Clinical Case Report

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Multifocal head and neck amyloidosis as a diagnostic clue of systemic lupus erythematosus (SLE)

A case report

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Abstract

Rationale: Amyloidosis accounts for 2% of head and neck tumors. Amyloidosis that develops in the head and neck region is localized amyloidosis. Multifocal amyloidosis in the head and neck region is extremely rare.

Patient concerns: The patient presented to the clinic of otolaryngology with nasal obstruction, anosmia and left neck mass for several months.

Diagnosis: A left nasopharynx tumor was revealed under nasopharyngeal scope. Eosinophilic, proteinaceous material was revealed under a pathology scope in the nasopharynx tissue and neck tumor. Congo red staining demonstrated pale congophilic amorphous material with apple-green birefringence under cross-polarized light, and multifocal amyloidosis was diagnosed. Amyloidosis secondary to systemic lupus erythematosus (SLE) was confirmed after a series of investigations.

Interventions: The patient underwent local excision for multifocal amyloidosis without following management. To control underlying SLE, the patient accepted steroid pulse therapy and immunosuppressants. The patient eventually achieved disease remission.

Outcomes: During the 6 months of follow-up in the outpatient department of otolaryngology and rheumatology, complications, recurrence of nasopharyngeal amyloidosis, and SLE flare-up were not observed.

Lessons: Head and neck amyloidosis involving the nasopharynx is a rare presentation of this disease. Head and neck multifocal amyloidosis should be taken as a hint of systemic disease. In head and neck amyloidosis, a comprehensive survey should be performed to clarify the underlying disease predisposing to amyloidosis and organ involvement.

Abbreviations: AA amyloidosis = reactive amyloidosis, AL amyloidosis = immunoglobulin light chain amyloidosis, SLE = systemic lupus erythematosus.

Keywords: amyloidosis, case report, head and neck, narrow-band image, nasopharynx, systemic lupus erythematosus

1. Introduction

Amyloidosis is a disease that results from extracellular deposition of insoluble misfolded fibrillar protein. Amyloidosis could be categorized into systemic or localized disease. Localized amyloidosis was defined as a single organ involvement of amyloid protein deposition and is rarely associated with systemic diseases. In contrast to localized amyloidosis, systemic amyloidosis involves more than 1 organ and multifocal lesions. Inflammatory diseases and some neoplastic diseases that produced misfolded fibrillary proteins, such as multiple myeloma and plasmacytic dyscaria, should be concerned as the cause of systemic amyloidosis.[1,2] However, the majority of amyloidosis discovered in the head and neck region was localized amyloidosis.[3–5] Reviewing the previous literature, multifocal amyloidosis that developed in the head and neck region was extremely rare, and only 1 case associated with lymphoma was reported.[6]

We reported a case of multifocal amyloidosis in the head and neck region resulting from SLE, and we would like to emphasize the importance of thoroughly investigating systemic disease in multifocal amyloidosis in the head and neck region.

The institutional review board of Taichung Tzu Chi Hospital approved this study. Informed written consent was obtained from the patient for publication of this case report and accompanying images

2. Case presentation

A 41-year-old female presented to the outpatient department of otolaryngology with nasal obstruction, loss of sense of smell and anterior neck mass for several months. An unmovable indurated

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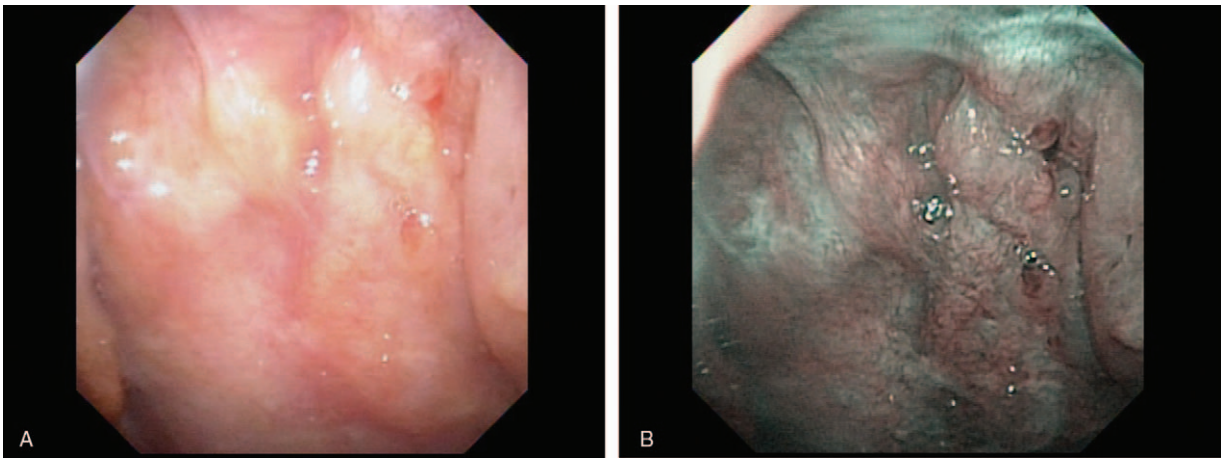

Figure 1. A. A bulging mass from the Rosenmuller fossa with a yellowish smooth surface. B. No angiodysplasia under narrow-band imaging.

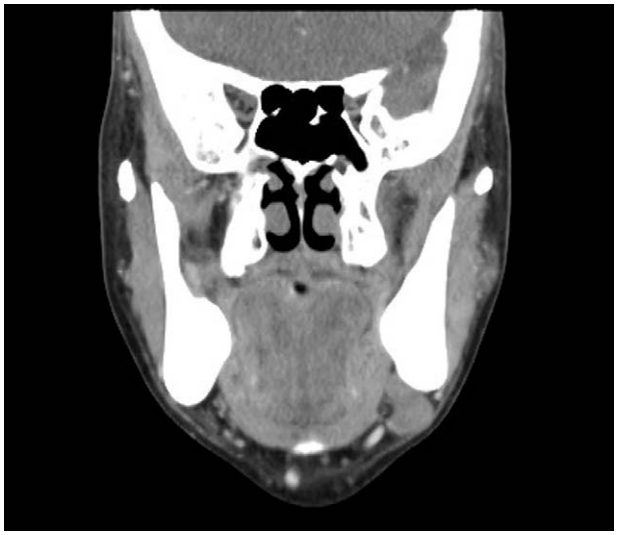

Figure 2. A $2.2 \times 1.5 \times 2.2$ cm enlarged lymph node at the level Ib of the left neck.

mass over the left submandibular area was noted. Ultrasound of the neck revealed a 3×2.2 cm round-shaped lymph node in the left level Ib. Left middle ear effusion was revealed by otoscope. Flexible nasopharyngoscopy demonstrated a bulging mass from the Rosenmuller fossa with yellowish smooth surface (Fig. 1A), which showed no angiodysplasia under narrow-band imaging (Fig. 1B). Further computed-tomography (Fig. 2) demonstrated a $2.2 \times 1.5 \times 2.2$ cm enlarged lymph node in level Ib over left neck.

The pathology report of the excisional biopsy of left lymph node and nasopharynx revealed eosinophilic, proteinaceous material (Fig. 3A). Congo red staining demonstrated pale congophilic amorphous material with apple-green birefringence when viewed under high intensity, cross-polarized light (Fig. 3B), which were typical finding suggestive of amyloidosis. Multifocal amyloidosis was identified. Immunohistochemistry analysis was also performed and AA amyloidosis was confirmed by the presence of anti-AA antibodies.[7]

Later, a complete blood count showed pancytopenia, a renal function test showed decreased estimated glomerular filtration rate and urine analysis showed proteinuria. Liver function test, chest radiograph and electrocardiogram all demonstrated normal results. Considering the clinical presentation and other laborato-

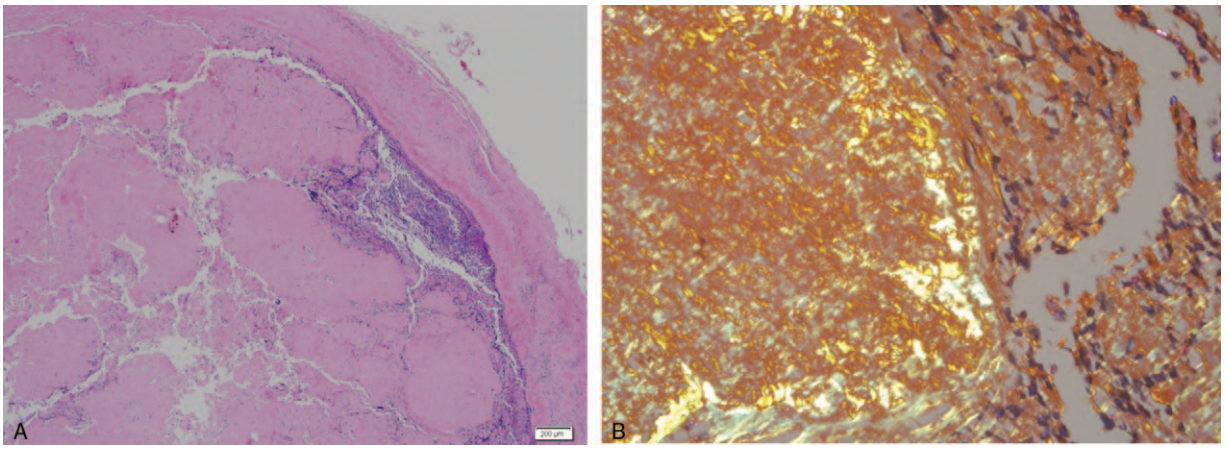

Figure 3. A. Eosinophilic, proteinaceous material in nasopharynx (40×). B. Congo red demonstrated pale congophilia with apple-green birefringence when viewed under high intensity, cross-polarized light (100×).

ry finding, autoantibodies, including serum anti-nuclear antibody, anti-β2 glycoprotein I antibody, and anti-double strand DNA antibody, were examined, which eventually all showed positive results.

After local excision of the nasopharynx and neck amyloidosis, no follow-up management for the multifocal amyloidosis was provided. Meanwhile, under the diagnosis of systemic lupus erythematosus (SLE) with active comorbidity, the patient was referred to a rheumatologist and accepted methylprednisolone pulse therapy (750 mg/day for 3 days) and cyclophosphamide (500 mg/week for 6 weeks) plus prednisolone (1 mg/kg/day) treatment followed by maintenance therapy with hydroxychloroquine (200 mg/day) and azathioprine (2 mg/kg/day).

Subsequently, the patient was disease free without any complications during the 6 months of follow-up in the outpatient department of otolaryngology and rheumatology. Thereafter, the patient accepted regular follow-up in the outpatient department of rheumatology for SLE.

Ethical committee approval was acquired from the institutional ethical review board of Taichung Tzu Chi Hospital, Taichung. (IRB number: REC107-39).

3. Discussion

The amyloidoses differ in the protein precursor undergoing aggregation, the target organs involved in amyloid deposition and, consequently, in their clinical features. To date, at least 28 different proteins have been identified as causative agents of amyloid diseases, ranging from localized cerebral amyloidosis in neurodegenerative conditions to systemic amyloidosis. The common types of amyloidoses are immunoglobulin monoclonal light chain amyloidosis (AL), reactive amyloidosis (AA), senile systemic amyloidosis (SSA), transthyretin amyloidosis (ATTR), fibrinogen amyloidosis (AFib), and apolipoprotein A-I amyloidosis (AApoAI).[7]

AA amyloidosis is related to chronic infection or inflammatory conditions, such as rheumatic disease, rheumatoid arthritis, and ankylosing spondylitis. The gold standard of diagnosis is Congo red staining pathology study results exhibiting amorphous deposition with apple-green birefringence under high intensity, cross-polarized light and immunohistochemical analysis with specific antibodies for the major amyloid precursors (AA, immunoglobulin light chains of κ or λ type, antitransthyretin).[1,2,7,8]

The most common form of systemic amyloidosis is AL amyloidosis, with a reported incidence of 8.9 per million person-years.[9] Amyloidosis is not uncommon in other chronic inflammatory processes but is rarely seen in SLE. The age of onset of amyloidosis is usually related to the age of onset of the inflammatory disease, its severity and the duration of the disease.[8] In previous case series, most of the patients had a history of SLE several years before the diagnosis of amyloidosis, ranging from 4 to 35 years.[8] In SLE patient, especially those presenting with polyarthritis, persistently high levels of acute phase of acute-phase reactants could be followed and accounted for as a risk factor for development of AA amyloidosis. However, not all cases with persistent increasing serum amyloid A protein developed AA amyloidosis, or not all cases with amyloidosis have higher level of SAA.[10]

Amyloid deposits have been reported in several organs in SLE patients.[8,11] In contrast to RA, in which high levels of acute phase reactants depending on IL-6, such as CRP and SAA are frequently found, patients with SLE had only modest elevations of serum Amyloid A protein, even in severe disease.[12]

A previous study demonstrated that amyloidosis in the head and neck region is typically localized disease and carries a good prognosis. The risk of systemic involvement is limited, and the nasopharynx is rarely involved.[13] The larynx is the most common site of head and neck amyloidosis. In a 20-year retrospective study directed by Rudy et al, 2018, 22 out of 865 patients had amyloidosis involving the head and neck region (mostly larynx), and 4 of them had multifocal involvement. Only 1 case of multifocal head and neck amyloidosis was secondary to marginal zone lymphoma.[6] In this study, we presented a case of head and neck multifocal amyloidosis secondary to occult underlying disease. Although the incidence is rare, multifocal amyloidosis should be taken as a hint of underlying occult disease predisposing to multiple amyloid protein deposition.[14–16]

The head and neck region has numerous blood vessels and lymphatic ducts. Given that fibrils of amyloid protein would be deposited along the blood supply and lymphatic drainage, multifocal lesions should be of concern for disease involving the head and neck region. Although localized amyloidosis was identified initially, a thorough head and neck investigation was warranted.

Treatment of amyloidosis varies with the type and involvement of disease. Systemic amyloidosis carries worse prognosis than localized amyloidosis.[1,13] It is crucial to investigate and eliminate underlying disease in systemic amyloidosis as soon as possible.[1,6,17]

4. Conclusion

Head and neck multifocal amyloidosis should be taken as a hint of systemic disease. In head and neck amyloidosis, a comprehensive survey to clarify the underlying disease predisposing to amyloidosis and organ involvement is warranted.

Author contributions

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