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A rare case of dysphagia: hypopharyngeal amyloidosis masquerading as a post-cricoid tumour

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Abstract
Amyloidoses are a group of disorders in which deposition of abnormal amounts of protein complexes (amyloid) occurs in a variety of tissues. The upper aerodigestive tract may be affected, particularly the larynx, but hypopharyngeal involvement is rarely reported. We present a unique case of amyloidosis of the post-cricoid region causing dysphagia.

This case report highlights the need for otolaryngologists to consider the possibility of submucosal amyloid deposition, in the absence of mucosal lesions, in patients who present with dysphagia secondary to an obstructive lesion of the post cricoid region.

Key words: Amyloid; Pharynx; Dysphagia

Case report

A 56-year-old lady, was referred to our ENT department with a year's history of worsening dysphagia, weight loss, increasing pain on swallowing and eventually the inability to swallow her own saliva resulting in frequent choking attacks. Her past medical history included seronegative polyarthritis over the last two years. Initial clinical examination demonstrated an emacitated lady with limited mouth opening, and swollen ankles, wrists and shoulders. No lymphadenopathy was found. She had been investigated locally with a barium swallow six months previously which demonstrated no mucosal abnormality of her oesophagus. Her symptoms persisted and subsequent flexible nasendoscopy revealed pooling of saliva and fullness of the tongue base and hypopharynx. Her vocal folds were fully mobile.

A follow-up barium swallow and computed tomography (CT) scan of the neck were arranged. The barium swallow this time demonstrated post-cricoid obstruction suggestive, but not characteristic, of a tumour. The CT scan revealed asymmetrical, yet concentric narrowing and generalized soft tissue thickening of the oesophagus from the level of the hypopharynx to the thoracic inlet (Figure 1) suspected to be an extrinsic lesion consistent with a neoplasm. A flexible upper gastrointestinal endoscopy under sedation was attempted but failed due to impassibility of the endoscope into the upper oesophagus beyond the level of the folds. She was referred, therefore, for direct rigid laryngoscopy, pharyngoscopy and upper oesophagoscopy. This proved technically difficult owing to limited mouth opening and rigidity of the tissues. The tongue base and posterior hypopharynx were biopsied deeply as the mucosa looked normal.

The hypopharyngeal biopsies revealed diffuse connective tissue thickening and the specimens stained positive with Congo Red. Plasma viscosity was persistently low and a normochromic, normocytic anaemia was present. Serum electrolytes, liver and thyroid function, autoimmune profile, angiotensin-converting enyzme and cortisol were all normal as were her chest X-ray, electrocardiogram and echocardiogram. Urinary Bence-Jones proteins were present and serum and urine electrophoresis with iso-electric

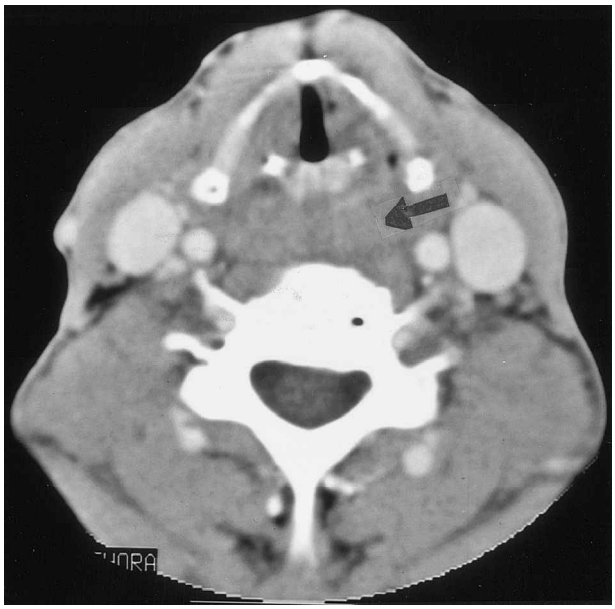

Fig. 1
CT scan of neck showing occlusive hypopharyngeal intrinsic mass.

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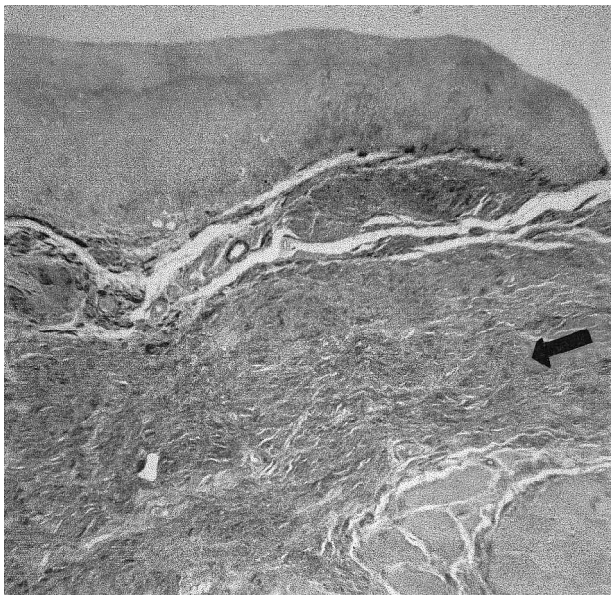

FIG. 2

Section of hypopharyngeal biopsy demonstrating marked amorphous sub-mucosal thickening with positive staining using 'amyloid P' immunohistochemistry ×100.

focusing revealed an abnormal band of kappa light-chains with a panhypoglobulinaemia. Bone marrow aspirate and trephine were performed revealing a monoclonal proliferation of plasma cells. Her diagnosis was therefore likely to be AL-type amyloidosis secondary to myeloma. Confirmation of diagnosis was achieved using amyloid P immunohistochemistry (Figure 2). Rectal biopsy provided further evidence of amyloid deposition. The patient was referred to the National Amyloidosis Centre, (Royal Free and University College Medical School, UCL) having been treated with analgesia, hydration and percutaneous gastrostomy for feeding. She had a serum amyloid P (SAP) scan performed which was able to quantify and localize the extent of her amyloidosis to the soft tissues of her joints, hypopharynx and elsewhere along her gastrointestinal tract. Her other organ systems appeared spared. She is being treated locally with a six-episode course of CVAMP chemotherapy for her myeloma with a good prognosis of progression halting, and a 50 per cent chance of regression of the amyloid deposits, noticable at one year.

Discussion

Amyloidoses are a group of abnormal tissue-damaging protein deposition disorders. Amyloid proteins are non-fibrillar SAP proteins (produced in all inflammatory reactions), linked to fibrillar components derived principally from immunoglobulin light-chain fragments (AL) or serum amyloid A protens (AA). It is these fibrillar components by which the amyloidosis is classified.[1] The fibrillar components, in excess, form beta-pleated sheet secondary protein structures which, when bound to SAP, render it relatively insoluble and therefore it is deposited in soft tissue intercellular spaces rather than cleared. It particularly affects the perivascular spaces of smooth and striated muscle. Clinical manifestations are therefore wide and varied being either organ-specific or systemic.

The two main types of systemic amyloidosis are, as above, AL and AA; the former being up to three times more common resulting in 250–400 new cases per year in the UK. Up to 10 per cent of patients with myeloma will have AL. Up to five per cent of patients with chronic inflammatory conditions have AA. Diagnosis is classically made by tissue biopsy and histological staining with Congo Red which imparts a unique apple-green birefringence under polarized light. Chemical classification is performed using immunohistochemistry. Clinically a quantitative test for diagnosis and surveillance was pioneered in 1987 – SAP scintigraphy.

No drug as yet has been shown to disperse amyloid and so treatment is aimed aggressively at the underlying causative disease process, e.g. anti-inflammatories and chemotherapy or liver transplant in hereditary amyloidosis.[2,3]

Historically prognosis has been poor, although recently it has been found that in those patients whose underlying disease responds well to therapy, organ function has been stabilized and an estimated 50 per cent will demonstrate, clinically, signs of amyloid deposit regression.[3]

Amyloid may affect several structures of the upper aerodigestive tract, the larynx being the most commonly involved, and usually as localized disease.[4] Nasopharyngeal amyloid has also been reported.[5] Hypopharyngeal amylodosis presenting with *dysphagia* has not been reported in the literature. Symptoms arise from direct infiltration or from amyloid neuropathy. The most common presenting symptoms in amyloidosis are fatigue, weight loss, oedema and syncope.[6] Most cases of dysphagia in amyloidosis are secondary to macroglossia,[7] or oesophageal involvement.[8] Patients usually undergo multiple investigations as illustrated above. Barium swallow findings are variable and pseudo-tumoral changes of the proximal oesophagus have been described,[9] as exemplified by our case. Confirmation of diagnosis necessitates biopsy if only to rule out malignancy. The presentation here appeared to be hypopharyngeal obstruction. The concentric narrowing and generalized tissue thickening in the absence of notable mucosal pathology raised the possibility of amyloidosis. Initial histology indeed reported normal mucosa and if specific Congo Red stains had not been requested the diagnosis would easily have been missed.

Our diagnosis led to further appropriate and targeted investigations to elucidate the underlying cause, in this case myeloma. This case highlights the need for otolaryngologists to consider amyloidosis, in the absence of mucosal lesions, in patients who present with dysphagia.

References

1 Husby G, Araki S, Benditt EP, Benson MD, Cohen AS, Frangione B, *et al.* The 1990 guidelines for nomenclature and classification of amyloid and amyloidosis; In: Natvig JB, Forre O, Husby G, Husebekk A, Skogen B, Sletten K, *et al.* eds. *Amyloid and Amyloidosis* 6th International Symposium, Dordrecht, 1990; 813–6

2 Raymond KA, Sneige NS, Batsakis JG. Amyloidosis in the upper aerodigestive tracts. *Ann Otol Rhinol Laryngol* 1992;**101**:794–6

3 Pepys MB, Hawkins PN, Gillmore JD, Madhoo S. *Specialist Services in Amyloidosis in the Immnological Medicine Unit,* Imperial College School of Medicine. 1999

4 Lewis JE, Olsen KD, Kurtin PJ, Kyle RA. Laryngeal amyloidosis: a clinicopathologic and immunohistochemical review. *Otolaryngol Head Neck Surg* 1992;**106**:372–7

5 Mufarji AA, Busaba NY, Zaytoun GM, Feiner HD. Primary localised amyloidosis of the nose and paranasal sinuses: A case report with immunohistochemical observations and a review of the literature. *Am J Surg Pathol* 1990;**14**:370–83

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6 Finsterer J, Wogritsch C, Pokieser P, Vesely M, Ulrich W, Grisold W, *et al.* Light chain myeloma with oropharyngeal amyloidosis presenting as bulbar paralysis. *J Neurol Sci* 1997;**147**:205–8
7 Jennings GH. Uncommon disease onsets with dysphagia. *Practitioner* 1969;**202**:808–15
8 Burakoff R, Robinow A, Cohen AS. Esophageal manometry in familial amyloid polyneuropathy. *Am J Med* 1985;**79**:85–9
9 Busuttil A, More AIR, Jones DG. Amyloid deposits in the trachea and oseophagus: Ultrastructure confirmation. *Laryngoscope* 1996;**86**:850–6

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