MMSG
CASE REPORT

Primary localised laryngeal amyloidosis - an atypical presentation

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Primary localised laryngeal amyloidosis is a rare disease that classically presents with dysphonia. We present a case of a 38-year-old woman who presented with a history of early morning haemoptysis, progressively worsening hoarseness and intermittent dysphagia. A bulky left false vocal cord was seen on examination. A computed tomography scan of the neck and trunk revealed thickening of the left side of the larynx with associated asymmetry. Direct laryngoscopy showed a round, well-circumscribed lesion on the left false vocal cord and histological examination of the lesion confirmed the presence of amyloid.

Systemic disease was ruled out and the patient was treated with endoscopic excision of the mass through carbon dioxide laser technology. The patient's symptoms improved and the patient is being followed up yearly to exclude disease recurrence. The report highlights the presentation, diagnosis and appropriate management of localised laryngeal amyloidosis.

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Introduction

Dysphonia, dysphagia and haemoptysis are common complaints in the ENT clinic, however localised amyloidosis causing this symptomatology is rare. This report describes the management of a patient with a benign disorder presenting with worrying symptoms.

Amyloidosis is a rare condition that progresses relatively slowly and constitutes a variety of heterogeneous disorders defined by abnormal deposits of extracellular fibrillar proteins. The deposition of amyloid in various organs and tissues around the body invariably causes organ dysfunction over time.[1]

Localized amyloidosis can be demonstrated in a single organ in the absence of systemic involvement and is typically benign in nature when isolated to an individual area in the head and neck region. Amyloid can be deposited at any laryngeal site however the true vocal cord is believed to be the most commonly affected.[2]

Case Presentation

A 38-year-old previously healthy woman presented to the Ear, Nose and Throat (ENT) department with a one-week history of early morning haemoptysis. The patient also complained of a six-month history of progressively worsening hoarseness and a shorter history of intermittent dysphagia. The patient, who previously smoked 20 cigarettes a day, initially attributed her hoarseness to smoking. The patient quit smoking in the three months before presentation, to no effect. Indirect laryngoscopy showed a bulky left false vocal cord. History and examination were otherwise unremarkable.

A computed tomography (CT) scan of the neck and trunk revealed thickening of the left side of the larynx with associated asymmetry (Figure 1, Figure 2). The thickening was characterised by loss of fat plane between the left side of the larynx and the thyroid cartilage anteriorly. A 7mm nodule straddling the longus colli muscles was observed, which was most likely in keeping with a Thornwaldt cyst. No abnormal enhancing of soft tissue and no loco-regional lymphadenopathy was noted. The base of tongue, parotid and submandibular glands appeared normal. No features of concern were observed elsewhere

Direct laryngoscopy revealed a round, well-circumscribed lesion on the left false vocal cord (Figure 3). The true vocal cord was visible underneath. Multiple biopsies were taken and sent for histology.

Histological examination of the left false vocal cord lesion showed the presence of amyloid. This was demonstrated by the staining of amorphous material with Congo red that displayed apple-green birefringence when viewed under high-intensity cross-polarised light. Amyloid deposits were present throughout. Vascular proliferation of stroma, which was covered by normal looking respiratory epithelium was also observed. Mild chronic inflammation with no evidence of atypia was noted.

Immunohistochemical staining of the amyloid deposits was performed using monospecific antibodies reactive with serum Amyloid A protein (SAA), apolipoprotein A1 (apoA1), Transthyretin (TTR) and with kappa and lambda immunoglobulin light chains. The amyloid stained with antibodies to lambda light chains. This confirmed amyloid of AL type (lambda subtype).

Figure 1 A CT scan of the neck showing thickening of the left side of the larynx. The arrow points towards the mass on the left false vocal cord.

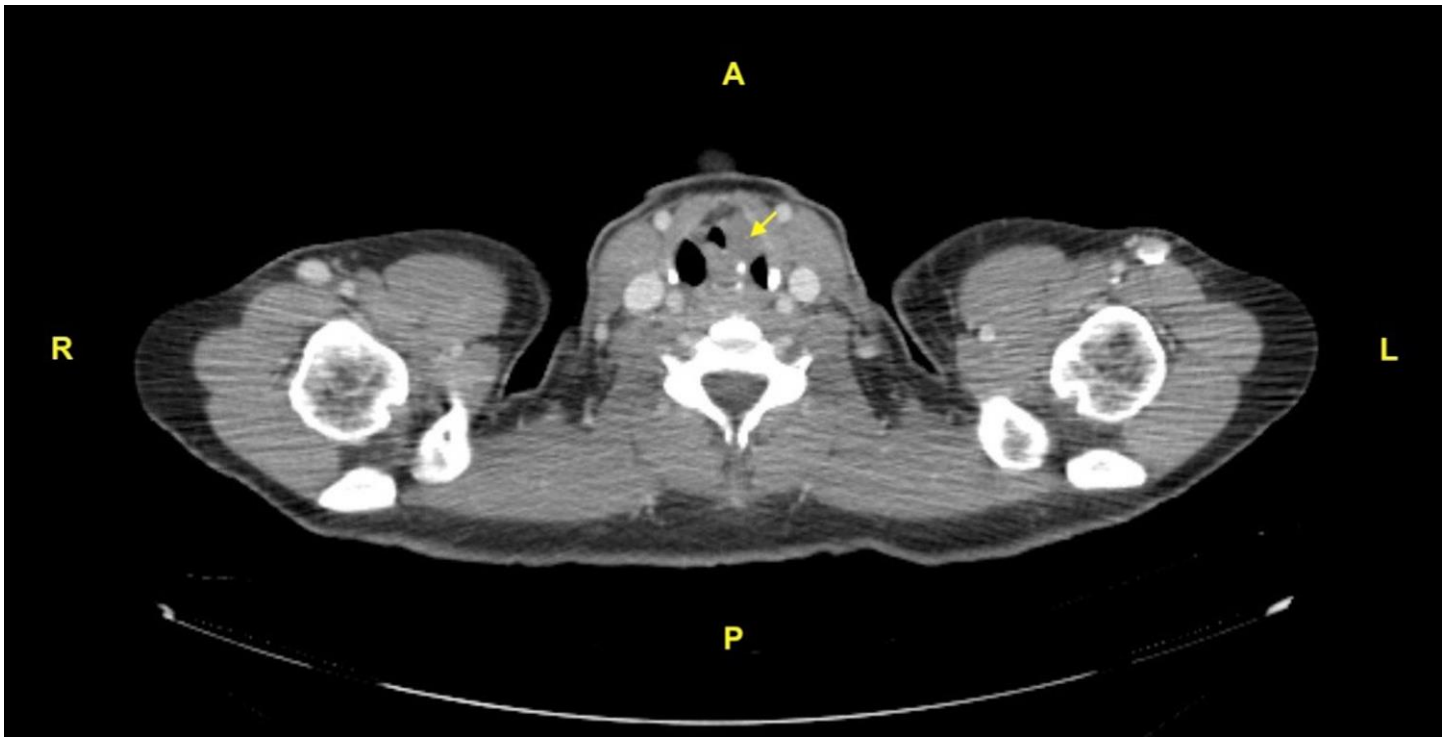
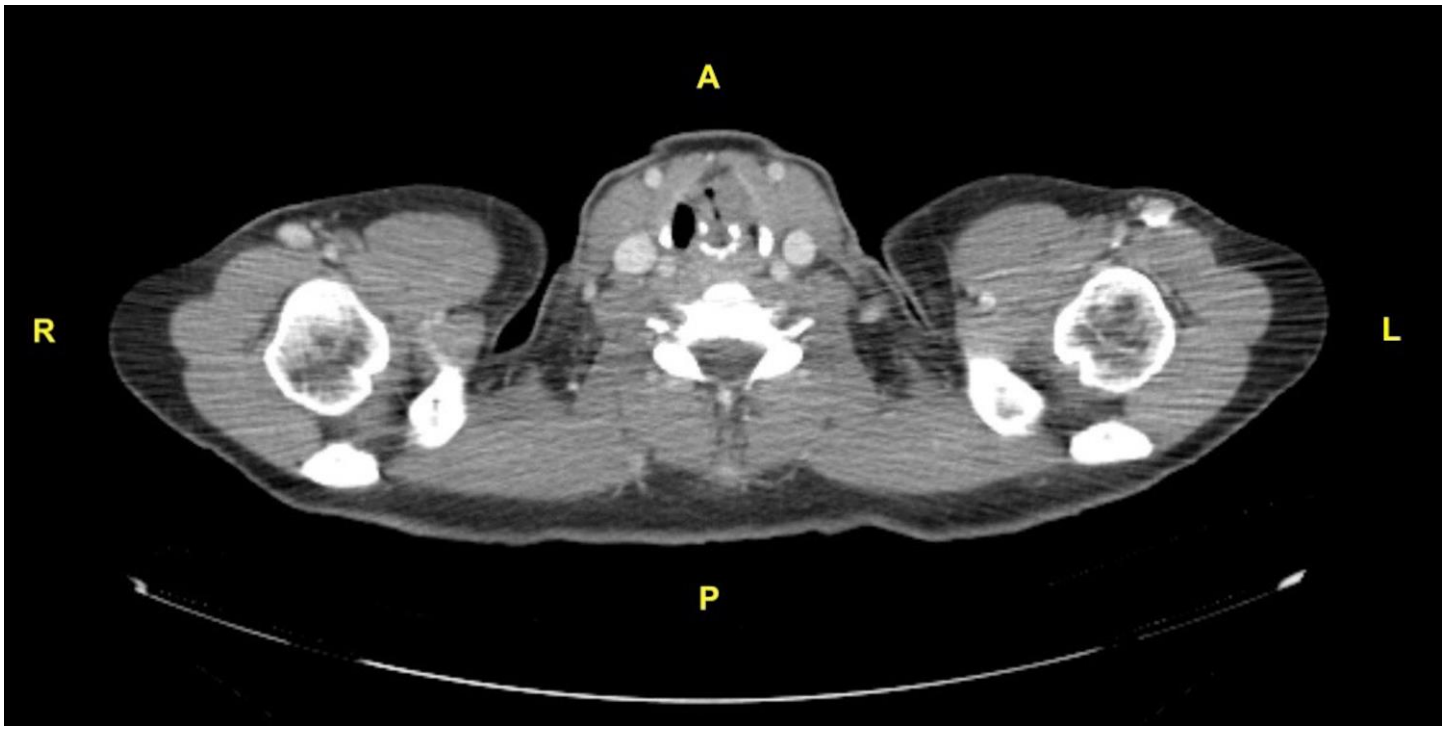


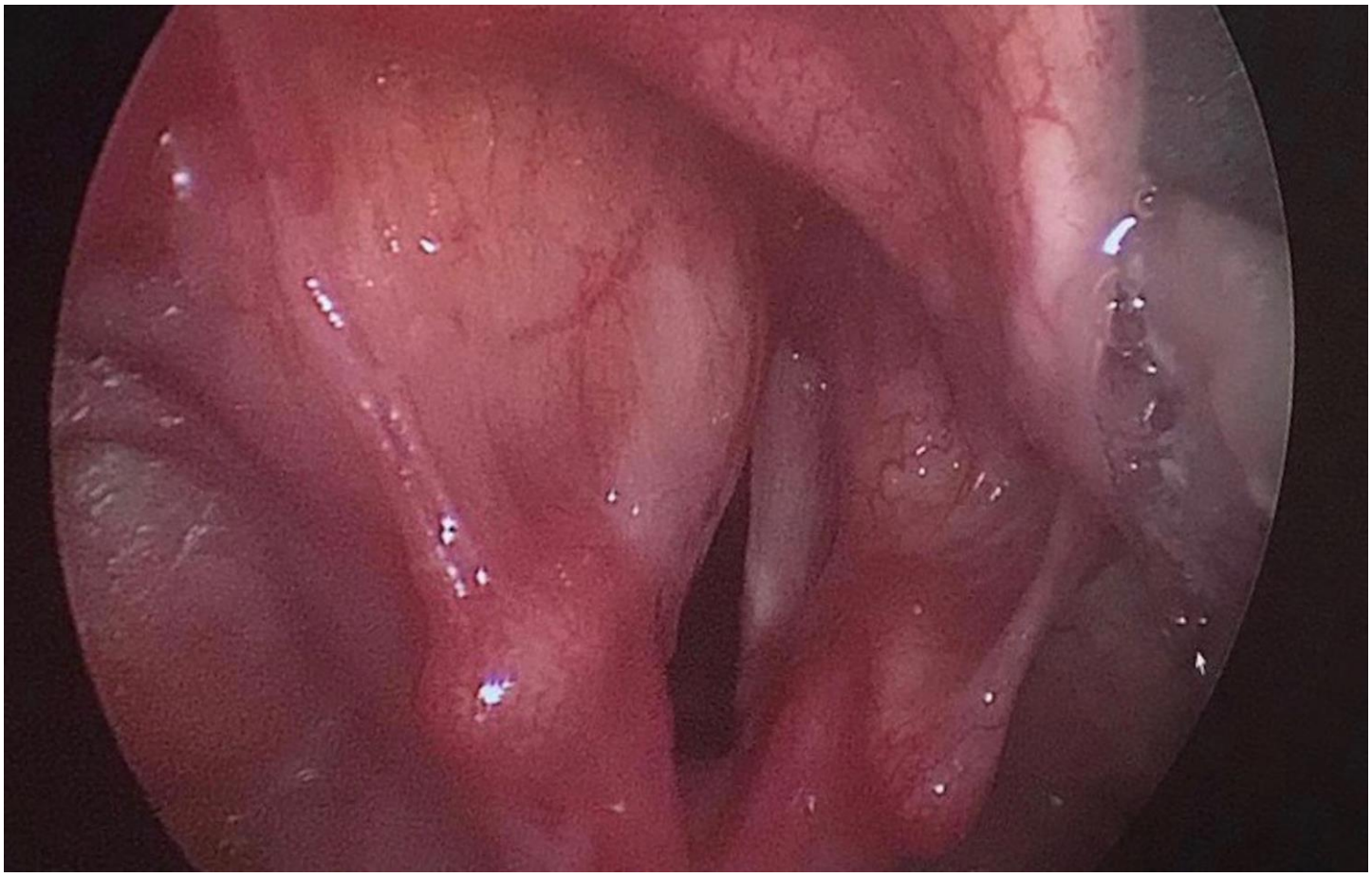
Figure 2 A CT scan of the neck showing thickening of the left side of the larynx with associated asymmetry



Serum Protein Electrophoresis showed no indication of an increase in free light chains, however an elevated kappa/lambda ratio was observed. A full blood count, renal profile, liver profile, serum paraproteins, CRP, serum albumin and NT-proBNP were within normal limits. An electrocardiogram (ECG) and an echocardiogram were normal with no evidence of cardiac amyloidosis. A bone marrow biopsy excluded an underlying plasma cell dyscrasia as there was no evidence of plasma cell clone. A CT scan of the thorax showed no thoracic involvement. Serum Amyloid P (SAP) scintigraphy was unremarkable. These investigations ruled out systemic amyloidosis.

The patient was diagnosed with localised laryngeal amyloidosis affecting the left false vocal cord. She was treated with endoscopic excision of the mass using carbon dioxide laser technology. The patient had an initial good response to treatment, however later complained about the development of a gravelly quality to her voice. Endoscopy showed a 0.5cm cyst overlying the left false vocal cord and was treated with a further two laser procedures. As a consequence to laser therapy, a granuloma was seen on follow up but this healed spontaneously. The symptoms resolved following the third laser procedure and the patient is being followed up once yearly.

Figure 3 Direct laryngoscopy showing thickening of the left false vocal cord.



Discussion

Primary localised amyloidosis of the larynx is very rare accounting for only 1% of benign laryngeal tumours.[3] It is characterised by the deposition of monoclonal light chains of the AL type.[4] Two theories have been described to give an explanation for the development of localised laryngeal amyloidosis. The first theory proposes that amyloid light chains are produced by plasma cell clones while the other theory is centred around the body's inability to remove light chain proteins leading to localized deposits.[5]

Amyloidosis typically presents non-specifically in patients aged 50 to 70 years old and has a preponderance for males over females with a ratio of 3:1.[5] In this case, our 38 year old female patient, presented with a sole nodule on the left false vocal cord. Other sites such as the orbits, the eyes and the salivary glands can also be affected. Submucosal deposits may be present in the oral cavity, stomatopharynx, nasopharynx, bronchotracheal tree and lungs as well as the nose, nasopharynx and paranasal cavities.[6]

Our patient presented with atypical symptoms. The most common presenting complaint in patients suffering from laryngeal amyloidosis is worsening hoarseness.[3] Symptoms such as cough and dyspnoea are also frequently observed, however dysphagia and haemoptysis are rarely reported.[3] Keeping in mind that laryngeal cancer can present similarly, a high index of clinical suspicion together with the appropriate investigations are needed to rule out the possibility of laryngeal cancer.[1]

Systemic involvement should be excluded and therefore causes of systemic disease such as rheumatic disease and tuberculosis must be ruled out. Typically, systemic amyloidosis involves the kidneys, affecting approximately 70% of patients, with nephrotic range proteinuria leading to renal failure in 50% of patients. It also affects the heart causing cardiomyopathy in around 60% of patients, manifesting as a thick-walled heart, low voltage ECG and pleural and pericardial effusions. Other forms of systemic involvement include cholestatic hepatopathy, peripheral and autonomic neuropathy, purpura and soft tissue infiltration, of which macroglossia is pathognomonic.[7]

Plasma cell dyscrasias, which include, Waldenström macroglobulinemia and multiple myeloma can also lead to amyloidosis and should therefore be looked for.[5] The build-up of abnormal amyloid protein leads to organ dysfunction. Therefore, in contrast to localised amyloidosis, systemic amyloidosis which affects various body organs, normally carries a very poor prognosis. Confirming the extent of amyloidosis guides management and serves to reassure the patient.[1]

The treatment of choice for localised laryngeal amyloidosis is surgery, ideally aided by laser technology. First line therapy involves endoscopic excision of the mass using carbon dioxide laser.[8] Spontaneous remission leaving no evidence of disease is possible however disease recurrence is a much more common outcome and therefore long-term follow up is advised for a minimum of 5 years.[3]

Key Messages

1. Primary localised laryngeal amyloidosis is a rare phenomenon that normally presents with hoarseness. However, physicians should be aware that it can also present with dysphagia and haemoptysis.
2. Hoarseness should not always be attributed to smoking and should be investigated to

rule out underlying pathology. Laryngeal amyloidosis should be considered as part of the differential diagnosis in patients presenting with persistent dysphonia.

3. Localised amyloidosis has a very high rate of recurrence and complications secondary to laser treatment may arise. Long-term follow up for a minimum of 5 years is therefore advised.
4. Localised laryngeal amyloidosis can present very similarly to laryngeal cancer. Physicians should have a reasonable degree of suspicion for both diagnoses and should confirm the diagnosis with a biopsy.
5. Localised and systemic amyloidosis have very different clinical outcomes, prognosis and management. Systemic involvement should therefore always be ruled out.

References

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