**Case Report**

**Rare Subtype of Localised Nasal Amyloidosis**

**Abstract**

**Introduction:** Localised amyloidosis is a rare finding in the nasal mucosa. Our objective was to present a case of nasal amyloidosis, illustrate the complexity of subtype analysis, and examine the evidence for management options.

**Methods:** Case note examination and literature review of nasal amyloidosis was undertaken using Pubmed and the Cochrane database.

**Results:** A patient presented with unilateral nasal obstruction and was found to have left sided nasal polyposis. Immunohistochemistry assisted the diagnosis of non-AA amyloid from the nasal biopsies. Investigations for systemic amyloidosis were negative.

**Conclusion:** This is the first documented case in the literature of localised nasal amyloid of non-AA subtype. Due to the rare presentation of this pathology there is limited data regarding optimal management to prevent recurrence.

**Keywords**

Nasal polyposis, Non-AA localised amyloidosis, nasal obstruction.

**Introduction**

Localised amyloidosis has been described in many diverse locations in the head and neck region including the salivary glands, eye, nose, paranasal sinuses, nasopharynx, oral cavity, pharynx, larynx, and tracheobronchial tree. 

It remains a rare diagnosis in the nasal cavity. In previously reported cases involving the nasal mucosa in which immunostaining was performed the subtype identified was Amyloid Light Chain (AL) amyloidosis. 

The definitive management of localised AL amyloidosis is not supported by high level evidence due to the small number of case reports and case series available. Presenting symptoms of localised amyloid deposits are related to the physical size and location of the mass and treatment is aimed at symptom relief. The prognosis of this form of the disease is excellent when compared with systemic amyloidosis. 

Conservative management, local and systemic steroids, debulking surgery and localised radiotherapy have been described in the past. Recurrence of localised nasal amyloidosis is frequently encountered as found in a recent review of reported cases. 

In our case report a detailed case note review was carried out including clinical presentation, examination, investigations, management and outcome. 

A qualitative review of the peer-reviewed literature in the English language reporting nasal amyloidosis was undertaken using Pubmed /Medline and the Cochrane database. The search terms included localised/systemic amyloidosis, non-AA amyloid and nasal/paranasal/sinonasal/ nasopharyngeal amyloid.

Our review focused on investigation modalities, histological subtypes, medical and surgical management, long-term outcomes and diagnostic advances in the last decade.

**Case report**

A 67 year old female presented to the ENT clinic with a one year history of nasal congestion and 2 episodes of epistaxis. She had a history of nasal trauma several years previously but no previous symptoms of rhinitis. She was found clinically to have left sided nasal obstruction caused by grade 3 fleshy polyps extending into the post-nasal space. She had no other relevant past medical history.

She underwent further investigation with a CT scan which identified left sided nasal polyposis containing areas of calcification. Biopsies were taken of this friable haemorrhagic left sided nasal mass at the time of debulking polypectomy and functional endoscopic sinus surgery.

The initial histological report was that of respiratory mucosa containing a heavy deposit of eosinophilic globules surrounded by multinucleate giant cells. On the basis of this she was referred to the haematology consultant and underwent clinical examination and serological investigations.
No further clinical abnormalities were identified. Her nasal symptoms returned 6 months postoperatively and she underwent a further CT which identified a recurrence of the nasal lesion. Her initial histology was reviewed and a diagnosis of amyloid was made based on Congo red staining with apple-green birefringence under polarised light. Figure 1-3.

She had further debulking surgery less than one year after her initial procedure, and histology again confirmed amyloid deposits.

She was referred to the UK National Amyloid Centre and further immunohistochemical staining of the histology specimens with serum amyloid A protein, and kappa and lambda immunoglobulin light chains were negative. This confirmed a diagnosis of non-AA type amyloid, which indicates that the possibility of AL amyloid can neither be excluded nor confirmed.

She was intensively investigated for evidence of systemic amyloid and none was found. Serum amyloid precursor (SAP) scintigraphy was negative and echocardiogram revealed no evidence of cardiac amyloid involvement. Serology for serum amyloid A, CRP, ESR, paraproteins, and free light chain ratio were all within the normal range.

Bone marrow had a normal appearance and showed no abnormal cell infiltration. In view of these results suggesting no systemic amyloid involvement she did not undergo treatment with chemotherapy. She continues to be closely monitored by the haematology and ENT departments.

**Discussion**

The term ‘amyloid’ was first applied to human tissue by Virchow in 1853 to describe the results of his experiments. It is defined as a pathological accumulation of insoluble β-pleated protein fibrils found mainly in the extracellular spaces of organs and tissues. The classical diagnostic appearance is due to affinity with Congo red staining and apple green birefringence when viewed with polarised light. The current nomenclature has moved away from the clinical terms of primary (idiopathic) and secondary (chronic inflammatory disease related) amyloidosis, and now requires determination of the chemical nature of the fibril protein.

Amyloid fibrils derived from immunoglobulin light chains indicates that the disease is AL amyloidosis. To date there are 27 amyloid fibril proteins. Immunohistochemistry staining with monospecific antibodies are used to determine the subtype. However there remains 20% of AL amyloid deposits which do not stain immunospecfically with the kappa or lambda light chains and are given the subtype non-AA amyloid, as AL cannot be excluded or confirmed by current techniques.

An essential component of the management of patients who are found to have isolated amyloid deposits on biopsy is a full investigation to rule out systemic involvement, due to the significant differences in management and prognosis of the localised and systemic forms of the disease. The prognosis of the most common type of systemic amyloidosis, AL, without chemotherapy treatment is 12 months. Techniques used to investigate systemic involvement include SAP scintigraphy, anterior abdominal wall or rectal biopsy, and echocardiogram, as well as haematological investigations.

Amyloidosis involving the nasal mucosa is a rare entity, and literature reports from 1928 to date have documented only 38 cases. 5 of these have been reported as systemic amyloidosis. Extensive literature review was carried out by Oluk et al. They reported that CT imaging has been used since 1984, and MRI since 2000. Immunohistochemistry was first described in nasal amyloid lesions in early 1990s. Recent advances in the immunohistochemical subtyping of
Rare Subtype of Localised Nasal Amyloidosis

amyloid has led to further understanding of the condition. Management of these lesions in the last decade is moving away from a purely surgical approach as the rate of recurrence despite surgical resection remains high.

From 2000 to 2012 we found from our literature review of localised nasal amyloidosis that 10 of 15 cases had documented surgical resection and there was recurrence in 4 of these.4, 15-18, 22-30 In 3 papers a conservative management approach was reported and no progression was found in these cases at last follow-up.16,24,28 Due to the rare presentation of this pathology there is limited data regarding optimal management to prevent recurrence. The small number of cases precludes the formation of evidence based protocols for either investigation modalities or management.

We have not found a previous reference to a nasal amyloid lesion of the non-AA subtype in those papers which have documented immunohistochemistry subtyping, and thus our case represents the first reported case in the English language of this subtype in the nasal mucosa.

Our case report of this uncommon nasal diagnosis aims to highlight the importance of prompt clinical and histological diagnosis. There is limited evidence in the literature on which management option will prevent recurrence of localised nasal amyloidosis, and this is an area where we await further research. The advances in immunohistochemical diagnostics in amyloid may hold the key to future treatment strategies.

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Conflict of Interest
All authors have no conflict of interest to declare. No extraneous funding was obtained.

Key Learning Points
• Localised amyloidosis is a rare diagnosis in the nose.
• Advances in immunohistochemical staining have allowed detailed subtyping.
• Accurate differentiation of localised disease from systemic amyloidosis is essential for optimal management.
• This is the first reported case of this amyloid subtype (non-AA amyloid) found in the nasal mucosa.
• Limited evidence in the literature exists regarding management strategies of these lesions which are known to recur despite surgical management.

References
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MCQ s
Stem A: Nasal Amyloidosis is an unusual diagnosis in nasal disease
Answer True or False to the following 5 statements:

a. The nasal cavity is the commonest subsite in the Head and Neck
b. Most cases are of the AA subtype
c. Surgery carries a higher risk of recurrence than conservative management
d. The localised form carries a better prognosis than the systemic form
e. Surgical treatment is carried out with curative intent

Stem B: Amyloid is defined as a pathological accumulation of insoluble β-pleated protein fibrils
Answer True or False to the following 5 statements:

a. Immunostaining in nasal amyloid has only been reported in the last 2 decades
b. Amyloid accumulates mainly intracellularly
c. The congo-staining appears red when viewed with polarised light
d. Non-AA subtype refers to AL amyloid deposits which do not stain immunospecifically with the kappa or lambda light chains
e. Non-Amyloid AL subtype refers to AL amyloid deposits which do not stain immunospecifically with the kappa or lambda light chains