The Journal of Laryngology & Otology (2006), ***120***, *778–780.*

doi:10.1017/S0022215106002155
Printed in the United Kingdom
First published online 25 July 2006

Clinical Record

Familial systemic amyloidosis associated with bilateral sensorineural hearing loss and bilateral facial palsies

R Hornigold, A V Patel, V M M Ward, A F O'Connor

Abstract

The Finnish type of familial amyloid polyneuropathy due to variant gelsolin is a rare form of familial amyloidosis. The subtype was first described in 1969 and is characterized by progressive cranial neuropathies, corneal lattice dystrophy and distal sensorimotor dysfunction. It is extremely uncommon, with only two families known to be affected in the UK. We discuss the case of a 70-year-old woman who presented with bilateral facial nerve palsies, bilateral sensorineural hearing loss and Finnish type familial hereditary amyloidosis. A literature search of the Medline database (1966–2005) was performed, using the keywords 'amyloid', 'hearing loss' and 'facial palsy'; however, this association appears to be a novel finding. We review the current literature and discuss otorhinolaryngological presentations of amyloidosis.

Key words: Amyloidosis; Finnish Type Familial Amyloid Neuropathy; Hearing Loss; Sensorineural Hearing Loss; Facial Paralysis

Introduction

Amyloidosis describes the extracellular deposition of abnormal fibrillar protein and encompasses a heterogeneous group of disorders. Deposits are mainly composed of protein fibrils, whose peptide subunits differ in the various forms of the disease. Amyloidosis may be hereditary or acquired and deposits may be focal or systemic in their distribution. Small deposits of amyloid within the joints, heart and vasculature accompany normal ageing and are usually asymptomatic.

Amyloidosis becomes problematic when the abnormal protein leads to disruption of the structure and function of affected tissues. Localized deposition of amyloid is associated with common disorders such as Alzheimer's disease and type II diabetes. Systemic amyloidosis may affect virtually any organ system and can be reactive, acquired or genetically inherited.

The most common form of hereditary systemic amyloidosis is familial amyloid polyneuropathy (FAP). This encompasses four autosomal, dominantly inherited subtypes with point mutations of the amyloid transthyretin protein (ATTR), a plasma protein consisting of 127 amino acids. We discuss a patient with the Finnish type of FAP (type IV), due to variant gelsolin, resulting from a point mutation at amino acid 187 (G654A or G654T).

Type IV FAP was first described in 1969[1] and is characterized by progressive cranial neuropathies, corneal lattice dystrophy and distal sensorimotor neuropathy without autonomic dysfunction. This type has been reported primarily in the Finnish population[1,2] and there are only two families known to be affected in the United Kingdom (H Lachman, personal communication). Onset is often within the fourth decade, with symptoms worsening with age. Gelsolin amyloid is deposited in vessel walls and perineural sheaths, leading to axonal loss; nerve roots appear to be more severely affected than distal nerves.[3] A literature search of the Medline database between 1966 and 2005, using the keywords 'amyloid', 'hearing loss' and 'facial palsy', was performed. Although facial paralysis has been reported in association with the Finnish type of FAP,[4] it has not been previously reported with bilateral sensorineural hearing loss. Sensorineural hearing loss has been previously reported in association with a new variant at the ATTR gene in position 44.[5]

Case report

A 70-year-old Ashkenazi Jewish woman with progressive, bilateral hearing loss presented to our department for hearing rehabilitation. She was known to suffer from familial systemic amyloidosis of the variant gelsolin type (Finnish type). She had initially presented with impaired hearing 22 years previously, at which time audiometry had demonstrated a mild, bilateral, high frequency sensorineural hearing loss.

Audiometry at current presentation showed moderate to severe, bilateral hearing loss, with a right-sided threshold of 60 dB across all frequencies and a left-sided loss of 70 dB over 250–4000 Hz and a 100 dB loss at 8000 Hz (Figure 1). Stapedial reflexes were intact, indicating a recruiting hearing loss and possible cochlear pathology. The patient was managing adequately with bilateral hearing aids, and there was no indication at the time to consider cochlear implantation.

In addition, the patient also suffered from four additional cranial nerve palsies. She had bilateral lower motor neurone facial nerve weakness (House–Brackman

From the Department of Otolaryngology, Guy's and St Thomas' Hospitals NHS Trust, London, UK.
Accepted for publication: 23 February 2006.

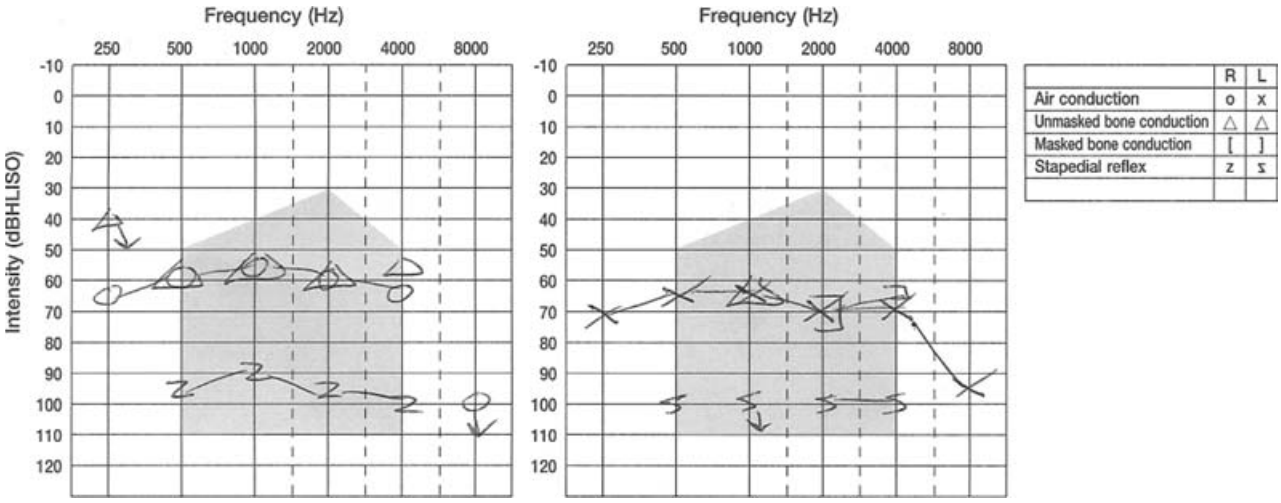

FIG. 1
Pure tone audiogram demonstrating moderate to severe bilateral hearing loss, with intact stapedial reflexes.

grade IV) that had deteriorated progressively over the last 26 years, limitation of down-gaze, patchy decreased sensation in the distribution of the maxillary division of the right trigeminal nerve, and a left hypoglossal nerve palsy. Examination of both the fundi and pupils was normal and no nystagmus was elicited. Neurological examination revealed loss of vibration sense in the lower limbs, diminished sensation affecting the hands and the back of both legs, and mild ataxia. She was also noted to have cutis laxa, particularly around the head and neck. Investigations in the past had shown no abnormality and a magnetic resonance imaging (MRI) scan of the brain was normal, with no posterior cranial fossa pathology.

The patient had a strong family history, with similar symptoms. Her paternal grandmother was reported to have had a 'twisted face' and her father suffered from bilateral facial nerve palsies and ataxia. Two sisters were also affected, one with bilateral facial nerve palsies, ptosis and external ocular weakness and the other with unilateral facial nerve palsy. One sister had undergone genetic testing, which had identified a mutation in gelsolin, and a diagnosis was made of hereditary systemic amyloidosis of the Finnish type. Neither of her sisters were thought to suffer from hearing loss and, to our knowledge, had not undergone audiological investigation.

Discussion

The Finnish type of familial amyloid polyneuropathy is rare in countries outside Scandinavia, and only two affected families are known in the United Kingdom. It is interesting that this case occurred in an individual of Ashkenazi Jewish descent, which has been associated with other autosomal recessive genetic disorders. Common manifestations of FAP are carpal tunnel syndrome, autonomic neuropathy and peripheral neuropathies.[6] Facial nerve palsies as a result of amyloidosis are rare but have been reported occasionally in focal amyloidosis,[7] systemic amyloidosis[8] and as part of Finnish type FAP.[5] Sensorineural hearing loss associated with deposition of amyloid in the cochlea has not previously been reported in the literature in association with this syndrome.

This case report describes a patient with bilateral facial palsies (House–Brackman grade IV) and intact stapedial reflexes, which may suggest VIIth nerve amyloid deposition distal to the nerve to the stapedius. The flat pattern of the audiogram and marked recruitment may well suggest strial disease. This would support a diagnosis of multiple pathology, with deposits in the cochlea in addition to those in the VIIth nerve in the facial canal, or there may be deposits within the cochlear nerve which are not disturbing facial nerve function at this point.

Currently, the only effective intervention in familial amyloid polyneuropathy is liver transplantation.[6] This is proposed as a curative treatment of FAP, and, in the majority of cases reported so far, has resulted in an improvement in general condition and a stabilization of all neuropathy. At present, the benefit–risk ratio seems acceptable when the procedure is performed early in the course of the disease. With time, the gene responsible for FAP may be targeted in gene therapy. At presentation, our patient was managing adequately with digital hearing aids, and no further intervention was required at the time. Like other situations in which facial nerve function is compromised by extrinsic pressure, good outcomes can be achieved by prompt decompression; however, this was obviously inappropriate in this case as the facial palsies had been present for over 20 years.

- **The Finnish type of familial amyloid polyneuropathy due to variant gelsolin is a rare form of familial amyloidosis**
- **This subtype was first described in 1969 and is characterized by progressive cranial neuropathies, corneal lattice dystrophy and distal sensorimotor dysfunction**
- **This paper reports the case of a 70-year-old woman who presented with bilateral facial nerve palsies, bilateral sensorineural hearing loss and Finnish type familial hereditary amyloidosis**

https://doi.org/10.1017/S0022215106002155 Published online by Cambridge University Press

Amyloidosis may present to the ENT department with symptoms due to localized deposits in the head and neck, which can involve the orbit, sinuses, nasopharynx, oral cavity, salivary glands and larynx.[8] Focal deposits of amyloid in the nasopharynx have been reported in association with conductive hearing loss,[9] as have focal deposits on the tympanic membrane in association with reactive amyloidosis.[10] Amyloidosis is a condition that is an almost inevitable consequence of ageing, and the familial amyloid polyneuropathies tend to present in the middle-aged population. It should therefore be considered in the differential diagnosis of middle-aged and elderly patients presenting with unexplained or multiple cranial nerve neuropathies.

References

1 Meretoja J. Familial systemic paramyloidosis with lattice dystrophy of the cornea, progressive cranial neuropathy, skin changes and various internal symptoms. *Ann Clin Res* 1969;**1**:314–24
2 Meretoja J. Genetic aspects of familial amyloidosis with corneal lattice dystrophy and cranial neuropathy. *Clin Genet* 1973;**4**:173–85
3 Kiuru-Enari S, Somer H, Seppalainen AM, Notkola IL, Haltia M. Neuromuscular pathology in hereditary gelsolin amyloidosis. *J Neuropath Exp Neurol* 2002;**61**:565–71
4 Darras BT, Adelman LS, Mora JS, Bodziner RA, Munsat TL. Familial amyloidosis with cranial neuropathy and corneal lattice dystrophy. *Neurology* 1986;**36**:432–5
5 Klein CJ, Nakumura M, Jacobson DR, Lacy MQ, Benson MD, Petersen RC. Transthyretin amyloidosis (serine 44) with headache, hearing loss, and peripheral neuropathy. *Neurology* 1998;**51**:1462–4
6 Plante-Bordeneuve V, Said G. Transthyretin related familial amyloid polyneuropathy. *Curr Opin Neurol* 2000;**13**:569–73
7 Massey EW, Massey JM. Facial diplegia due to amyloidosis. *South Med J* 1986;**79**:1458–9
8 Braganza RA, Tien R, Hoffman HT, Haghighi PH. Amyloid of the facial nerve. *Laryngoscope* 1992;**102**:1372–6
9 Patel A, Pambuccian S, Maisel R. Nasopharyngeal amyloidosis. *Am J Otolaryngol* 2002;**23**:308–11
10 Korzets A, Ben-Tovim R, Zohar Y, Zevin D. Amyloidosis of the middle ear in a chronically hemodialyzed patient. *Isr J Med Sci* 1990;**26**:209–11

Address for correspondence:
Mr A Fitzgerald O'Connor,
Department of Otolaryngology,
Guy's and St Thomas' Hospitals NHS Trust,
London SE1 9RT, UK.

Fax: +44 207 9558878
E-mail: r_hornigold@yahoo.com

Mr A F O'Connor takes responsibility for the integrity of the content of the paper.
Competing interests: None declared