Sinonasal Globular Amyloidosis Simulating Malignancy: A Rare Presentation

Binay Kumar¹ · Bhawna Pant² · Vikrant Kumar² · Meghna Negi¹

Received: 6 October 2015 / Accepted: 2 January 2016 / Published online: 16 January 2016
© Springer Science+Business Media New York 2016

Abstract Primary localized amyloidosis in the head and neck region is a rare entity. The most commonly involved organ is larynx. Primary amyloidosis localized to the sinonasal tract is extremely rare. We report one such case along with a brief review of the associated literature. The aim of reporting this case is to emphasize the fact that sometimes nasal amyloidosis can also present with signs and symptoms of nasal and nasopharyngeal malignancy. The definitive diagnosis in such cases depends upon histopathology and further confirmed by immunohistochemistry. A 55-year old male presented with recurrent episodes of nasal bleed, bilateral nasal obstruction, and bilateral hearing loss from last 7 years. On clinical examination a mass was found in the nasal cavity on both sides reaching up to the nasopharynx. Contrast enhanced CT scan revealed that the mass was extending up to the skull base and destroying bony landmarks of the nasal cavity and paranasal sinuses. Mass was proved to be amyloidosis after histopathological examination. It showed multiple blotches of globular submucosal deposit of amyloid, on staining with Congo red. Immunohistochemistry confirmed AL amyloidosis with expression of mixed kappa and lambda light chain immunoglobulin ($\kappa > \lambda$). No evidence of systemic amyloidosis was found after proper work up. It was managed by conservative surgery.

Keywords Amyloidosis · Globular · Nose

Introduction

Amyloid deposition in tissue was first described by Rokitsky in 1842, but it was Virchow who coined the term “amyloid” in 1853 [1]. Localized amyloidosis is rare, constituting 10–20 % of amyloidosis cases, commonly affecting the head and neck region [2, 3]. Larynx is the most commonly affected site (61 %) followed by oropharynx (23 %), trachea (9 %), and orbit (4 %). Only 3 % of cases occur in the nasopharynx [4, 5]. Sinonasal globular amyloidosis is extremely rare. We report one such case along with a brief review of the literature. Identification of specific type of amyloid protein is important because it may have significant prognostic and therapeutic ramifications.

Case Report

A 55-year old male presented with bilateral nasal obstruction, recurrent nasal bleed and bilateral hearing loss for last 7 years. On clinical examination, the nasal cavity was occupied on both sides by a mass which was pale pink, non tender and soft to firm in consistency. It was situated in between the septum and the lateral wall above the inferior turbinate. Posterior rhinoscopy examination showed a similar mass in the nasopharynx. The diagnostic nasal endoscopy confirmed the findings (Fig. 1). There was minimal bleeding on manipulating the mass. Audiogram showed bilateral conductive hearing loss. Contrast enhanced CT scan of nose and paranasal sinuses revealed wide spread extent of mass causing bony destruction and eroding skull base, suggestive of malignant lesion (Fig. 2).

Tissue was sent for histopathological examination which showed multiple globular submucosal eosinophilic deposits with a lamellated appearance reminiscent of corpora amylacea along with focal linear extracellular amyloid

✉ Binay Kumar
binaypgi@gmail.com

¹ Department of Pathology, Government Medical College, Haldwani-Nainital, Uttarakhand, India

² Department of ENT, Government Medical College, Haldwani-Nainital, Uttarakhand, India

Fig. 1 Images from rigid endoscopy demonstrating a *pale pinkish* looking nasal mass between the septum and the lateral wall above the inferior turbinate

Fig. 2 CECT of the nose and PNS showing enhancing mass extending from nasal cavity to sella and supra seller region with destruction of medial wall of maxillary sinus, nasal septum, hard palate, pterygoid process on both sides

deposition in a perivascular distribution (Fig. 3). Confirmation was done on Congo red staining by apple green birefringence on polarizing microscopy (Fig. 4). Immunohistochemistry was done which showed expression of both kappa and lambda AL chain (IgG) with comparatively weak expression of λ (Figs. 5, 6) in the amyloid material but reverse type of expression in nearby lympho-plasmacytic infiltrate (Figs. 7, 8). Patient underwent investigations such as liver function tests, renal function tests, serum alkaline phosphatase, urine analysis for Bence Jones protein, serum electrophoresis for M protein, chest X-ray, abdominal ultrasound, ECG, echocardiogram, and abdominal fat aspiration to rule out systemic amyloidosis.

The disease was limited to sinonasal tract only, thus the diagnosis of isolated globular nasal amyloidosis was made. Since the patient was symptomatic, conservative surgery was done under general anesthesia. Postoperative period was uneventful. Patient is in regular follow up and is symptomatically relieved.

Discussion

Amyloidosis most commonly affects individuals between 50 and 70 years with a male to female predominance of 3:1–3:2 [6]. Symptoms are related to the size of mass and

Fig. 3 Blotches of extracellular globular lamellated, homogenous fragmented eosinophilic material in subepithelial and perivascular region (H & E; 100×)

Fig. 4 Apple green birefringence on polarized microscopy (Congo red stain; 100×)

Fig. 5 Immunohistochemistry for amyloid light chain protein show kappa overexpression in amyloid material and nearby lymphoplasmacytic infiltrate (AL-k; 100×)

Fig. 6 Immunohistochemistry for amyloid showing lambda light chain immunoglobulin expression in amyloid material and nearby lymphoplasmacytic infiltrate (AL-lambda; 100×)

Fig. 7 Immunohistochemistry for amyloid light chain protein show kappa expression in nearby lymphoplasmacytic infiltrate at other foci (AL-k; 400×)

Fig. 8 Immunohistochemistry for amyloid showing lambda light chain immunoglobulin expression in nearby lymphoplasmacytic infiltrate at other foci (AL-lambda; 400×)

sites of involvement. Sinonasal amyloidosis presents with symptoms of chronic rhinosinusitis, epistaxis (due to vessel wall invasion/deposition), glue ear and posterior nasal drip [6, 7]. On examination, the mass is usually seen as pale pink or yellowish polypoidal lesion. The extension is better assessed radiologically by a CT scan or MR imaging. Enhancement with contrast may be seen on both CT and MRI. Advanced cases may show bony erosion on CT scan. As it happened in our case, all signs and symptoms as well as radiological findings were in favor of sinonasal malignancy. Duration of disease was pointing towards some benign pathology. The diagnosis of amyloidosis was confirmed by tissue biopsy [7].

Amyloidosis can be either in systemic or in localized form [8]. Clinically, it is difficult to distinguish between primary, secondary, familial, and senile forms of amyloid from one another. Majority of systemic amyloidosis have immunoglobulin light chain amyloid (AL) or primary type. The localized amyloidosis is extremely rare [8] but can be seen in the head and neck region. It can be either idiopathic wherein there is no evidence of coexisting disease or secondary (amyloid associated—AA proteins) which may be associated with chronic inflammatory diseases such as tuberculosis, rheumatoid arthritis etc. [9]. Isolated nasal amyloidosis is extremely rare. Review of literature from 1928 to date have documented only 38 cases of amyloidosis involving nasal mucosa out of which five cases were of systemic amyloidosis [10]. About 23 cases of isolated sinonasal amyloidosis have been reported on review of the literature [6] of which only 15 cases were true idiopathic isolated amyloidosis [11]. Up to 1935, there were only seven reported cases of sinonasal amyloidosis [12]. Mufarrij et al. [13] found seven subsequent cases from 1935 to 1990. A Medline search up to 2001 revealed five other reported cases [14–18]. Further search revealed three more case reports of sinonasal amyloidosis in English literature [19–22].

Review of literature shows that idiopathic primary nasal amyloidosis more frequently affects women than men, affects all age groups, and nasal obstruction is the most common presenting symptom. Facial pain associated with bony erosion is a worrying feature [5]. Meticulous surgery produces substantial symptomatic improvement in these patients [11]. Systemic amyloidosis should be ruled out by a detailed clinical examination and investigations such as peripheral blood smear, liver function tests, serum electrophoresis, radiographic imaging, electrocardiography and bone marrow biopsy. Abdominal fat aspiration is as sensitive as rectal mucosal biopsy (75–90 %) to rule out systemic amyloidosis [11]. Amyloidosis is characterized ultrastructurally as nonbranching fibrils highly organized in antiparallel β -pleated sheet conformation. The pathogenesis is multifactorial. It is believed to result from

combination of immune deregulation or persistent stimulus causing excess production of precursor proteins and inability to break down the immunoglobulin/immunoglobulin precursor proteins, with their resultant polymerization in to insoluble amyloid fibrils which deposit in the extracellular space [7]. Histologically, amyloid is eosinophilic amorphous hyaline material. It can be diagnosed by Congo red staining wherein a characteristic apple green birefringence is seen under polarizing microscope, though the congophilia is lost after pretreatment of the tissue with potassium permanganate in cases of AA, β_2 -microglobulin (β_2 M), apolipoprotein A1 (ApoA1) amyloid [23]. Amyloid fibril proteins can be classified immunohistochemically in to 27 different types [10] using antibodies directed against amyloid P component, AA amyloid, apolipoprotein A1 (ApoA1), β_2 -microglobulin (β_2 M), transthyretin (ATTR), immunoglobulin-derived λ light and κ -light chains (AL), lactoferrin (ALac), lysozyme (ALys), keratopithelin (Aker), etc. [24] and confirmation is done by mass spectroscopy. A given biochemical form of amyloid protein can occur in a variety of clinical settings. Amyloid is deposited in a linear or globular pattern and vascular, perisinusoidal, or stromal distribution. Globular lamellated pattern of deposition has been reported in the liver and gastrointestinal tract involving stomach and small bowel due to deposition of AA amyloid [25]. Globular amyloid frequently coexist with linear amyloid, though morphologically distinct, and is not predictive of amyloid subtype and of uncertain pathogenesis [25]. This is the second case report of isolated primary nasal–nasopharyngeal amyloidosis containing both the λ and κ light chains [15]. Recent evidence in lung suggests that these deposits are due to a low grade B cell clonal proliferation [26]. Usually the plasma cells are monotypic and/or B cells clonal [27]. Globular localized nasal amyloidosis has not been reported to date.

Localized amyloidosis is a slowly expansile non-destructive lesion with a benign clinical course. Endoscopic removal without compromising the function of involved organ is preferred treatment. Close follow up is required as it has a high chance of recurrence (50 %) [6, 7]. Bony erosion is seen in advanced lesion [6], as seen in our case. High-dose intravenous melphalan followed by autologous stem cell transplantation (HDM/SCT) produces complete hematologic responses in about 40 % of treated patients, as measured by complete loss (CR) of clonal plasma cells in the bone marrow and disappearance of the monoclonal LC by IFE and assay for free LCs. Hematologic responses can be followed in the subsequent 6–12 months by improvement in organ function and quality of life. The immunomodulators thalidomide and lenalidomide have activity; lenalidomide is well tolerated in doses lower than those used for myeloma and, in combination with

dexamethasone, produces complete hematologic remissions and improvement in organ function. The proteasome inhibitor bortezomib has also been found to be effective in single and multicenter trials. The primary therapy in AA amyloidosis is treatment of the underlying inflammatory or infectious disease. Treatment that suppresses or eliminates the inflammation or infection also decreases the SAA protein concentration. Tumor necrosis factor and interleukin-1 antagonists can be effective in syndromes related to cytokine elevation. For this disease, there is also a fibril-specific agent: eprodisate was designed to interfere with the interaction of AA amyloid protein with glycosaminoglycans and to prevent or disrupt fibril formation [27].

Conclusion

Nasal amyloidosis may present with nasal obstruction, epistaxis, ear blockage, facial pain, or localized bony destruction. It should be kept as differential diagnosis by ENT surgeon while evaluating patients with nasal mass. Confirmatory diagnosis requires histopathological examination of tissue from nose and further immunohistochemistry. Proper tests should be done to exclude systemic amyloidosis. Most of the patients with localized amyloidosis in head and neck area are relieved symptomatically by surgery but they should be followed up for recurrence or the appearance of systemic form of disease. Isolated primary globular nasal amyloidosis is a rare entity. This case also emphasizes that nasal amyloidosis can also behave like a malignant tumour causing extensive bony destruction.

References

1. Durbec M, Ambrun A, Barnoud R, Poupert M, Pignat JC, Merrot O. Localized nasopharyngeal amyloidosis. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:160–2.
2. Pang KP, et al. Amyloidoma of the nose in a pediatric patient: a case report. *Am J Otolaryngol*. 2001;22:138–41.
3. Barnes L. Miscellaneous disorders of the head and neck. In: Barnes L, editor. *Surgical pathology of the head and neck*, vol. 3. 2nd ed. New York: Marcel Dekker; 2001. p. 2191–3.
4. Glenner GG. Amyloid deposits and amyloidosis: the β -fibrillosis (second of two parts). *N Engl J Med*. 1980;302(24):1333–43.
5. Scott PP, Scott WW Jr, Siegelman SS. Amyloidosis: an overview. *Semin Roentgenol*. 1986;21(2):103–12.
6. Naidoo YS, Gupta R, Sacks R. A retrospective case review of isolated sinonasal amyloidosis. *J Laryngol Otol*. 2012;126:633–7.
7. Gean-Marton AD, et al. Focal amyloidosis of the head and neck: evaluation with CT and MR imaging. *Radiology*. 1991;181:521–5.
8. Panda NK, Saravanan K, Purushotaman GP, et al. Localised amyloidosis masquerading as nasopharyngeal tumor: a review. *Am J Otolaryngol Head Neck Med Surg*. 2007;28:208–11.
9. Tsikoudas A, Martin-Hirsch DP, Woodhead CJ. Primary sinonasal amyloidosis. *J Laryngol Otol*. 2001;115:55–6.
10. Cunningham A, Kalwani S, Alsanjari N, Fayad G. Rare subtype of localized nasal amyloidosis. *Otorhinolaryngol*. 2013;6(1):60–3.
11. Pearlman AN, Jeffe JS, Zynger DL, Yeldandi AV, Conley DB. Localized amyloidosis of the nasal and paranasal mucosa: a rare pathology. *Am J Otolaryngol Head Neck Med Surg*. 2010;31:130–1.
12. Kramer R, Som ML. Local tumour like deposits of amyloid in the larynx: report of a case and review of literature. *Arch Otolaryngol*. 1935;21:324–34.
13. Mufarrij AA, Busaba NY, Zaytoun GM, et al. Primary localized amyloidosis of the nose and paranasal sinuses. A case report with immunohistochemical observations and a review of the literature. *Am J Surg Pathol*. 1990;14:379–83.
14. Birchall D, Fields JM, Poon CL. Case report: focal amyloidosis of the maxillary antrum: plain film, CT and MR appearances. *Clin Radiol*. 1997;52:392–4.
15. Lim JS, Lebowitz RA, Jacobs JB. Primary amyloidosis presenting as a nasopharyngeal mass. *Am J Rhinol*. 1999;13:209–12.
16. Kobayashi T, Taguchi O, Ysui H, et al. A case of amyloidosis of the tracheobronchial tree and inferior nasal concha. *Jap J Thorac Dis*. 1971;35:1378–82.
17. Dominguez S, Wienberg P, Claros P, et al. Primary localized nasopharyngeal amyloidosis. A case report. *Int J Pediatr Otorhinolaryngol*. 1996;36:61–7.
18. Clevens RA, Wiatrak BJ, Myers MW. Multifocal amyloidosis of the pediatric airway. *Arch Otolaryngol Head Neck Surg*. 1995;121:229–32.
19. Kenny PP, Chee Lincoln WJ, Busmanis Inny. Amyloidoma of the nose in a pediatric patient: a case report. *Am J Otolaryngol*. 2001;22(2):138–41.
20. Teo DT, David PL, Sethi DS. Recurrent localized sinonasal amyloidosis: a case report. *Otolaryngol Head Neck Surg*. 2003;129:270.
21. Chin SC, Girish F, Kao CH, et al. Amyloidosis concurrently involving the sinonasal cavities and larynx. *Am J Neuroradiol*. 2004;25:636–8.
22. Penner CR, Muller S. Head and neck amyloidosis: a clinicopathological study of 15 cases. *J Oral Oncol*. 2006;42(4):421–9.
23. Westermark GT, Johnson KH, Westermark P. Staining methods for identification of amyloid in tissue. *Methods Enzymol*. 1999;309:3–25.
24. Kebbel A, Röcken C. Immunohistochemical classification of amyloid in surgical pathology revisited. *Am J Surg Pathol*. 2006;30(6):673–83.
25. Hemmer PR, Topazian MD, Gertz MA, Abraham SC. Globular amyloid deposits isolated to the small bowel: a rare association with AL amyloidosis. *Am J Surg Pathol*. 2007;31(1):141–5.
26. Grogg KL, Aubry MC, Vrana JA, Theis JD, Dogan A. Nodular pulmonary amyloidosis is characterized by localized immunoglobulin deposition and is frequently associated with an indolent B-cell lymphoproliferative disorder. *Am J Surg Pathol*. 2013;37:406–12.
27. Seldin DC, Berk JL. Amyloidosis, chap. 112. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. *Harrison's principles of internal medicine*, vol. 1, 19th ed. McGraw-Hill; 2015. p. 722–723.