unique staining patterns have been discovered as a result of the adoption of antiparallel beta-pleated sheet conformation.[2] An apple-green birefringence can be displayed under polarized light after staining with Congo red and an intense yellow-green fluorescence is demonstrated with the use of thioflavin T.

Clinically, amyloidosis can manifest in several different forms: primary versus secondary, heredofamilial versus acquired, and generalized versus localized. The most frequent types encountered in clinical practice are the amyloid light chain (AL, primary) and a protein called the AA protein (secondary), both of which might involve multiple organ systems (e.g. kidney, heart, and liver). Isolated deposition of fibrillar proteins in an organ may result in organ-specific syndromes (e.g. Alzheimer's disease and primary localized amyloidosis of the bladder).[3] In the head and neck region, the most common site of amyloid depositions is in the larynx, and other sites include the orbit, skin, tongue, salivary glands and cervical lymph nodes.[4] Localized nasopharyngeal amyloidosis is an extremely rare condition, and few cases have been reported.[5]

Compared with the USA and Western European countries, nasopharyngeal carcinoma is endemic in some countries of Southeast Asia. Consequently, when a nasopharyngeal mass is visualized at otolaryngologic clinics in Taiwan, nasopharyngeal carcinoma should be the first priority to be considered, especially in adult populations.

We report an unusual case of amyloidosis localized to the nasopharynx, which was an unexpected diagnostic finding, following biopsy of the nasopharyngeal mass. We also review the literature regarding its pathogenesis, clinical manifestations, diagnostic methods and management options.

Case Report

An 86-year-old man presented to our department with the chief complaint of intermittent postnasal drip for several years. His past medical history was as

*Correspondence to: Dr Ching-Yin Ho, Department of Otolaryngology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: cyho@vghtpe.gov.tw • Received: December 14, 2009 • Accepted: May 17, 2010

follows: (1) duodenal ulcer; (2) drug-induced hepatitis; (3) allergic rhinitis; and (4) bilateral sensorineural hearing loss. Initially, he did not pay much attention to the postnasal drip. There were no associated symptoms of epistaxis, persistent nasal obstruction, facial pain or visual change. He denied smoking and drinking alcohol. The family history was noncontributory.

On physical examination of our patient, no obvious neck mass was palpated. Nasal endoscopy revealed an irregular, yellowish-colored, smooth-surfaced bulging at the left aspect of the nasopharynx (Figure 1A). Bilateral intact eardrums with good mobility were found on pneumatic otoscopy. Pure tone audiometry showed nearly symmetric sensorineural hearing loss bilaterally. Otherwise, there were no remarkable findings in other parts of the body.

Under the tentative diagnosis of suspected nasopharyngeal malignancy, nasopharyngeal biopsy was undertaken. However, pathological analysis showed squamous and respiratory mucosal tissue with infiltration of inflammatory cells and deposition of globules of a pink-colored amyloid substance in subepithelial connective tissue (Figure 2A). The amyloid substance stained a red color with Congo red solution and gave apple-green birefringence under polarized light (Figure 2B). There was no evidence of malignancy in this biopsied specimen.

On admission, chest X-ray showed nonspecific interstitial infiltration in both lung fields. Magnetic resonance imaging (MRI) demonstrated a hypointense submucosal soft-tissue mass on the left aspect of the nasopharyngeal wall with local extension to the oropharynx on a T2-weighted sequence, and showed slight enhancement on a postcontrast T1-weighted sequence (Figure 3). Sonography of the abdomen disclosed no significant findings. To exclude systemic amyloidosis, anterior abdominal wall fat pad biopsy was conducted, and no pathological process was identified. As a result,

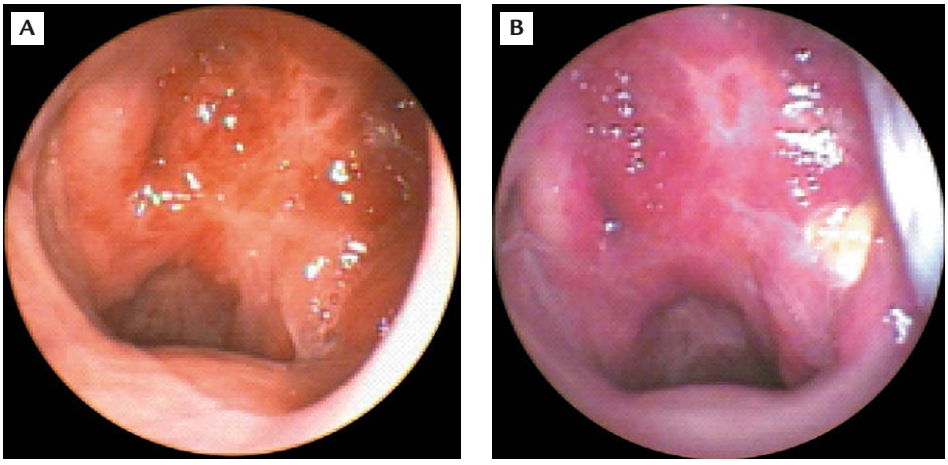

Figure 1. (A) Nasal endoscopy shows a heterogeneously reddish, smooth-surfaced exophytic tumor in the nasopharynx. (B) The lesion remained in place without progression over the 3-year follow-up period.

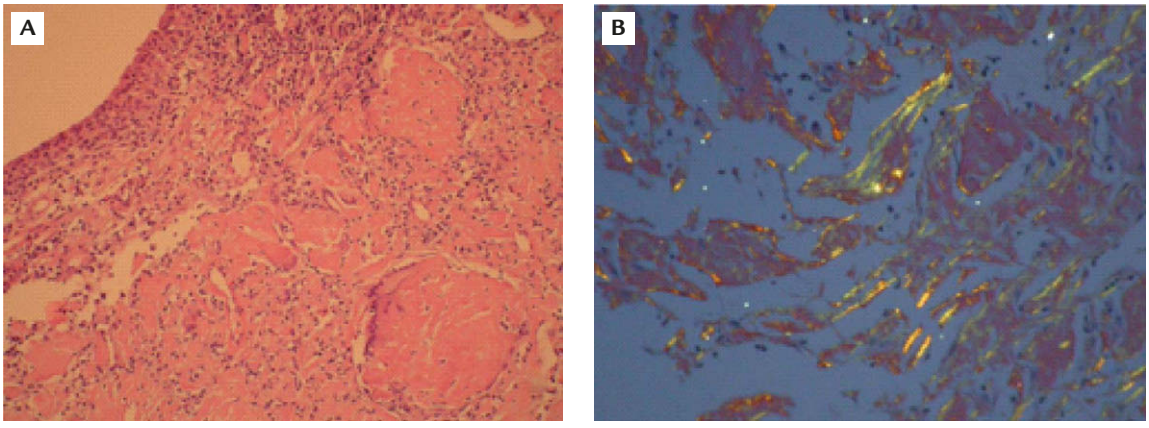

Figure 2. (A) Routine light microscopy shows deposition of lobules of an eosinophilic amorphous substance with encasement of blood vessels in submucosal connective tissue (hematoxylin & eosin, 25×). (B) Polarized-light microscopy shows the amorphous substance with an apple-green birefringence after staining with Congo red (25×).

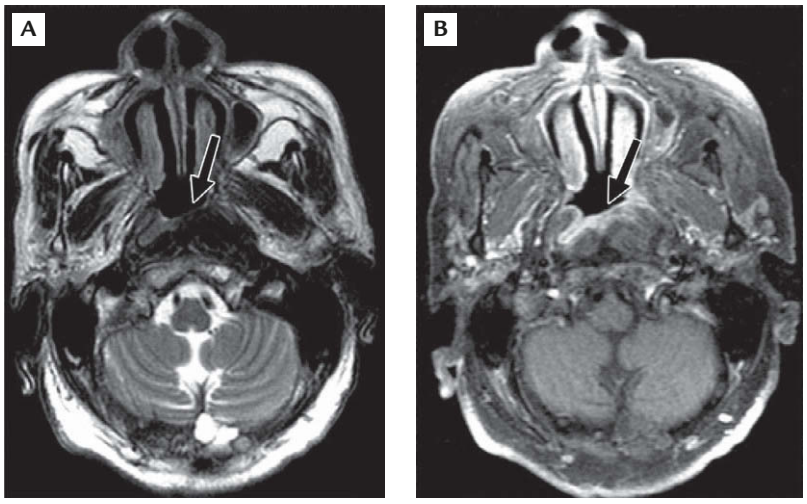

Figure 3. (A) Axial T2-weighted magnetic resonance imaging shows a hypointense, submucosal soft-tissue mass in the nasopharynx (arrow). (B) Axial gadolinium-enhanced T1-weighted magnetic resonance imaging shows heterogeneous enhancement of the lesion, mainly at the left aspect of the nasopharynx (arrow).

under the final diagnosis of localized amyloidosis of the nasopharynx, this patient has undergone regular follow-up at our outpatient clinic for more than 3 years without progression of local disease (Figure 1B) or development of systemic symptoms.

Discussion

Amyloidosis refers to diseases characterized by extracellular eosinophilic deposition of insoluble polymeric fibrillar proteins in tissues and organs. More than 25 distinct biochemical forms of precursor proteins have been identified, many of which circulate as constituents of plasma. Fibril formation is also associated with codeposition of nonfibrillar substances including proteoglycans, glycoprotein, serum amyloid P-component, and apolipoprotein E. Clinically, amyloidosis can be categorized as primary, when associated with plasma cell dyscrasia, or secondary, when occurring as a complication of an underlying disease in which there is ongoing or recurrent inflammation.[6] Heredofamilial amyloidoses comprise a heterogeneous group of dominantly inherited disorders with several distinct patterns of organ involvement. Amyloidosis of the upper aerodigestive tract generally behaves as a benign, localized condition, with the larynx being the most common site of amyloid deposition.[4] The majority of patients with head and neck amyloidosis have no underlying chronic systemic disease (i.e. primary form). Nasal or nasopharyngeal amyloidosis is a very rare condition with few case reports seen in the English scientific literature. Both sexes may be affected, with a great variation in age of disease onset (8–86 years old). The presenting symptoms consist of nasal obstruction, recurrent epistaxis, postnasal drip and ear problems due to eustachian tube obstruction with resultant middle ear effusion.[7] Occasionally, it may manifest as a clinical picture simulating an apparent malignancy with cervical nodal metastasis.[8] Grossly, the appearance has been described as a yellowish or whitish polypoid, firm mass.

The diagnosis of amyloidosis can be ascertained only by tissue biopsy, although a detailed history and systematic review of clinical manifestations might be suggestive of this condition. For patients with single organ involvement, a direct biopsy on the clinically involved site is recommended. In these patients, it is less likely that biopsies of unaffected tissues will reveal amyloids.[9] However, due to marked differences in prognosis between systemic and localized types, it is still necessary to differentiate by performing aspiration biopsy of subcutaneous fat, or a rectal biopsy. The amyloid deposits appear as amorphous hyaline material on light microscopy. On Congo red staining, green birefringence is revealed under polarized light, and electron microscopy shows 8–10-nm wide, straight, and unbranching fibrils.

There are no specific features on imaging studies of nasopharyngeal amyloidosis. Usually, computed tomography and/or MRI are performed. Computed tomography scans demonstrate focal amyloidosis as a well-defined, submucosal, homogeneous, hyperdense, soft tissue mass in association with calcifications.[10] Following administration of a contrast agent, the lesion exhibits slight or no enhancement. A "fluffy" appearance of bones surrounding the lesion has been shown,

which is thought to result from an osteoblastic reaction provoked by submucosal deposition of amyloid fibrils.[11] MRI studies show a submucosal mass with low signal intensity in both T1- and T2-weighted images, and mild enhancement in postcontrast T1-weighted images. However, Motosugi et al reported a case of localized nasopharyngeal amyloidosis, which showed high signal intensity on T2-weighted images and marked early enhancement in the periphery of the mass on dynamic contrast-enhanced MRI.[12] This phenomenon was attributed to plasmacyte infiltration, which occasionally occurs with amyloidosis, leading to hypervascularity.

Currently, there is no universally effective, specific therapy for systemic amyloidosis. Treatment generally varies with different types of amyloidosis and is aimed at the underlying primary disorders. It has previously been shown that regression of symptoms can occur as well as a decrease in amyloid burden following successful treatment of underlying disorders.[13] For localized amyloidosis of the nasopharynx, surgical resection is usually chosen as the treatment modality for symptomatic relief. However, the extent of surgical excision has changed from radical excision to a more conservative approach. The rationale behind this alteration is that a conservative surgical approach may be associated with a slower rate of recurrence.[14] Unfortunately, failure to prevent recurrence by means of surgical excision has been found in the majority of case reports. Simpson et al have suggested a reduction in the recurrence rate following laser resection.[15] Emerging treatment approaches employing agents that disrupt fibril formation, destabilize amyloid deposits, or interfere with interaction between amyloidogenic proteins and accessory molecules have shown promising results in animal models, and clinical applications are underway.[16] Currently, there are no reports showing progression of localized amyloidosis to the systemic form. In addition, a survival benefit from surgical excision of nasopharyngeal amyloidosis has not been demonstrated. Finally, complete removal of amyloid tumors in the nasopharynx may greatly impair normal physiological functions. For the above reasons, careful observation with regular follow-up by nasal endoscopy and imaging studies is a reasonable therapeutic option.

In conclusion, amyloidosis is a rarely encountered entity in the nasopharyngeal region. Most cases of amyloidosis manifest initially as nonspecific symptoms and signs. A definitive diagnosis can be established via biopsy with adequate pathological analysis. Radiographical studies can aid in delineating the local extent of disease and observation alone can be instituted safely in selected patients.

References

1. Westermark P, Benson MD, Buxbaum JN, Cohen AS, Frangione B, Ikeda S, Masters CL, et al. Amyloid: toward terminology clarification. Report from the Nomenclature Committee of the International Society of Amyloidosis. *Amyloid* 2005;12: 1–4.
2. Merlini G, Bellotti V. Molecular mechanisms of amyloidosis. *N Engl J Med* 2003;349:583–96.
3. Malek RS, Wahner-Roedler DL, Gertz MA, Kyle RA. Primary localized amyloidosis of the bladder: experience with dimethyl sulfoxide therapy. *J Urol* 2002;168:1018–20.
4. Pribitkin E, Friedman O, O'Hara B, Cunnane MF, Levi D, Rosen M, Keane WM, et al. Amyloidosis of the upper aerodigestive tract. *Laryngoscope* 2003;113:2095–101.
5. Panda NK, Saravanan K, Purushotaman GP, Gurunathan RK, Mahesha V. Localized amyloidosis masquerading as nasopharyngeal tumor: a review. *Am J Otolaryngol* 2007;28:208–11.
6. Lachmann HJ, Goodman HJ, Gilbertson JA, Gallimore JR, Sabin CA, Gillmore JD, Hawkins PN. Natural history and outcome in systemic AA amyloidosis. *N Engl J Med* 2007;356: 2361–71.
7. Patel A, Pambuccian S, Maisel R. Nasopharyngeal amyloidosis. *Am J Otolaryngol* 2002;23:308–11.
8. Zhuang YL, Tsai TL, Lin CZ. Localized amyloid deposition in the nasopharynx and neck, mimicking nasopharyngeal carcinoma with neck metastasis. *J Chin Med Assoc* 2005;68:142–5.
9. Andrews TR, Colon-Otero G, Calamia KT, Menke DM, Boylan KB, Kyle RA. Utility of subcutaneous fat aspiration for diagnosing amyloidosis in patients with isolated peripheral neuropathy. *Mayo Clin Proc* 2002;77:1287–90.
10. Gean-Marton AD, Kirsch CF, Vezina LG, Weber AL. Focal amyloidosis of the head and neck: evaluation with CT and MR imaging. *Radiology* 1991;181:521–5.
11. Chin SC, Fatterpeckar G, Kao CH, Chen CY, Som PM. Amyloidosis concurrently involving the sinonasal cavities and larynx. *AJNR Am J Neuroradiol* 2004;25:636–8.
12. Motosugi U, Ichikawa T, Araki T, Endo S, Masuyama K, Nakazawa T. Localized nasopharyngeal amyloidosis with remarkable early enhancement on dynamic contrast-enhanced MR imaging. *Eur Radiol* 2007;17:852–3.
13. Raymond AK, Sneige N, Batsakis JG. Amyloidosis in the upper aerodigestive tracts. *Ann Otol Rhinol Laryngol* 1992;101: 794–6.
14. Lesserman JA FD. Endoscopic treatment of amyloidosis of the nasopharynx. *Am J Rhinol* 1995;9:43–7.
15. Simpson GT 2nd, Strong MS, Skinner M, Cohen AS. Localized amyloidosis of the head and neck and upper aerodigestive and lower respiratory tracts. *Ann Otol Rhinol Laryngol* 1984;93:374–9.
16. Lachmann HJ, Hawkins PN. Novel pharmacological strategies in amyloidosis. *Nephron Clin Pract* 2003;94:c85–8.