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Clinical Record

Nasopharyngeal amyloidosis: an unusual cause for epistaxis

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Abstract

Objective: We report the first case of nasal and nasopharyngeal amyloidosis secondary to multiple myeloma; this case also represents the fourth report of systemic nasal or nasopharyngeal amyloidosis.

Method: Case report and review of the world literature concerning nasal and nasopharyngeal amyloidosis epidemiology, presentation and management.

Results: Nasal and nasopharyngeal amyloidosis is rare. The presentation, clinical course and treatment are discussed for the presented patient. The amyloid tumour, which recurred in correlation with the progressive transformation of the multiple myeloma, was treated surgically. Subsequent localised radiotherapy decreased the size and growth rate of the tumour.

Conclusion: Amyloid should be considered as a cause of resistant or recurrent epistaxis provided a mass lesion is seen on radiological imaging. Radiotherapy may be a treatment option in nasal and nasopharyngeal amyloidosis.

Key words: Nasal Cavity; Nasopharynx; Amyloid; Myeloma

Introduction

Amyloid rarely involves the head and neck region, and occurs even less frequently in the nasal and nasopharyngeal area.[1–31] We report the first case in the English literature of nasopharyngeal amyloidosis secondary to multiple myeloma.[1–24] We aim to raise awareness of the unusual complications of amyloid. Therefore, we include a literature review of nasopharyngeal amyloidosis, with the intention of increasing awareness of the diagnosis and management of this rare disease.[1–24]

Case report

A 61-year-old man presented to the ENT out-patient department with a two-month history of left nasal obstruction, loss of sense of smell and left-sided conductive hearing loss. His past medical history included multiple myeloma, diagnosed three years previously, with associated mediastinal lymphadenopathy. There was a medical history of allergic rhinitis.

A large, left-sided nasal polyp and polypoidal mass on the right middle turbinate was visualised on nasopharyngoscopy. Visualisation of the overlying external eustachian orifice revealed no significant findings. Tympanometry of the left ear demonstrated otitis media with effusion. Pure tone audiometry revealed a mild to moderate, mixed hearing loss in the left ear and a moderate, high frequency loss in the right ear.

The patient was treated with topical steroids and listed for excision and biopsy of the nasal cavity polyp and left myringotomy.

Myringotomy findings revealed an effusion.

Nasal cavity biopsies revealed eosinophilic, proteinaceous material with a mixed infiltrate of plasma cells (acute and chronic) (see Figure 1). Staining of the amorphous material with Congo red demonstrated pale congophilia with apple-green birefringence when viewed under high intensity, cross-polarised light. Immunohistochemical analysis established a diagnosis of λ light chain amyloid. No computed tomography (CT) scan was performed at this stage.

Three months later, the patient was admitted to the accident and emergency department with a three-day history of progressively worsening epistaxis and deterioration of hearing in the left ear. Examination demonstrated re-growth of the left-sided nasal polyp. The patient was listed for resection of this mass under general anaesthetic.

On examination six weeks after this procedure, there was recurrence of the amyloid tumour, which now extended to the posterior wall of the nasopharynx.

At this stage, the patient's paraprotein levels had risen from 35 to 36.5 g over the previous three months, and he was referred to the National Amyloid Centre. There, the patient's mediastinal lymphadenopathy was thought clinically to be almost certainly secondary to amyloid infiltration, and the patient was thus diagnosed with secondary amyloidosis.[32] A serum amyloid precursor scan, performed to search for other secondary amyloid deposits, found no other tissue to be involved by amyloid.

Following an increase in bone marrow plasma cells from 22 to 70 per cent, three months after his nasopharyngeal amyloid resection, the patient commenced chemotherapy with the vincristine, adriamycin and dexamethasone regime, for his myeloma. Unfortunately, the chemotherapy did not reduce the aggression of the neoplasm. A CT scan

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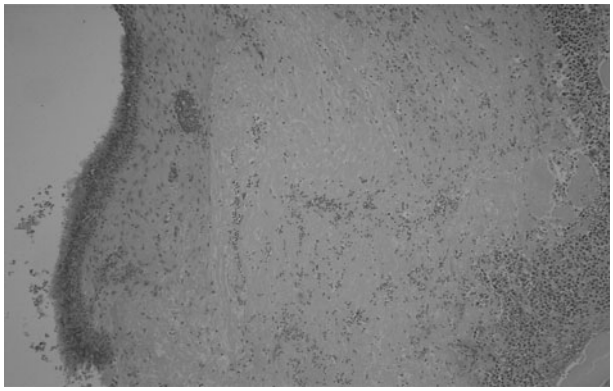

FIG. 1
Photomicrograph of nasal cavity biopsy specimen, showing diffuse material staining with Congo red (×100).

performed three months later (Figure 2) showed an invasive mass present in the left maxillary antrum, ethmoids and sphenoidal air sinuses. The mass extended into the middle cranial fossa with associated bone destruction of the left maxillary antrum, ethmoids, pterygoid plates, greater wing of the sphenoid, pituitary fossa and part of the clivus. The posterior fossae and orbits remained largely unaffected.

In light of the progression of the multiple myeloma, the patient's chemotherapy regime was changed to cyclophosphamide, thalidomide and dexamethasone. This led to an improvement, and over a period of six months his paraprotein levels reduced from 13 g/l to 31 g/l; however, a new CT scan showed that the nasopharyngeal amyloidosis continued to penetrate into nearby structures, as in the previous scan.

At this point, a trial of localised radiotherapy to the nasopharyngeal amyloid mass was introduced. A CT scan taken after several cycles of radiotherapy (without contrast due to unknown renal status) showed a decrease in nasopharyngeal amyloid (Figure 3).

Discussion

Myeloma is a monoclonal plasma cell tumour with an incidence of 40 per million in the UK population, and accounts for 1 per cent of all cancers in the Western World.[33,34] It is an incurable, multi-system disease, postulated to be caused by a cytogenetic error late in B cell differentiation, originating in the bone marrow, and often complicated by subsequent anaemia and bone marrow failure.[35] Amyloidosis occurs as a complication of multiple myeloma in 5–15 per cent of patients.[35]

Amyloid is a non-branching, fibrillar protein which is resistant to proteolysis and thus remains deposited in most intracellular regions.[34] Amyloid deposition complicates many chronic diseases.[33] Over-accumulation of amyloid results in amyloidosis, defined as a pathological accumulation of protein fibrils between cells in various tissues and organs of the body. Clinically, amyloidosis can be categorised as primary, when associated with some immunocyte dyscrasia, or secondary, when occurring as a complication of an underlying chronic inflammatory or tissue destructive process. Hereditary or familial amyloidosis constitutes a separate, albeit heterogeneous group with several distinctive patterns of organ involvement.[34]

Amyloid fibrils associated with a plasma cell dyscrasia are derived from the N-terminal region of monoclonal immunoglobulin light chains and are classified as Amyloid Light chain (AL) amyloid deposition.[35] Common clinical

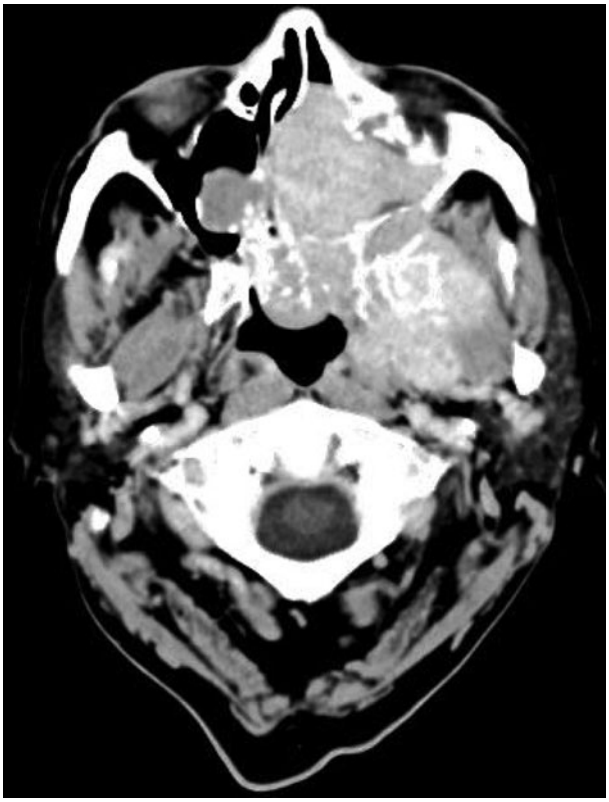

FIG. 2
Axial computed tomography scan with contrast, demonstrating invasion of nasopharyngeal amyloid tumour in the left maxillary antrum, ethmoids and sphenoidal air sinuses.

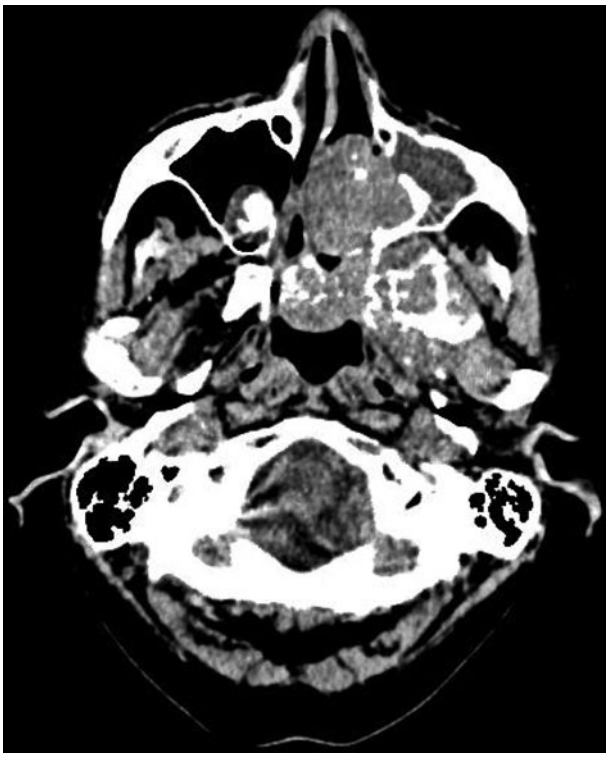

FIG. 3
Axial computed tomography scan without contrast, demonstrating a reduction in the nasopharyngeal amyloid tumour mass following localised radiotherapy.

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presentations of amyloid include nephrotic syndrome, restrictive cardiomyopathy and sensorineual neuropathy.[36]

Head and neck amyloidosis is rare. There have been 28 case reports of nasal or nasopharyngeal amyloidosis deposits in the English language literature between 1928 and 2004.[1–24] Only three of these cases occurred secondary to systemic amyloidosis.[5,9,16] Elcock and Grimaldi reported the case of a 72-year-old woman with known Waldenstrom's macroglobulinaemia presenting with epistaxis, nasal obstruction and a mass in the nasal cavity.[5] Dubey *et al.* described a 64-year-old woman with systemic primary amyloidosis presenting with increasing nasal obstruction, epistaxis and progressive widening of the dorsum of the nose.[9] In this case, anterior rhinoscopy revealed a pale, polypoid, friable mass at the level of the middle turbinate in both nasal cavities. Zundel *et al.* gave an account of a 56-year-old man with known systemic amyloidosis and renal failure presenting with intermittent epistaxis; on examination, the patient had near-total perforation of the nasal septum.[11]

Nasal and nasopharyngeal amyloidosis affects both genders, with a wide age range of reported cases (eight to 86 years). The most common presenting complaint is nasal obstruction due to the tumour invading the nasal chamber, followed by epistaxis. In several reports, the amyloid tumour has been described as polypoidal, firm and submucosal.[1–24] Some cases, all of which involved localised amyloidosis, had amyloid masses described as yellowish or whitish and hard.[8,14,15,17,18,22] Excluding one case,[15] all these descriptions were associated with a relevant ENT past surgical history.[8,14,17,18,22] These patients may perhaps have had localised primary amyloid secondary to surgical or medical intervention.

Nasopharyngoscopy and CT scanning have been performed in cases of nasal and nasopharyngeal amyloidosis from 1984 onwards.[6] Prior to this, several reports described the use of sinus X-rays to visualise the amyloid mass.[3–5] Magnetic resonance imaging (MRI), which enables more detailed visualisation, has been featured in case reports from 2000 onwards.[18,20]

The radiological appearance of focal amyloidosis is non-specific. Computed tomography scans show amyloid as a well defined, radiopaque, high attenuation, soft tissue mass associated with calcification. Fatterpeckar *et al.* (who described a case of localised nasopharyngeal amyloidosis) noted a 'fluffy' appearance in the bone adjacent to the amyloid, leading them to postulate that deposition of proteinaceous amyloid fibrils in the submucosal layers of the sinonasal cavities incited an osteoblastic reaction, resulting in the fluffy bone appearance.[22] Pang *et al.* reported a CT appearance of bilateral turbinate masses with osteotic changes.[20] Magnetic resonance imaging characteristics are described in one case report only, as consisting of a hypo-intense, soft tissue mass with low to intermediate signal intensity in both T1- and T2-weighted images, making amyloid difficult to differentiate from muscle tissue.[18]

Histological examination of biopsied material using congo staining has previously been the method of choice for amyloid diagnosis.[4–24] Immunohistochemical techniques, first implemented in 1990 and included in several reports thereafter, enable the biochemical diagnosis of amyloid as either systemic or localised.[10,13,14,17,20]

The recently developed SAP scan was used in the current case to demonstrate the location and quality of amyloid deposits in organs throughout the body. Radiolabelled SAP component, specifically and quickly localises to amyloid deposits, in direct relation to the amount of amyloid present. Thus diagnosis and quantification of whole body deposits by whole body scintigraphy is realised via SAP. Unfortunately, the reliability of the test is questionable, as hollow or moving organs cannot be assessed. Tsikoudas et al. used SAP scanning to rule out the possibility of systemic amyloidosis.[19]

Nasal and nasopharyngeal amyloidosis may be resected surgically. Thirteen out of a possible 26 articles available for review describe resection of nasal or nasopharyngeal amyloidosis.[1,2,5,7–15,18] Only one of the three patients with secondary amyloidosis underwent surgical resection, as the remaining patients were unsuitable for surgical intervention owing to their poor health status.[5,9,16] Earlier cases used comparatively extensive surgical methods. Ottosen performed a conchotomy, and Garrett used a Caldwell–Luc procedure to perform a rhinotomy.[2,3] However, in a recent report a patient was treated with a turbinectomy, although one must note that she had previously defaulted and that, in the interim, the tumour had grown considerably in size.[20] There is evidence that a conservative surgical approach to nasal and nasopharyngeal amyloidosis improves outcomes. Lesserson and Finn found that their previous attempt to remove an amyloid tumour (i.e. transoral removal via laser with forceps punch biopsy) resulted in amyloid recurrence on bilateral sides of the palate, particularly on pressure areas of the palate.[14] Their subsequent surgical intervention avoided the traction used in their earlier approach and was performed transnasally under local anaesthetic and intravenous sedation. Three years' follow up revealed no recurrence of disease.[14]

Most of the case reports located failed to prevent recurrence of amyloid tumour by surgical methods.[1–24] Some omitted follow-up details,[1,2,3,8,10,19] and several reported ill patients who died soon afterwards.[3,5,15,17]

- **Nasal or nasopharyngeal amyloidosis is a rare cause of epistaxis**
- **Treatment is surgical to achieve symptomatic relief, although recurrence is common**
- **A conservative surgical approach may be associated with a slower rate of recurrence**
- **Chemotherapy has not been shown to be of benefit in the treatment of nasopharyngeal amyloidosis; however, in the presented case radiotherapy produced useful remission**

The cyclophosphamide-thalidomide-dexamethasone chemotherapy regime slowed progression of multiple myeloma in our patient; however, it did not ameliorate the symptoms or signs of amyloidosis. We thought it possible that reduction in the rate of plasma cell production could in turn reduce the amyloid produced and subsequently deposited in the nose and nasopharynx. One other case report, of localised nasal and nasopharyngeal amyloidosis, describes a female with Non-Hogkins lymphoma for whom chemotherapy was introduced as empirical treatment. After 45 days of melphalan, the trial was abandoned owing to non-progression of symptoms.[4]

The current case represents the first report of nasal and nasopharyngeal amyloidosis (either systemic or localised) treated with localised radiotherapy. Several cycles of localised radiotherapy led to a dramatic decrease in the size of the amyloid tumour (see Figure 3), with an associated improvement in symptoms and signs. Perhaps this could be considered in future cases of nasal or nasopharyngeal amyloidosis.

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Conclusion

Nasal or nasopharyngeal amyloidosis is a rare cause of epistaxis and/or nasal obstruction in cases of known, chronic illness. It may be associated with a past history of surgical or medical ENT conditions. Immunohistochemical techniques now enable a definitive diagnosis. A SAP scan is suitable as a supportive investigation for assessing the extent of spread of systemic amyloidosis in visceral organs. Computed tomography and MRI imaging (although non-specific for nasal or nasopharyngeal amyloidosis) enables evaluation of disease progression. Treatment by surgical excision provides symptomatic relief, but there is a high incidence of recurrence. In the presented case, localised radiotherapy decreased the mass of the nasopharyngeal amyloid tumour.

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