

# Localized Sinonasal Amyloidosis

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## Abstract

Localized amyloidosis involving the nasal mucosa is rare, with only 38 published cases reported to date. We report a case of amyloidosis localized to the sinonasal tract. A 61-year-old man presented with a 1-year history of left-sided nasal obstruction. Endoscopic examination and computed tomography revealed the presence of a nasal mass originating from the left inferior turbinate. The patient subsequently underwent an examination under anesthesia and an excision biopsy of the nasal mass. Histology confirmed amyloidosis with no immunospecific stains. Systemic amyloidosis testing was negative, leading to a diagnosis of localized sinonasal amyloidosis of nonamyloid A (AA) subtype. To our knowledge, this is the second reported case of non-AA subtype of the sinonasal tract. The patient was managed conservatively and is currently under close follow-up.

## Keywords

localized, amyloidosis, sinonasal, nasopharyngeal, nasal

## Case Report

A 61-year-old Caucasian man presented to the otolaryngology clinic with a 1-year history of left nasal obstruction associated with copious green discharge and recurrent epistaxis. The patient denied any associated facial pain, facial numbness, or visual symptoms. There was also no history of weight loss, fevers, or night sweats. His medical history included hypertension, controlled on dual antihypertensive therapy, and an elevated body mass index of 38. He was a nonsmoker with minimal alcohol intake.

Flexible nasendoscopy in clinic revealed a substantial left-sided nasal mass. General examination and otoscopy were otherwise unremarkable. An urgent computed tomography (CT) of the paranasal sinuses demonstrated thickening of the posterior aspect of the left inferior turbinate, extending into the nasopharynx. The striking opacification of the maxillary sinus was considered secondary to middle meatal occlusion by the mass.

Due to the suspicious lesion, further imaging was requested. A CT scan of the chest, neck, abdomen, and pelvis was unremarkable. A magnetic resonance imaging was also organized after the initial diagnostic work-up which demonstrated similar findings to the

initial CT images (See Figure 1). An examination under anesthesia demonstrated a friable exophytic mass originating from the posterior aspects of the left inferior turbinate and extending through the choana into the nasopharynx. An excision biopsy of the nasal mass was undertaken for histological analysis. It exhibited large deposits of amorphous eosinophilic material and the presence of amyloid on Congo-red staining with apple-green birefringence when viewed with polarized light (See Figure 2). Immunohistochemistry was negative for serum amyloid A (SAA) protein and kappa and lambda immunoglobulin light chains.

The patient was referred to the U.K. National Amyloidosis Centre (NAC), where he was assessed for systemic disease. Investigations included full blood

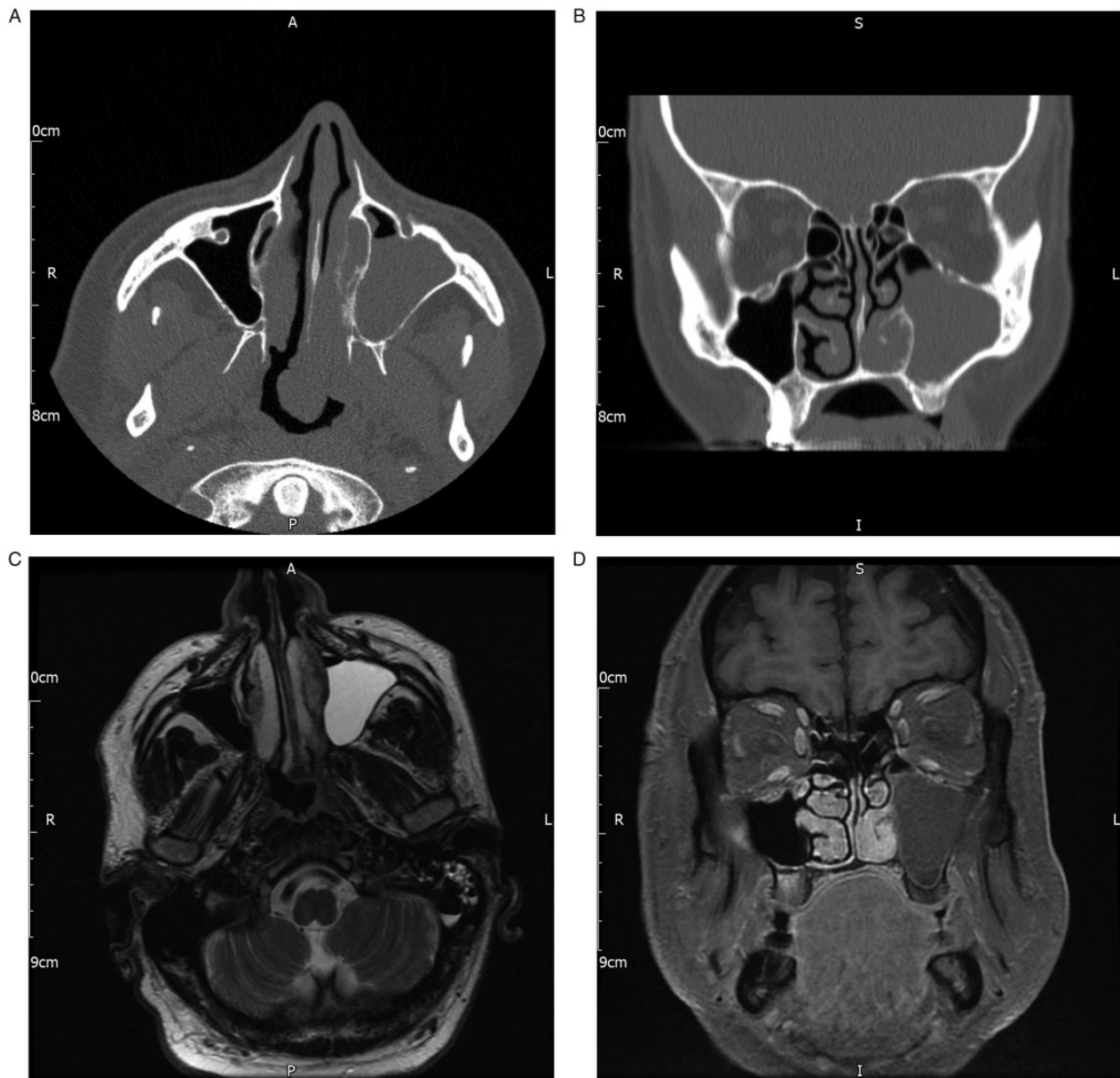
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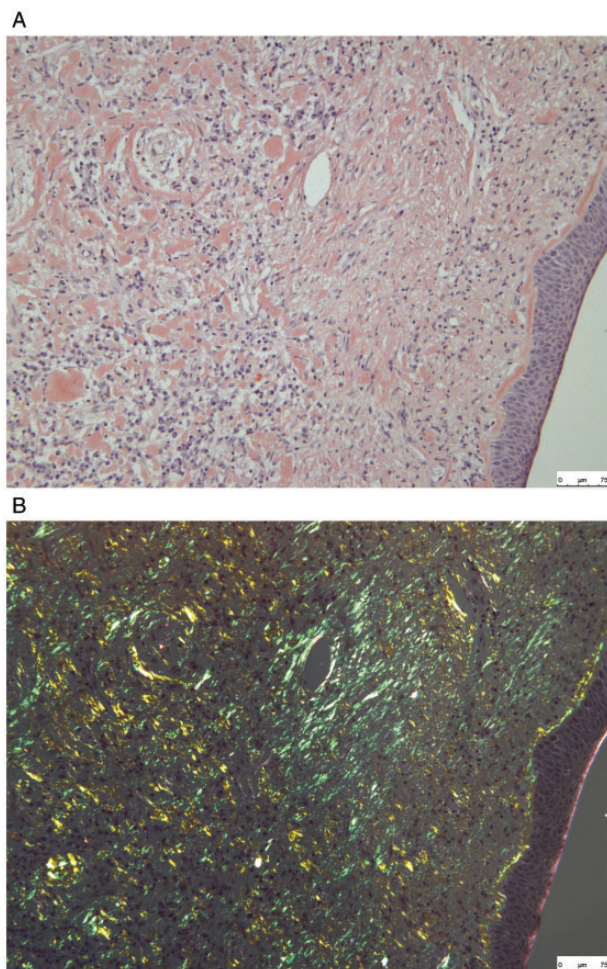




**Figure 1.** A, Axial CT image showing the mass originated from the posterior aspects of the left inferior turbinate, extending into the postnasal space. B, Coronal CT image: the opacification in the left maxillary sinus was a simple retention cyst not an extension of the tumor. There are also subtle reactive bone changes within the left inferior turbinate and lateral wall as compared to the contralateral side. C, Axial magnetic resonance imaging (MRI) T2-weighted image shows soft tissue density mass in the left maxillary sinus, which is hyperintense postcontrast enhancement and is seen closely abutting the left inferior turbinate extending posteriorly into the nasopharynx. D, Coronal MRI T1-weighted image shows soft tissue density mass in the left maxillary sinus, which is isointense to the adjacent skeletal muscle.

count, renal function tests, serum paraprotein, serum free light chains, N-terminal pro-brain natriuretic peptide (NT-proBNP), urinalysis, electrocardiogram, echocardiogram, and a serum amyloid P component (SAP) scintigraphy scan. There was also no evidence of monoclonal protein by serum or urinalysis. Renal function

tests showed a subnephrotic stage 1 chronic kidney disease with proteinuria in the context of longstanding hypertension. The echocardiography was normal and NT-proBNP was 160 ng/L, illustrating no evidence of cardiac amyloidosis. The SAP scintigraphy also did not reveal any visceral amyloid deposits. The battery of tests



**Figure 2.** A, Amyloid on Congo red ( $\times 100$ ) showing red stain of the amorphous eosinophilic material. B, Apple-green birefringence under high-intensity cross-polarized light ( $\times 100$ ).

did not show any evidence of systemic amyloidosis. The patient was consequently diagnosed with localized sinonasal amyloidosis.

No further surgical treatment was required following the initial diagnostic procedure. However, the patient's mild renal impairment necessitated a referral to the nephrology team. At 6 months, there was no local recurrence of disease. The patient will be followed up annually by the otolaryngology team to monitor recurrence with endoscopic examination of the nasopharynx as well as a review at 2 years with the NAC.

## Discussion

Amyloidosis is the generic term to describe a group of rare but serious conditions caused by an abnormal protein called amyloid. The exact pathogenesis is still not well understood; however, it is known to be caused by a buildup of the insoluble amyloid fibrillar protein in

organs and tissues throughout the body. Amyloidosis is usually a systemic disease affecting multiple organs, but it can also be localized (10%–20%).<sup>1</sup> The estimated incidence of all systemic amyloidosis in the United Kingdom exceeds 8 per million inhabitants per year and prevalence of systemic amyloidosis is 20 per million.<sup>2</sup> It commonly affects adults in the fifth decade and seventh decade.<sup>1</sup> Amyloid disease is classified by its chemical profile using an A for the amyloid followed by an abbreviation for the fibril protein, with more than 30 subtypes described to date. The main types of systemic amyloidosis are light chain amyloidosis (AL amyloidosis), amyloid A amyloidosis (AA amyloidosis), and the transthyretin-derived amyloidosis (ATTR amyloidosis) and are summarized in Table 1.<sup>3–7</sup>

Diagnosis is confirmed by histopathology, apple-green birefringence on Congo-red staining. Immunohistochemistry analysis sometimes further identifies the precursor protein subtype. This is performed by staining of the amyloid deposits using monoclonal antibodies targeting SAA protein and kappa and lambda immunoglobulin light chains. When these tests are negative, AA amyloidosis can be excluded with a high degree of certainty. However, up to 30% of AL amyloidosis deposits and up to 20% of ATTR amyloidosis deposits cannot be typed reliably using current techniques. Therefore, in these cases, the main differential diagnosis is between AL and hereditary ATTR.<sup>8</sup> In some cases, further typing of the amyloid fibril proteins by mass spectrometry may sometimes be of additional value. Subtyping is particularly important to characterize when suspecting systemic disease as misdiagnosis can lead to inappropriate administration of chemotherapy.

Scintigraphy with radioisotope labeled SAP scan is the gold-standard test providing an estimate of total amyloid deposition in the body. It has a sensitivity of 90% to detect AA and AL amyloidosis in visceral organs including the spleen, liver, kidneys, and adrenal glands.<sup>9</sup> The SAP scan has a low detection rate of cardiac amyloidosis, and therefore an echocardiogram is usually requested alongside. Other investigations include bone marrow aspirate, abdominal fat, and rectal biopsies. It is important to thoroughly evaluate these patients for systemic amyloidosis. Unlike the localized form, systemic involvement significantly shortens life expectancy.

Localized amyloidosis predominantly occurs in the head and neck region, most commonly affecting the larynx and oropharynx. Less frequently involved sites include the trachea, orbit, nasopharyngeal, and sinonasal region. Localized nasal amyloidosis is rare; there have been more than 38 published cases reported to date.<sup>10</sup> The most common presenting symptom for sinonasal amyloidosis is nasal obstruction, the main complaint in this case. Other presenting symptoms



**Table 1.** Classification of Amyloidosis (Nonexhaustive).

Amyloid Type		Precursor Protein	Cause/Association	Prevalence (%)
Systemic	AL amyloidosis	Immunoglobulin light chain (kappa or lambda)	Caused by plasma cell dyscrasia Occurs in absence of coexisting disease	50–60
	Amyloid with MM		MM	20–30
	Reactive amyloidosis (AA)	Serum AA	Chronic disease/inflammation results in production of serum AA (eg, rheumatoid arthritis, tuberculosis)	10
	Senile amyloidosis (nonhereditary ATTR)	Unmutated TTR (wild-type)	Aging	10–20
	Hereditary amyloidosis (hereditary ATTR)	Mutated TTR	Familial-inherited abnormal proteins with mutation	1
Localized	Localized AL	Immunoglobulin light chain	No systemic involvement Mostly occurs in head and neck region • Larynx (61%) • Oropharynx (23%) • Trachea (9%) • Orbit (4%) • Nasopharynx (3%)	10

Abbreviations: AA, amyloid A; AL amyloidosis, light chain amyloidosis; ATTR, transthyretin-derived amyloidosis; MM, multiple myeloma; TTR, transthyretin protein.

include postnasal drip, recurrent epistaxis, and Eustachian tube dysfunction.<sup>11</sup> The endoscopic appearance has been previously reported as a heterogeneously reddish, smooth exophytic nasal mass.<sup>12</sup> Localized amyloidosis usually appears as a well-defined, homogeneous, smooth soft tissue mass without any evidence of bony erosion.<sup>13</sup> It has also been reported to appear as densely calcified lesions on CT.<sup>14</sup> In our case, the CT demonstrated a thickened inferior turbinate without calcification but with subtle reactive bony changes. Investigation of both localized amyloidosis and systemic amyloidosis follow the same regime; however, management differs considerably in the systemic form and depends on the subtype.

The main aim of treatment in systemic amyloidosis is suppression of amyloid precursor synthesis either with chemotherapy or anti-inflammatory agents. In contrast, there is no definitive treatment established for localized amyloidosis. Surgical resection has historically been the preferred treatment option. However, in the last decade, management of nasal amyloidosis has moved away from a purely surgical approach.<sup>10</sup> This is due to the high rate of recurrence, as high as 50%, despite surgical excision.<sup>7,15</sup> Adjuvant chemotherapy and steroids have been shown to be of little clinical benefit.<sup>16</sup> Localized amyloidosis has never been reported to progress to systemic disease. The localized form follows a slow and benign clinical course with a generally favorable prognosis of a 90.6% five-year overall survival. Current literature is insufficient to address long-term follow-up.

Nevertheless, regular follow-up is advised. To our knowledge, this is the second reported case of non-AA subtype of the sinonasal tract.<sup>10</sup>

### Learning Points

- Although rare, it is important to consider localized amyloidosis as a differential diagnosis in sinonasal masses.
- Localized amyloidosis and systemic amyloidosis have significantly different treatments, management, and prognosis.
- Immunohistochemistry enables identification of amyloid subtypes and informs treatment.

### Authors' Contribution

NWW, TA, SM, and MB were involved in the clinical care of the patient, literature review, and manuscript preparation. JG contributed to the acquisition and analysis of pathological data. All authors read and approved the final manuscript.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical Approval

This study was approved by our institutional review board.

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## Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

## Statement of Informed Consent

Patient consent has been obtained.

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