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CASE REPORT

A Rare Case with Recurrent Abdominal Pain as the First Symptom: AL Amyloidosis with Colon Involvement Combined with Pulmonary Adenocarcinoma

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Background: Amyloidosis combined with lung cancer is a rare occurrence. To date, there are no reported cases of amyloid light-chain(AL) amyloidosis solely affecting the colon combined with pulmonary adenocarcinoma.

Case Summary: Here, we describe a case of a 66-year-old woman who presented with recurrent abdominal pain and was eventually diagnosed with AL amyloidosis with colon involvement and pulmonary adenocarcinoma. We also review the relevant literature and discuss the relationship between amyloidosis and lung malignancies. Significantly, lung cancer may contribute to the deposition of amyloid through paraneoplastic mechanisms. And in published case reports, the pathological type of lung cancer associated with AL amyloidosis was all adenocarcinoma.

Conclusion: Such cases are rare but provide new insights into the relationship between amyloidosis and lung malignancies. The mechanism of amyloid protein deposition in relation to lung cancer or malignancies remains unknown, further research in this field is warranted.

Keywords: amyloidosis, adenocarcinoma, lung cancer, comorbidity

Introduction

Amyloidosis is a group of diseases caused by various factors that result in protein misfolding and the formation of amyloid substances containing reverse parallel β-folded sheet structures. These substances infiltrate and deposit in the interstitial spaces of organs, ultimately leading to multi-organ damage and progressive multi-organ dysfunction. Commonly affected organs include the heart, kidneys, skin, and peripheral nervous system, with the digestive system also frequently involved. AL amyloidosis is a systemic disease characterized by the excessive production of λ-chain by monoclonal plasma cells, leading to the deposition of monoclonal immunoglobulin light chain fragments in the form of amyloid fibrils, resulting in progressive tissue and organ dysfunction. Systemic light-chain amyloidosis remains the most common type, accounting for 55% of all cases.[1]

Reports of cases of AL amyloidosis combined with lung cancer are rare. According to our research, only three cases of confirmed AL amyloidosis combined with lung cancer have been reported.[2–4] Our case is the first reported instance of AL amyloidosis solely affecting the colon combined with pulmonary adenocarcinoma, and the patient has shown good recovery in subsequent follow-ups.

Case Report

A 66-year-old woman was admitted to our hospital due to recurrent abdominal pain for three years. Three years earlier, the patient was first admitted to our hospital with the episode of abdominal pain, accompanied by moderate anemia,

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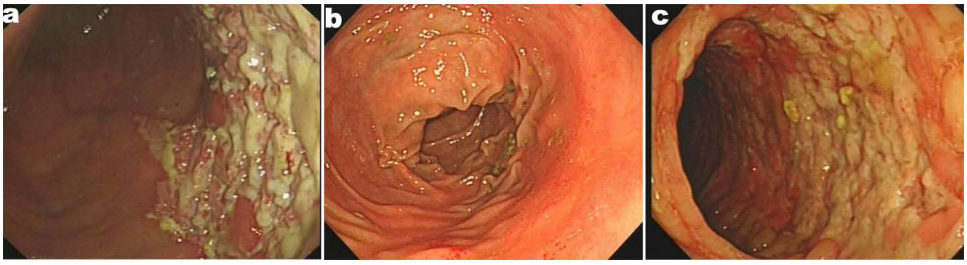

Figure 1 (**a**) First colonoscopy: extensive ulceration of transverse colon with a granular appearance and a yellowish-white moss; (**b**) Follow-up colonoscopy: the ulcers were in remission, red erosion of the mucosal surface can be seen in the transverse colon; (**c**) Colonoscopy at this admission: extensive ulceration of transverse colon with a granular appearance, mucosa hyperemia and a yellowish-white moss.

hypoproteinemia, and abnormal immunoglobulins, without cough, chest pain, or hemoptysis. Enhanced abdominal computed tomography showed transverse colon dilation with thickened bowel walls. Colonoscopy demonstrated extensive ulceration of transverse colon with a granular appearance and a yellowish-white moss.(Figure 1a) However, pathology report at that time did not indicate any specific lesions. Although the symptoms improved, the diagnosis of colonic lesions were undetermined, treatment with mesalazine and thalidomide continued after she was discharged.

During follow-up, her abdominal pain recurred but improved with symptomatic treatment. Her anemia and hypoproteinemia significantly improved, and enhanced abdominal computed tomography also showed improvement in the thickened bowel walls of the transverse colon. Follow-up colonoscopy showed the ulcers were in remission, red erosion of the mucosal surface can be seen in the transverse colon.(Figure 1b) Consequently, she discontinued mesalazine and thalidomide herself.

It should be noted that, her immunoglobulin levels were abnormal (IgG 16.9g/L↑, κ-chain 1.25g/L↓, λ-chain 2.94g/L↑) at her first admission. She was also admitted to the hematology department at that time, where bone marrow aspiration and immunofixation electrophoresis were performed, leading to a diagnosis of monoclonal gammopathy of undetermined significance (MGUS), and she was advised to a follow-up observation.

In addition, a chest computed tomography showed a ground-glass nodule in the upper lobe of the left lung at her first admission. During the follow-up two years, there was progressive enlargement of the pulmonary nodules.(Figure 2) After multidisciplinary consultation, surgical resection was recommended. The patient underwent thoracoscopic lung nodule resection at another hospital, and postoperative pathology report indicated pulmonary adenocarcinoma.

At this admission for recurrent abdominal pain, physical examination revealed mild abdominal distension and tenderness in the upper abdomen without rebound tenderness or muscle rigidity. Enhanced abdominal computed tomography showed thickened, edematous ascending colon walls and transverse colon dilation. Colonoscopy indicated aggravation of lesions, extensive ulceration of transverse colon with a granular appearance, mucosa hyperemia and a yellowish-white moss recurred.(Figure 1c) Pathology report showed chronic inflammation with inflammatory necrosis exudation and granulation tissue proliferation in the transverse colon, amyloid deposits around the mucosal stroma and small blood vessels can be seen, with positive Congo red staining. Reviewing the initial pathological sections of colon (three years ago), Congo red staining was also positive.(Figure 3) Based on these findings, a diagnosis of amyloidosis was considered, and she was referred to the hematology department for further treatment.

In the hematology department, laboratory tests showed some positive results which supported the diagnosis of AL amyloidosis.(Table 1) Flow cytometric analysis revealed the presence of abnormal clonal plasma cells 1.83% (expressing CD56+CD38+CD138+, not expressing CD117-CD28-CD45-CD19-), no clonal B lymphocytes detected.

Aspiration biopsy of bone marrow showed small amount of monoclonal plasma cell proliferation (about 1%) with no abnormal morphology, reticulin stain (-), iron stain (+), Congo red (-), oxidized Congo red (-), immunohistochemistry showed CD138+ plasma cells about 1%, CD19-, CD56-, restrictive expression of Lambda and Kappa (-).

Pelvic X-ray, skull lateral X-ray and enhanced cardiac magnetic resonance imaging showed no obvious abnormalities. Lumbar magnetic resonance imaging revealed degenerative changes in the lumbar spine, L2/3, L4/5, L5/S1 disc herniation; L5/S1 endplate inflammation.

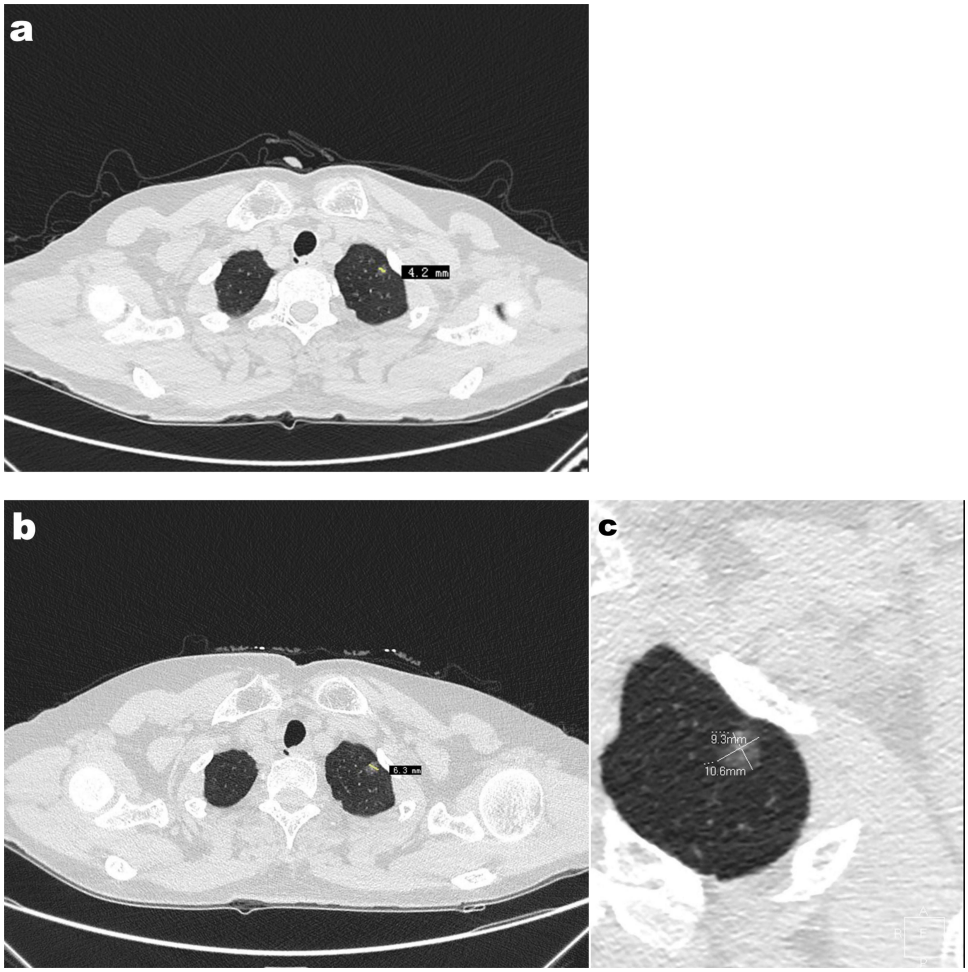

Figure 2 Computed tomography(CT) images: (**a**) Chest CT scan showed a ground-glass nodule(4.2mm) in the upper lobe of the left lung; (**b** and **c**) The nodule was progressively enlarged during the follow-up two years(6.3mm to 9.3mm).

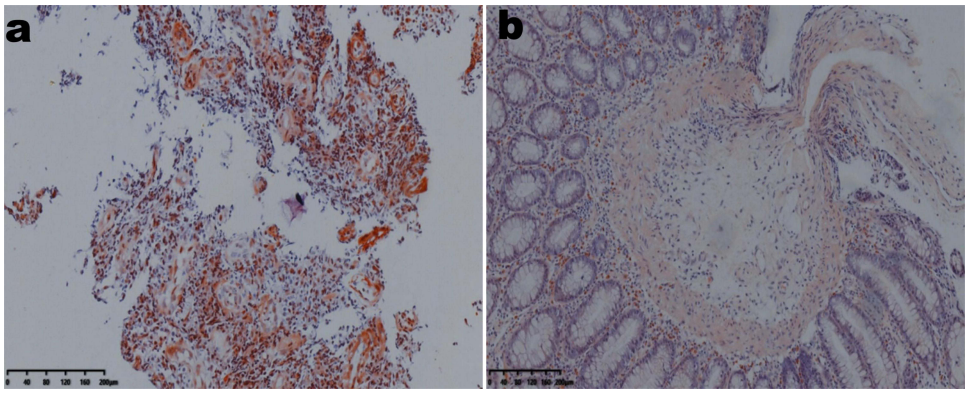

Figure 3 (**a** and **b**) Both Congo red staining of transverse colon biopsy specimen was positive.

The patient was eventually diagnosed with AL amyloidosis with colon involvement, and she was treated with Bortezomib plus dexamethasone initially, later adjusted to Melphalan, lenalidomide, and dexamethasone due to fever and fatigue. Final diagnosis: AL amyloidosis with colon involvement combined with pulmonary adenocarcinoma. The patient's abdominal pain significantly improved after chemotherapy for AL amyloidosis, and she showed good recovery over more than three years of follow-up.

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Table 1 Summary of Significant Laboratory Tests

	Value		Normal Range
Routine tests			
Hb(g/L)	92	↓	115–150
WBC(*10^9/L)	4.31	Normal	3.50–9.50
PLT(*10^9/L)	375	↑	125–350
CRP(mg/L)	40.82	↑	<0.5
ESR(mm/h)	65	↑	0–20
Total protein(g/L)	57.1	↓	65.0–85.0
Albumin(g/L)	27.4	↓	40.0–55.0
Serum immunoglobulin			
IgM (g/L)	0.32	↓	0.40–2.30
IgG (g/L)	14.7	Normal	7.00–16.00
IgA (g/L)	0.94	Normal	0.70–4.00
κ-chain (g/L)	1.00	↓	1.70–3.70
λ-chain(g/L)	3.09	↑	0.90–2.10
Serum protein electrophoresis			
α1-globulin(%)	5.3	Normal	1.0–5.7
α2-globulin(%)	13.6	↑	4.9–11.2
β-globulin(%)	9.7	Normal	7.0–13.0
γ-globulin(%)	19.6	↑	9.8–18.2
Albumin(%)	51.8	↓	57.0–68.0
M-protein	Positive		
Quantitative assay of serum free light chains			
κ-chain(mg/L)	18.08	Normal	3.30–19.40
λ-chain(mg/L)	119.77	↑	5.71–26.30
κ/λ ratio	0.1510	↓	0.2600–1.6500
Quantitative assay of urine free light chains			
κ-chain(mg/L)	50.00	↑	0.39–15.10
λ-chain(mg/L)	20.88	↑	0.81–10.10
κ/λ ratio	2.4038	Normal	0.4600–4.0000
Serum monoclonal immunoglobulin	IgG-λ		
Urine monoclonal immunoglobulin	None		

Discussion

Amyloidosis and Lung Cancer

In the 1970s, a co-existence of amyloidosis and lung cancer was discovered. In 1975, Japanese researchers accidentally observed amyloidosis in the kidneys, spleen, liver, and adrenal glands while inducing experimental lung cancer by applying carcinogens to rabbit bronchi.[5] Unfortunately, the relationship between lung cancer and amyloidosis was not further explored. In 1981, a study of 120 lung cancer autopsy cases identified amyloid in four oat cell carcinomas and one squamous lung carcinoma, suggesting different mechanisms between tumor amyloid deposits and systemic amyloidosis.[6]

AL Amyloidosis and Lung Cancer

In 1992, Benharroch et al[2] reported a case of a 51-year-old female with progressive systemic sclerosis, who, upon autopsy, was found to have bronchioloalveolar carcinoma (a type of pulmonary adenocarcinoma) and extensive amyloidosis (AL).

In 2010, Miyazaki et al[3] reported a case of primary systemic AL amyloidosis with rare lung nodules composed of adenocarcinoma and amyloid deposits. A 60-year-old female patient was found to have proteinuria and lung nodules

during a physical examination. And the pathology report of lung lobe showed adenocarcinoma with amyloid deposits surrounding the tumor. Immunohistochemistry showed that receptors for advanced glycation end-products (RAGE) were mainly positively stained in the tumor cells. She was ultimately diagnosed with primary systemic AL amyloidosis with nephrotic syndrome, and her condition improved over three years of follow-up.

In 2017, Okamoto et al[4] reported a 71-year-old female patient diagnosed with primary systemic AL amyloidosis with nephrotic syndrome and cardiomyopathy, combined with pulmonary adenocarcinoma. Furthermore, positive staining for RAGE was detected only in the lung tumour cells. The patient died three months after treatment.

It is notable that, the prior onset of lung cancer may contribute to the deposition of amyloid through paraneoplastic mechanisms. RAGE, a receptor for amyloid protein, is constitutively expressed in the lungs and typically downregulated in lung cancer tissues. Interestingly, RAGE that can bind amyloids showed strong expression in primary lung adenocarcinoma tissue in the early stages. The expression of RAGE in pulmonary adenocarcinoma may be a complication of latent amyloidosis. Clinicians should be aware that RAGE-positive lung cancer may be a complication of underlying amyloidosis that could impact more severely on the prognosis of the patient than the cancer itself.

Secondary Amyloidosis and Lung Cancer

In 1985, Focan et al[7] reported a 70-year-old male patient with diffuse joint pain and aplastic anemia. Autopsy revealed progressive systemic sclerosis and amyloidosis involving the gastrointestinal tract and bone marrow (considered secondary amyloidosis), as well as squamous cell carcinoma in the lungs. Although the association between systemic sclerosis, aplastic anemia, amyloidosis, and lung cancer might be coincidental, some pathogenic factors can be proposed.

In 2003, Ramón Barceló et al[8] reported a case of amyloid A(AA) amyloidosis combined with lung squamous cell carcinoma. The patient died of cancer-related respiratory infection and septic shock. In 2021, Wang et al[9] reported a case of lung squamous cell carcinoma combined with amyloidosis detected by PET-CT, the patient underwent surgery to remove the lung cancer, followed by chemotherapy. He did not receive any treatment against amyloidosis. Unfortunately, he died of a severe respiratory infection after the fourth cycle of chemotherapy.

In 2018, Zhao et al[10] reported a case of primary pulmonary adenocarcinoma combined with syphilis-induced secondary amyloidosis. A 55-year-old female patient was found to have lung nodules and multiple lung cysts on CT scans. She underwent thoracoscopic lobectomy, and the nodules were found to be adenocarcinoma with extensive amyloid deposits throughout the left upper lobe. Additionally, the patient was found to have a syphilis infection, leading to the suspicion that the pulmonary amyloidosis was secondary to the syphilis infection. Fortunately, no severe adverse effects appeared and no signs of local recurrence or distal disease were found at 6-month follow-up visit.

Cases of amyloidosis combined with lung cancer are rare, with more reports of AA amyloidosis combined with lung cancer compared to AL amyloidosis. Lung cancer might play a pathogenic role in the development of secondary amyloidosis. However, the exact mechanism linking amyloid protein formation to solid tumors remains unclear.

Amyloidosis and Other Malignant Solid Tumors

The incidence of amyloidosis among cancer patients is very rare(0.4%, 16/4033).[11] Among solid tumors, renal cell carcinoma (RCC) appears to account for one-quarter to one-half of all amyloidosis-associated cancers.[12] Compared to other solid tumors, there are more reported cases of lung cancer and basal cell carcinoma of the skin, possibly suggesting a specific relationship between lung cancer and amyloidosis. The mechanism linking tumors and AA amyloidosis may involve immune responses exacerbated by the tumor and its microenvironment or by immunotherapy. Serum amyloid A (SAA) is an important driver of AA amyloidosis in patients with solid tumors, but other factors, such as genetic susceptibility or immune adaptation, are key in amyloid protein deposition.

Prognosis of Amyloidosis

In recent years, the survival of AL amyloidosis patients has improved steadily, with median overall survival (OS) increasing from 1.4 years in the 1980s to 4.25–4.6 years in the 2010s.[1,13] However, amyloidosis with gastrointestinal involvement may have a poorer prognosis. In a study of 155 systemic amyloidosis patients, the median overall survival for those with gastrointestinal involvement (8 months) was shorter than for those without (16 months).[14]

Conclusion

The unique aspects of this case are: 1) Its rarity, the reports of AL amyloidosis combined with lung cancer are very few, which have involved multiple systems mostly, whereas our case is the first reported case of AL amyloidosis solely affecting the colon combined with pulmonary adenocarcinoma. 2) The patient's favorable prognosis, likely due to early diagnosis and lack of involvement beyond the colon.

Among the reported cases, the pathological type of lung cancer associated with AL amyloidosis was all adenocarcinoma, while the pathology type of lung cancer combined with secondary amyloidosis is predominantly squamous cell carcinoma.[8] Whether there is a relationship between the pathology type of lung cancer and the subtype of amyloidosis requires further study with more cases.

Although our patient had the rare condition of AL amyloidosis combined with lung cancer, early diagnosis and lack of involvement beyond the colon contributed to a favorable prognosis. Therefore, early diagnosis and early treatment are particularly important. For patients with amyloidosis, clinicians need to pay attention to lung cancer screening. The mechanism of amyloid protein deposition in relation to lung cancer or malignancies remains unknown, further research in this field is warranted.

Abbreviations

AL, amyloid light-chain; MGUS, monoclonal gammopathy of undetermined significance; RAGE, receptor for advanced glycation end-products; AA, amyloid A; RCC, renal cell carcinoma; SAA, Serum amyloid A;OS, overall survival.

Ethics Approval and Consent to Participate

Ethics approval is not required for this type of study. Written consent to participate in this study was obtained from the patient.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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