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Primary amyloidosis of the larynx

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Abstract
The history, examination and operative findings of primary amyloidosis of the larynx are very suggestive of carcinoma, indicating the need for careful histological examination. Staining with Congo red shows a characteristic birefringence. Systemic amyloidosis may be present.

Key words: Laryngeal diseases; Amyloid

Introduction

The importance of this lesion lies in its possible confusion with invasive squamous cell carcinoma. There is a risk of either missing concomitant systemic amyloidosis or exhaustively investigating for this when it is not present through failure to appreciate the nature of the disease. Current classifications of amyloidosis are based on the biochemical nature of the protein subunits. We describe a case which highlights the role of birefringence from Congo red staining in confirming the diagnosis.

Case report

A 72-year-old man was referred with a three-week history of a sore throat, hoarseness and tightness in the area of the larynx. Otherwise he felt well with no weight loss, dysphagia or any other symptoms. He admitted to drinking two pints of beer and four whiskies per day as well as being a longstanding pipe smoker (4–5 oz per week). There was a past history of tobacco/alcohol amblyopia. He appeared cachectic but denied any weight loss. There was no evidence of lymphadenopathy on palpation of the neck. Examination by indirect laryngoscopy revealed a small mass in the supraglottis. A chest X-ray was normal. Computer tomography from the level of the hyoid bone down through the larynx in 5 mm contiguous slices revealed a right-sided supraglottic mass extending into the aryepiglottic fold and anteriorly across the midline through the pre-epiglottic space. There was no evidence of destruction of the underlying thyroid cartilage or lymph node enlargement.

Investigations

The outpatient findings were confirmed under general anaesthesia and biopsies taken from the left aryepiglottic fold. These were reported as consisting of pseudostratified respiratory-type columnar epithelium with underlying connective tissue containing mucous glands. There were extensive deposits of extracellular, amorphous, hyaline material, within the connective tissue and lying free, along with hyaline thickening of vessel walls. The specimens were stained with Congo Red and then viewed under polarized light. This showed focal light green birefringence, a staining characteristic highly suggestive of amyloid deposition. There was no evidence of any malignancy.

Further investigations were carried out to exclude systemic amyloidosis. The full blood count and differential count erythrocyte sedimentation rate (ESR) were normal, as were urea and electrolytes, liver function tests and the blood calcium level. No proteins were present in the urine. Protein electrophoresis of the blood showed a normal distribution of immunoglobulins.

Discussion

Aetiology and pathogenesis

Amyloidosis is a disorder of protein metabolism in which autologous proteins are deposited intracellularly as fibrils. Systemic amyloidosis occurs in four different clinical settings as shown in Table I (Pepys, 1987). Localized amyloidosis of the larynx is a rare condition (McAlpine and Fuller, 1964). Amyloid deposits in the larynx were, for a long time, confused with vocal fold nodules. It is now certain that the hyaline deposits in these common lesions of the vocal fold are of fibrin and other products of local blood exudation; they bear no relation to the rare amyloid (Michaels, 1984). A primary lesion localized to the larynx was first described in 1875 (Burow and Neumann, 1875) but despite many cases being described since then the real pathogenesis underlying the condition has not yet been fully elucidated.

The intracellular deposits of protein fibrils may be focal, localized to a particular tissue or organ, or distributed systemically. They rarely regress, instead tending to increase inexorably in size disrupting first the structure and then the function of the tissue in which they lie. It is rare for the larynx to be the first site of systemic amyloidosis (Briggs, 1961), but this should be

TABLE I
CLINICAL SETTINGS OF SYSTEMIC AMYLOIDOSIS (PEPYS, 1987)

(1)	As a complication of immunocyte dyscrasia; the fibrils are derived from immunoglobulin light chains and the constituent protein designated AL (A: amyloid, L: light chain)
(2)	Associated with chronic inflammatory or infectious disease; the fibrils (designated AA) are derived from the acute-phase reactant serum amyloid protein
(3)	As a familial disorder; fibrils derived from genetic variant forms of pre-albumin
(4)	In up to a quarter of aged individuals; fibrils derived from plasma pre-albumin

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excluded (Friedman, 1986) as it carries a grave prognosis for there is no effective therapy (Pepys, 1987). A case has been reported where systemic disease only became evident six years later (Talbot, 1990).

One would expect the ESR to be raised in generalized or secondary amyloidosis but in our case this was normal. Normal urea and electrolytes ruled out renal involvement and the normal protein electrophoresis excluded a myeloma. In addition, there were no Bence-Jones proteins present in the urine. This was an important finding as localized amyloidosis is occasionally a complication of the rare, primary extra-skeletal plasmacytoma, one of the most frequent sites of which is the larynx (Friedmann, 1986).

Histopathology

The most commonly used test is histological staining with Congo red. Amyloid deposits are congophilic and produce an apple-green birefringence when viewed between crossed Nicol's prisms. This must be distinguished from the pseudoamyloid so often found in vocal nodules. This, however, has no fibrillary substance and is composed of an amorphous granular degeneration of ground substance with collagen fibres sparsely interspersed between fibroblasts (Michaels and Hyams, 1979). Potassium permanganate can be used to distinguish the constituent proteins as amyloid ocute-phase (AA) protein dissolves whereas amyloid light chain (AL) is resistant and still seen in the section.

Management

Most evidence suggests that immune mechanisms are involved in the pathogenesis of human and experimental amyloidosis and it can complicate immune deficiency states. Substances which compromise the immune response such as steroids, immuno-suppressive agents and ionizing radiation can accelerate it (Friedmann, 1986).

Consequently, the treatment for primary localized amyloid of the larynx is surgical (Raymond *et al.*, 1992). This may be with the aid of a laser (McIlwain and Shepperd, 1986). A recent report has demonstrated the advantage of the carbon dioxide laser over the scalpel (Talbot, 1990). It is very slow growing, and even spontaneous regression is possible (Simpson *et al.*, 1984). Nevertheless, recurrence may become manifest after several years so long-term follow-up is necessary (Hardingham, 1987). In secondary amyloidosis abatement of the amyloid deposits may follow control of the promoting and underlying disease.

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