Case Report

Amyloidosis and Respiratory Tract Involvement: Report of Two Cases

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Amyloidosis is a group of diseases in which amyloid deposit in the extracellular space in an abnormal insoluble fibrillar form. The most important amyloid precursors are immunoglobulin light chain (AL) and serum amyloid-associated protein (AA). Amyloidosis can manifest as localized or systemic disease and respiratory system is one of the target organs that can be involved by amyloid. The authors report two cases of pulmonary amyloidosis presented with diffuse interstitial pulmonary amyloidosis and tracheobronchial involvement.

Keywords: *Amyloidosis, Respiratory tract involvement, Diagnosis, Management*

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Amyloidosis is a heterogeneous group of diseases in which amyloid, a normally soluble plasma protein, deposits in the extracellular space in an abnormal insoluble fibrillar form[1]. The main fibrillar component of amyloid can be derived from any one of 23 precursor proteins. The most important amyloid precursors are immunoglobulin light chain (AL amyloid) and serum amyloid-associated protein (AA amyloid)[2]. When amyloid deposits in tissues it may produce atrophy of parenchymal cells, interfere with mechanical function or impair vasoconstriction of blood vessels and lead to hemorrhage[3]. Amyloidosis can manifest as localized or systemic disease[4]. Respiratory system is one of the target organs that can be involved by amyloid[5]. The authors report two cases of pulmonary amyloidosis.

Case Report

Case 1

A 69-year-old man presented with progressive dyspnea on exertion for three months. He also had a non-productive cough and 3 kg weight loss. He was a non-smoker. Chest radiograph revealed bilateral multiple lung nodules. A CT scan of the chest revealed multiple pulmonary nodules varying in sizes with some centrilobular nodules and tree-in-buds appearance of both lungs (Fig. 1, 2). Bronchoscopy was performed and transbronchial lung biopsy at the superior segment of right lower lobe demonstrated amyloid

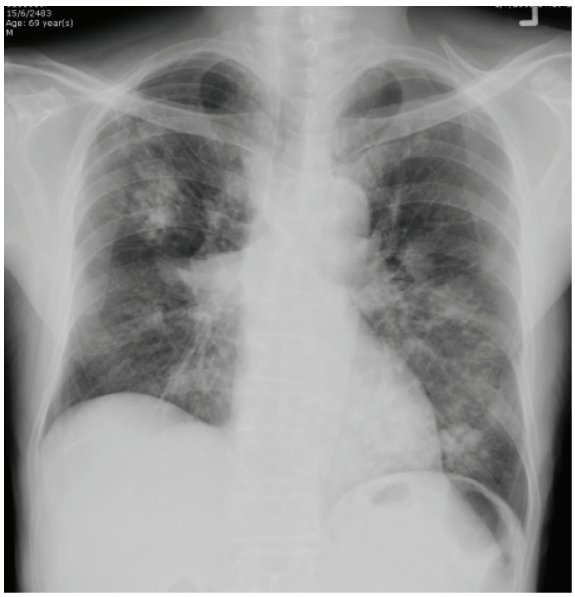

Fig. 1 Chest x-ray revealed bilateral multiple pulmonary nodules and interstitial infiltrates

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deposit tissue. Bone marrow biopsy also demonstrated amyloidosis. Immunohistochemical study confirmed AL amyloidosis. This case was classified as diffuse interstitial pulmonary amyloidosis, which occurs most often in systemic AL amyloidosis. Treatment with oral melphalan and prednisolone was planned but the patient was lost to follow-up.

Case 2

A 67-year-old man presented with two years history of cervical lymphadenopathy and multiple cutaneous masses at cheek, back, and both arms. Lymph node and skin biopsy revealed amyloid deposit tissue. He had a history of pulmonary tuberculosis 25 years earlier. Whole body CT scan was performed to investigate other organ involvement by amyloid. Findings from chest CT demonstrated minimal reticulonodular infiltration at the right upper lobe. Bronchoscopy was performed to investigate amyloid deposit in the lung and excluded other chronic granulomatous infections, which were a common cause of this abnormal x-ray pattern. The bronchoscopic finding revealed multiple whitish nodules at trachea and both bronchi (Fig. 3). Tissue biopsy from tracheal nodule was consistent with amyloidosis. This patient was diagnosed with systemic amyloidosis with tracheobronchial amyloidosis. Type of amyloid could not be determined from immunuhistochemistry in this case but the patient did not have other evidence of plasma cell dyscrasia or chronic inflammatory diseases from further investigations. Management of this case was follow up and his symptom and sign was stable.

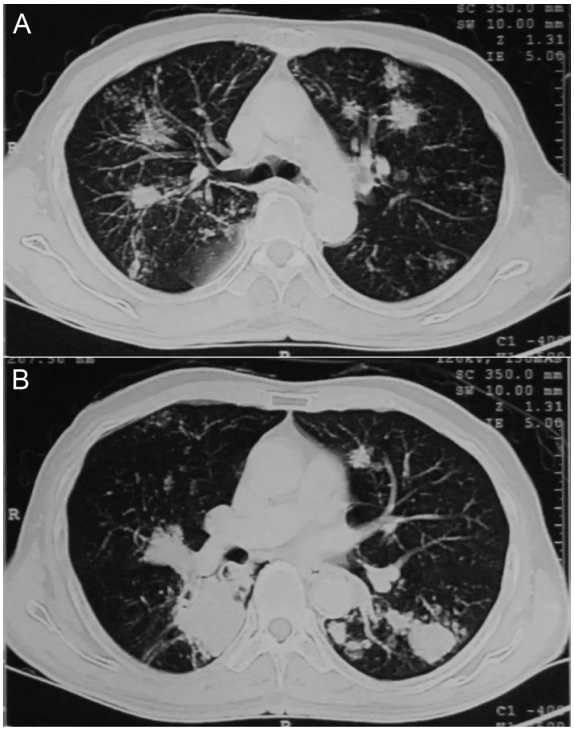

Fig. 2 (A, B) CT scan of chest demonstrated varying in sizes of multiple pulmonary nodules with some centrilobular nodules and tree-in-buds appearance in both lungs

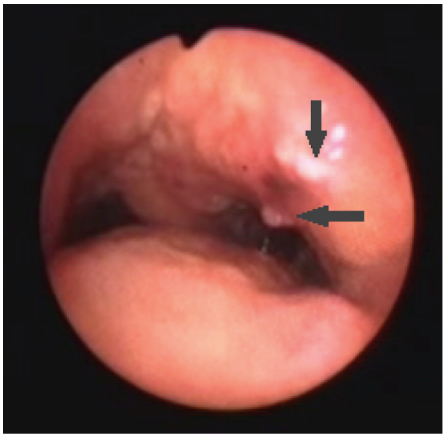

Fig. 3 Bronchoscopic finding revealed the whitish nodules at trachea (arrow)

Discussion

Amyloidosis may involve any portion of the respiratory tract and can manifest as localized or systemic disease[4]. Common three distinct forms of pulmonary amyloidosis are diffuse interstitial pulmonary amyloidosis, nodular parenchymal amyloidosis, and tracheobronchial amyloidosis[3]. Diffuse interstitial amyloidosis is the least common form of pulmonary amyloidosis[6]. The patient may present with dyspnea and cough, but rarely hemoptysis. Chest radiograph reveals either reticulonodular or miliary pattern. CT scan finding shows small nodules, patchy ground glass opacities, or alveolar opacities but rarely honeycombing[7]. This form occurs most often in systemic amyloidosis, especially in AL type amyloidosis, and less commonly in AA type[8]. In case 1, the finding is compatible with systemic AL amyloidosis, which involves skin, lymph nodes, and lung, presenting with diffuse interstitial pulmonary amyloidosis.

Pulmonary nodular parenchymal amyloidosis is usually localized[9] and presents as an abnormal

immune response of bronchial associated lymphoid tissue (light chain derivation, rare cases of amyloid associated protein). Radiographic finding shows solitary or multiple nodules varying in sizes from 0.5-15 cm[10]. These nodules are well-defined, with lobulated margins, and usually subpleural in distribution[11]. They grow slowly, and frequently cavitate or calcify[12]. Clinical symptoms are minimal with the occasional incidental finding from chest radiograph, but it may be associated with cough, dyspnea, or hemoptysis.

Tracheobronchial amyloidosis is the characterized by amyloid deposits in the trachea and large bronchi either in form of plaques or masses that mimic an endobronchial tumor[13,14]. This form of amyloid deposit in the respiratory tract is localized and most often by light-chain derivation[3]. The localized abnormal immune response of bronchial-associated lymphoid tissue may be the pathogenesis of this form. The patient can be asymptomatic or present with a cough, stridor, hemoptysis, or symptoms associated with bronchial obstruction[15-17]. Interestingly, case 2 presented as a systemic form of amyloidosis due to evidence of other organ involvement, such as skin and lymph node, but the bronchoscopic finding was compatible with tracheobronchial amyloidosis, which is usually found in localized form.

Diagnosis of amyloidosis requires tissue characteristic histopathology with Congo red staining, which showed an apple-green birefringence appearance under cross-polarized light microscopy, which is the diagnostic gold standard[5]. Immunohistochemistry is necessary to determine the fibril protein type. After amyloidosis is diagnosed, the evidence of other organ involvement must be evaluated to differentiate localized or systemic form[1]. Treatment depends on symptoms, fibril types and whether it is a localized or a systemic form[8]. In symptomatic localized amyloidosis such as tracheobronchial or nodular amylodosis, bronchoscopic therapy or surgical resection may be required[13]. In contrast, treatment of systemic amyloidosis requires treating the underlying disease in AA amyloidosis and to give chemotherapy in AL form.

Conclusion

Amyloidosis is a rare disease and can involve the respiratory system in various forms. The common forms are diffuse interstitial pulmonary amyloidosis, nodular amyloidosis, and tracheobronchial amyloidosis. Diagnosis of amyloidosis is difficult and requires tissue examination stain with Congo red. Immunohistochemistry is necessary to determine the fibril type. The management of pulmonary amyloidosis depends on symptoms and whether it has systemic involvement.

Potential conflicts of interest

None.

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โรค amyloidosis ในระบบทางเดินหายใจ: รายงานผู้ป่วย 2 ราย

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โรค amyloidosis เป็นกลุ่มโรคซึ่งเกิดจากการสะสมของสาร amyloid ในรูปที่ไม่ละลายบริเวณนอกเซลล์ โดยสารต้นกำเนิดของ amyloid ที่สำคัญ ได้แก่ อิมมูโนโกลบุลินชนิด light chain (AL) และโปรตีน amyloid-associated (AA) ซึ่งโรค amyloidosis นั้นสามารถแสดงออกแบบเฉพาะที่หรือมีการสะสมในหลายอวัยวะของร่างกาย โดยระบบทางเดินหายใจเป็นอวัยวะหนึ่งที่สามารถเกิดการสะสมของสาร amyloid ได้ ผู้นิพนธ์ได้รายงานผู้ป่วย 2 ราย ที่ได้รับการวินิจฉัยเป็นโรค amyloidosis ที่เกิดในระบบทางเดินหายใจ ในรูปแบบของ diffuse interstitial pulmonary amyloidosis และ tracheobronchial amyloidosis