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Article

A case of primary systemic amyloidosis with prominent hematemesis and biomechanical implications of amyloid deposition

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Abstract: This article reviews a case of primary systemic amyloidosis characterized by vomiting blood. The patient was treated at the Affiliated Central Hospital of Shandong First Medical University for vomiting blood. Gastroscopy pathology showed amyloid deposition and restricted expression of plasma cell light chains, with elevated free light chains in hematuria. Bone marrow biopsy confirmed primary systemic amyloidosis. Amyloid deposition significantly altered tissue biomechanical properties, including increased stiffness and reduced elasticity in affected organs such as the gastrointestinal tract and heart, contributing to organ dysfunction. The patient received a chemotherapy regimen (D-CyBorD), achieving partial remission. However, irreversible multi-organ involvement persisted, underscoring the progressive nature of amyloid-induced biomechanical and functional damage. This study highlights the interplay between amyloid pathology, biomechanical tissue changes, and clinical outcomes, emphasizing the need for early diagnosis and multidisciplinary management.

Keywords: primary systemic amyloidosis; mayo staging; multisystem involvement; hematemesis; Congo red staining; biomechanics; mechanical properties

1. Introduction

Primary systemic amyloidosis (AL amyloidosis) is a rare but severe disease characterized by the deposition of amyloid fibrils in various tissues and organs, leading to progressive organ dysfunction. The amyloid fibrils in AL amyloidosis are primarily composed of misfolded immunoglobulin light chains, produced by clonal plasma cells, typically originating from a monoclonal gammopathy. The disease can involve multiple organs, including the heart, kidneys, liver, and gastrointestinal system, and its presentation is often insidious, with symptoms overlapping those of many other systemic diseases. AL amyloidosis is associated with a poor prognosis, especially when the heart or kidneys are involved, as it can lead to irreversible organ damage and ultimately organ failure [1].

The clinical manifestations of AL amyloidosis are highly variable, ranging from nonspecific constitutional symptoms such as fatigue, weight loss, and fever to organ-specific symptoms depending on the tissues affected by amyloid deposition. Gastrointestinal involvement, although less common, can present as a challenging diagnostic dilemma due to its nonspecific symptoms, which often mimic more prevalent conditions like gastrointestinal bleeding or malabsorption. In some cases, gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and malabsorption are the first signs of systemic amyloidosis, delaying the correct diagnosis and treatment [2].

The diagnosis of AL amyloidosis is often delayed due to its rarity and the nonspecific nature of its symptoms. The gold standard for diagnosis involves tissue biopsy, where Congo red staining and subsequent confirmation under polarized light reveal the characteristic apple-green birefringence of amyloid deposits [3]. Immunohistochemistry can identify the specific type of amyloid protein, and serum or urine electrophoresis can detect the presence of monoclonal light chains, which are indicative of an underlying plasma cell dyscrasia. Recent advances in imaging techniques and biomarkers have improved the diagnostic accuracy, allowing for earlier detection and more personalized treatment strategies.

In terms of treatment, chemotherapy and stem cell transplantation remain the cornerstones of therapy for AL amyloidosis. The goal of treatment is to reduce the production of the offending monoclonal light chains, thereby decreasing amyloid deposition and halting further organ damage [4]. Chemotherapeutic regimens, such as cyclophosphamide, bortezomib, and dexamethasone (CyBorD), have shown promising results in inducing remission and improving survival outcomes. However, despite the effectiveness of these treatments in controlling the plasma cell clone, the reversal of amyloid-related organ damage remains challenging, particularly in patients with advanced organ involvement. The prognosis for patients with AL amyloidosis is largely determined by the extent of organ involvement at the time of diagnosis, with heart and kidney involvement conferring the worst outcomes [5].

While significant progress has been made in the understanding and management of AL amyloidosis, there remain many unmet needs in the diagnosis and treatment of this complex disease. Novel therapies, including targeted monoclonal antibodies and proteasome inhibitors, are under investigation and hold promise for improving outcomes for patients with AL amyloidosis [6–10]. Additionally, multidisciplinary care, involving specialists in hematology, cardiology, nephrology, and gastroenterology, is essential for optimizing patient care and managing the diverse and often severe manifestations of the disease.

The pathogenesis of AL amyloidosis begins with the production of abnormal monoclonal light chains by plasma cells in the bone marrow. These light chains misfold and aggregate into amyloid fibrils that are deposited in various tissues, leading to the characteristic organ dysfunction seen in the disease. The amyloid deposits disrupt normal cellular function and structure, causing inflammation, fibrosis, and organ failure. As the disease progresses, the accumulation of amyloid fibrils can cause irreversible damage to critical organs such as the heart, kidneys, and liver, with cardiac involvement being the leading cause of death in these patients [11–13].

Given the complexity of the disease, timely and accurate diagnosis is critical for improving outcomes. Early identification and intervention can prevent further organ damage, and emerging therapies targeting the underlying plasma cell disorder may offer new hope for patients who were previously considered to have limited treatment options. In addition, biomarkers such as the levels of free light chains, cardiac biomarkers, and imaging techniques like Magnetic Resonance Imaging (MRI) and echocardiography can provide essential insights into disease progression and treatment response [14].

AL amyloidosis is a rare but life-threatening disease with a variable clinical presentation and a poor prognosis, particularly when major organs such as the heart

and kidneys are involved. While diagnostic advances have improved the ability to detect this condition early, significant challenges remain in terms of effective treatment and long-term management. Through a comprehensive understanding of the pathophysiology, clinical features, and available treatment options, this paper seeks to highlight the critical need for early diagnosis and individualized therapeutic strategies in the management of AL amyloidosis [15–18].

Systemic amyloidosis is a systemic plasma cell disease in which amyloid protein is deposited in the extracellular matrix of multiple tissues and organs throughout the body, causing damage to tissue and organ function. It can be divided into primary, secondary, and familial amyloidosis according to the cause and clinical manifestations [1]. Among them, primary systemic amyloidosis (PSA), also known as AL amyloidosis, has the highest incidence and a poor prognosis. The disease has diverse clinical manifestations, most commonly affecting the heart, kidneys, liver, lungs, thyroid, tongue, skin, and peripheral nerves, while gastrointestinal involvement is uncommon, with an incidence of only about 5% [2]. Due to the diverse clinical manifestations of PSA and the lack of specific examinations, diagnosis is often delayed. This study reports a case of PSA with vomiting as the prominent manifestation, aiming to deepen the understanding of this disease and promote its early diagnosis and treatment.

2. Tests

The patient is a 44-year-old female who came to the hospital because of "abdominal pain and bloating for 2 months, cough for 1 month, and vomiting blood for 18 h". Abdominal pain and bloating occurred 2 months ago, and cough occurred 1 month ago, and no special treatment was given. 18 h ago, she vomited bright red blood mixed with dark red blood clots and gastric contents, about 1000 mL, accompanied by upper abdominal pain and a small amount of black stool. Past history: 26 April 2024. Gastroscopy: superficial gastritis with erosion, duodenal bulb inflammation; see **Figures 1** and **2** for details. Pathology: Moderate to severe inflammation of the duodenal bulb mucosa with erosion and amyloid deposition in the interstitium.

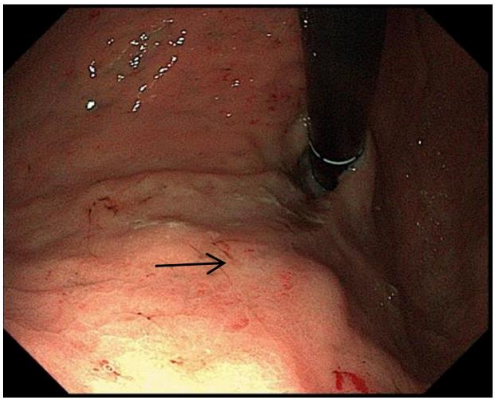

Figure 1. Erosion and congestion can be seen in the gastric fundus.

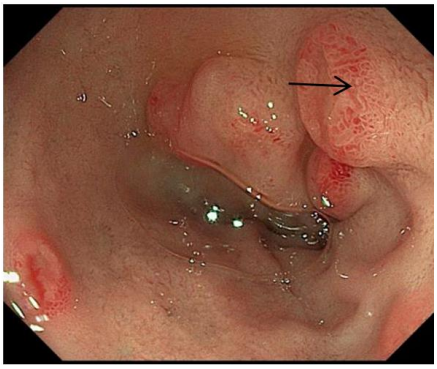

Figure 2. Congestion, edema, and erosion can be seen in the duodenal bulb.

Physical examination: BP 93/63 mmHg, chronic disease facial features, shortness of breath, severe pitting edema of both lower limbs, and no other obvious abnormalities in physical examination. Laboratory test: White blood cells 22.21 × 10^9/L, hemoglobin 98 g/L, platelets 950 × 10^9/L, alanine aminotransferase 90.5 U/L, aspartate aminotransferase 330.8 U/L, albumin 22.3 g/L, total bilirubin 66.7 μmol/L, γ-glutamyl transferase 1093 U/L, total cholesterol 12.28 mmol/L, low-density lipoprotein 9.7 mmol/L, fibrin degradation products 32.6 μg/mL, troponin T 32.46 ng/L, N-terminal B-type natriuretic peptide precursor 1391 ng/L, erythrocyte sedimentation rate 77 mm/h.

Serum free light chain κ 11.89mg/L, free light chain λ 4260.87 mg/L. Serum protein electrophoresis: γ band 10.8%, $\alpha 2$ band 18.8%, $\alpha 1$ band 5%, $\beta 1$ band 4.3%, $\beta 2$ band 11%, albumin 50.1%, see **Figure 3** for details.

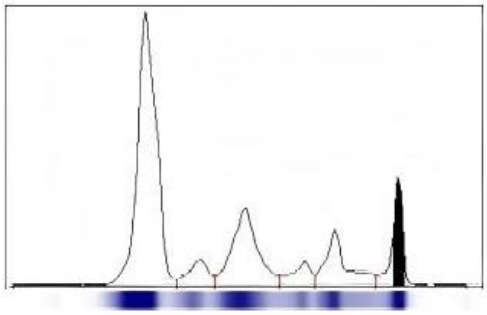

Figure 3. Serum protein electrophoresis results (Albumin $\alpha 1$, $\alpha 2$, $\beta 1$, $\beta 2$, γ).

Urine protein 4+, 24-hour urine protein 13.695 g. Urine $\alpha 1$-microglobulin > 220 mg/L, urine microalbumin 22,172 mg/L, urine transferrin 51.27 mg/L, urine $\alpha 2$-macroglobulin 8.05 mg/L, urine light chain κ 51.87 mg/L, urine light chain λ 187.27 mg/L. Immunofixation electrophoresis, immunoglobulins, abnormal leukocyte morphology, 16 rheumatism items, and renal function were all normal.

Electrocardiogram: sinus rhythm, low voltage in limb leads, *T* wave changes. Cardiac ultrasound: mild regurgitation of mitral and tricuspid valves. Enhanced CT of the chest and abdomen: multiple nodules in both lungs; multiple enlarged lymph nodes in the mediastinum and hilum, interstitial changes, bilateral pneumonia, and increased bilateral pleural effusions; uneven enhancement of the liver during the arteriovenous phase; diffuse thickening of the stomach wall; edema of the right colon; slightly widened portal vein; varicose veins at the gastric fundus; abdominal and pelvic

effusions; subcutaneous edema in the chest and abdomen.

Bone marrow smear: active proliferation of three bone marrow lines, 4.5% plasma cells, flow cytometry analysis showed 3.93% monoclonal plasma cells. Bone marrow puncture pathology: immune tissue showed CD138 positive plasma cell proliferation and light chain lambda restricted expression.

Second pathological examination of previously submitted tissues: consistent with amyloid deposition and plasma cell light chain restricted expression. Immunohistochemistry and special staining: CD38 (+), CD138 (+), Kappa (+), Lambda (-), Congo red (amyloid+), crystal violet (amyloid weak+), see **Figure 4** for details.

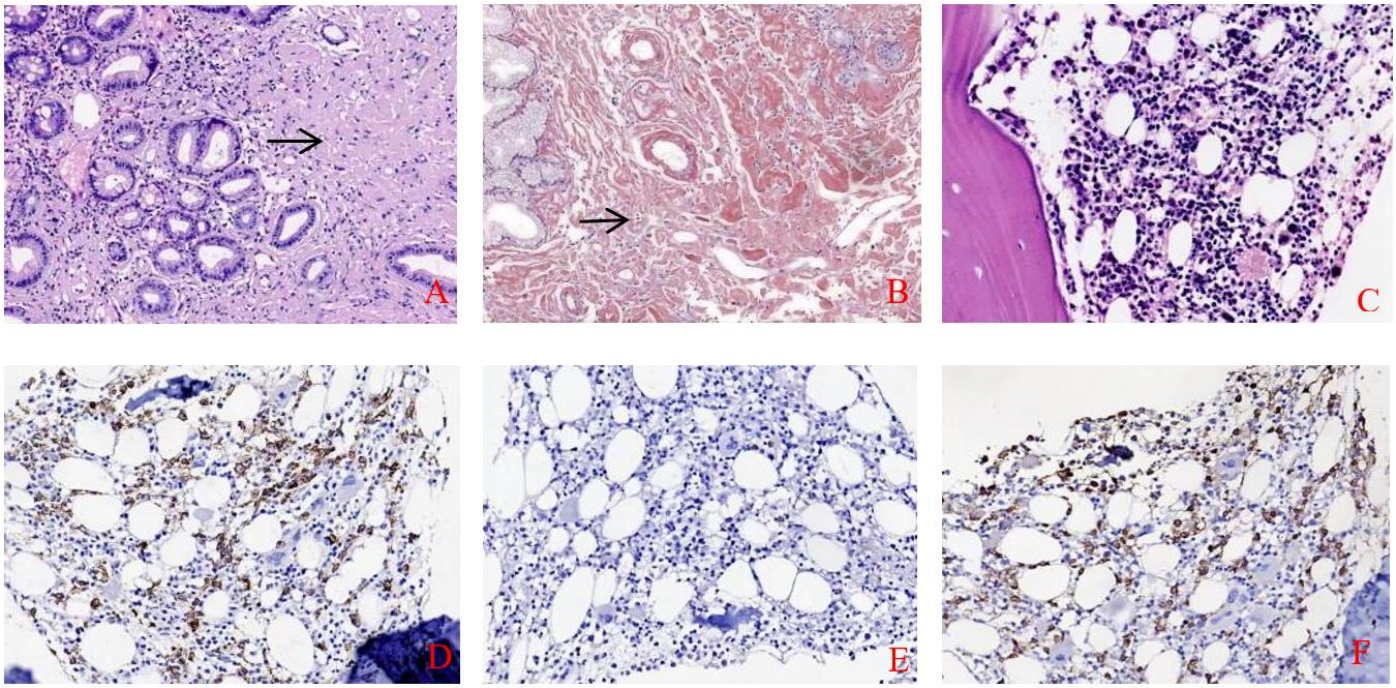

Figure 4. Duodenal and bone marrow biopsy. **(A)** Pink staining can be seen in the interstitial cells of the duodenum, and the arrow indicates the deposition of pink amorphous substances (HE staining × 100); **(B)** the arrow indicates that after Congo red staining, the amorphous substances appear brick red (Congo red staining × 100); **(C)** amyloid substances are deposited in the extracellular matrix of bone marrow cells (HE staining × 200); **(D–F)** Immunohistochemistry shows CD138, κ light chain (+), λ light chain (+) (immunofluorescence × 200).

The patient's plasma cell count in the bone marrow was found to be less than 10%, which did not meet the diagnostic criteria for multiple myeloma. However, taking into account the patient's gastrointestinal symptoms, bone marrow pathology, serological results, and immunoelectrophoresis findings, a diagnosis of PSA stage III was made. Stage III of PSA indicates widespread organ involvement, which typically correlates with poorer prognosis and more aggressive disease. The findings were consistent with amyloid deposition affecting multiple organ systems, contributing to the patient's symptoms.

Given the diagnosis of PSA, the patient was started on a chemotherapy regimen consisting of daratumumab, bortezomib, cyclophosphamide, and dexamethasone (D-CyBorD), a combination therapy used to target the underlying pathophysiology of amyloidosis. Daratumumab, a monoclonal antibody targeting CD38 on plasma cells;

bortezomib, a proteasome inhibitor; cyclophosphamide, a chemotherapy agent; and dexamethasone, a corticosteroid, are often used in combination to manage the hematologic aspects of amyloidosis.

However, due to the patient's history of massive hematemesis (vomiting blood), caution was exercised in administering dexamethasone. The dose of dexamethasone was reduced to mitigate the risk of further gastrointestinal bleeding, which could be exacerbated by high doses of corticosteroids. The treatment protocol was as follows: dexamethasone 20 mg on days 1, 2, and 8; daratumumab 400 mg on days 1, 2, 8, and 15; cyclophosphamide 0.4 g on days 7 and 14; dexamethasone 10 mg on day 14; bortezomib 1.5 mg on days 14 and 21; and dexamethasone 5 mg on day 21.

Throughout the treatment, the patient experienced low immunity, which led to repeated episodes of fever. Symptomatic treatments were given to manage these infections, though they complicated the clinical course. Despite these challenges, after 3 weeks of treatment, some improvement was observed. The patient's edema (swelling) and stomach discomfort improved, and there was no further occurrence of hematemesis. Laboratory results showed a dramatic reduction in the serum free light chain λ level to 139.86 mg/L and κ level to 15.4 mg/L. The serum free light chain difference, a critical marker in amyloidosis, dropped by 97%, from a higher baseline value to 124.46 mg/L, indicating a significant reduction in the amyloid-producing plasma cells. This marked improvement in light chain levels suggested partial relief and a positive response to the chemotherapy.

Despite these improvements in hematologic and clinical status, the patient's renal function and heart-related indicators continued to worsen progressively. This deterioration in organ function, despite the partial remission achieved through chemotherapy, is a common feature of advanced PSA, where amyloid deposition can lead to irreversible organ damage. Unfortunately, three days after the chemotherapy regimen was completed, the patient suffered a recurrence of acute vomiting blood, and despite rescue efforts, the patient ultimately succumbed to multi-organ failure.

This case highlights several key aspects in the treatment and management of primary systemic amyloidosis. Despite a good initial response to chemotherapy, the prognosis remains poor due to the irreversible nature of amyloid-induced organ damage, particularly in advanced stages of the disease. The treatment approach, which involved dose adjustments of corticosteroids to avoid gastrointestinal complications, was tailored to the patient's specific clinical circumstances. However, the progressive nature of organ dysfunction in advanced PSA remains a challenge, and this case underscores the need for continued research into more effective therapies that can better address both the hematologic and organ-specific manifestations of the disease.

3. Discussion

PSA is a rare disease, occurring in 8.9 per million people, caused by abnormal immunoglobulin light chain deposition, primarily affecting elderly individuals over 65 [3].

The specific pathogenesis of PSA is still unclear, but studies have shown that the disease may be related to factors such as genetic susceptibility, chronic infection, and abnormal immune response. The main pathological feature of this disease is the

deposition of amorphous amyloid substances in the extracellular matrix, which appear brick red after Congo red staining, and apple green birefringence is its specific manifestation under polarized light microscopy [4].

Due to the lack of specific clinical symptoms and imaging features, early diagnosis is prone to missed or misdiagnosis. In addition, most patients are already in the progressive stage of the disease when diagnosed, so the prognosis is poor. PSA patients may show systemic symptoms (such as fatigue and weight loss) and manifestations of damage to specific organs, which may eventually lead to multiple organ failure and death [5]. In this case, the patient's main manifestations were involvement of the gastrointestinal tract, heart, kidney, liver, lung, and other organs.

Amyloid can be deposited in the submucosal layer or blood vessel wall of various parts of the gastrointestinal tract, which then manifests as non-specific symptoms such as abdominal distension, abdominal pain, gastrointestinal bleeding or fatigue, weight loss, and in rare cases, intestinal obstruction, perforation, or bleeding may occur [6]. Endoscopy can reveal mucosal erythema, erosion, fine granular changes, and even ulcer bleeding. Colonoscopy can reveal characteristic submucosal hematoma and blood bubbles [7]. The patient was admitted to the hospital due to hematemesis, accompanied by abdominal pain, abdominal distension, black stools, etc. CT showed diffuse thickening of the gastric wall and edema of the right colon. Previous gastroscopy showed acute and chronic inflammation with erosion. Gastroenteroscopy was not performed here, so there are certain defects in the diagnosis. To clarify the cause of bleeding, the patient's previous tissues were sent for pathological examination. The results showed amyloid deposition, restricted expression of plasma cell light chains, positive Congo red staining, and positive immunohistochemistry CD138. There was no obvious abnormality in coagulation function. It was considered that the patient's hematemesis might be caused by amyloid degeneration involving the gastrointestinal mucosa, leading to ulcer bleeding, which is consistent with other reports [6].

Cardiac involvement is an important sign of poor prognosis in PSA patients. If timely intervention is not carried out, most patients will face life-threatening situations within 1 to 2 years after diagnosis [8]. About 72% of PSA patients will experience heart-related symptoms [9]. Cardiac markers such as brain natriuretic peptide and troponin can be used to assess the degree of cardiac involvement and prognosis [10]. In this case report, the patient had chest tightness, shortness of breath, severe edema of both lower limbs, multiple serous effusions, and elevated N-terminal B-type natriuretic peptide precursor and troponin T, indicating cardiac involvement. Amyloid protein deposition in the myocardial interstitium can cause hardening of the heart muscle and decreased contractility, leading to restrictive cardiomyopathy, causing patients to experience exertional dyspnea, limb edema, and ascites [7]. Li et al. [11] found that patients with myocardial involvement in amyloidosis all had ventricular thickening, abnormal diastolic function, and low voltage in the limb leads on the electrocardiogram, which is not completely consistent with this case.

The patient was a middle-aged female. Laboratory tests showed urine protein 4+, increased 24-hour urine protein, progressive increase in serum creatinine and urea, and increased urine free light chains, consistent with massive proteinuria, severe edema, hyperlipidemia, and hypoalbuminemia. Nephrotic syndrome caused by amyloid

deposition in the kidneys was considered. According to the literature, about 38% of patients showed renal involvement [9]. Amyloid deposition in the glomeruli, renal interstitium, and/or renal arteries can lead to proteinuria, nephrotic syndrome, and eventually renal failure [5]. Studies have shown that decreased glomerular filtration rate and increased proteinuria indicate poor survival [12].

When PSA affects the liver, patients may experience loss of appetite, fatigue, abdominal distension, edema, liver discomfort and pain, liver enlargement, weight loss, etc. [13], but most patients may be asymptomatic. Patients with abdominal symptoms, progressive increase in transaminase, alkaline phosphatase, and total bilirubin levels, abnormal blood lipids and coagulation, enhanced CT showing uneven liver enhancement, widened portal vein, obvious gastric varices, abdominal effusion, low albumin, and no obvious liver enlargement still indicate liver involvement.

When amyloid affects the lungs, the main manifestations are diffuse alveolar septal deposition, interstitial lung, pulmonary consolidation, and solitary or multiple pulmonary nodules [14,15]. Clinical manifestations include chronic cough, recurrent lung infections, hypoxemia, and progressive dyspnea in severe cases. In our case, the patient had a cough, and chest CT showed multiple nodules in both lungs, bilateral pneumonia, and interstitial changes, which were consistent with the manifestations of interstitial amyloid infiltration.

In addition, skin manifestations such as waxy rash and macroglossia have been mentioned in many cases [16,17]. Such manifestations were not present in the present case.

The patient showed symptoms of a chronic progressive disease with multiple system damage, but bone marrow cytology showed no significant abnormalities, thus excluding the possibility of multiple myeloma and other diseases. The patient's autoimmune disease and malignant tumor indicators were negative, so secondary systemic amyloidosis was excluded. According to the Mayo staging criteria updated in 2012 [18], this patient had two risk factors: free light chain difference 4248.98 mg/L > 180 mg/L and troponin T 32.46 ng/L > 25 ng/L, and was diagnosed with PSA stage III. According to the severity of cardiac involvement, the patient's systolic blood pressure was ≤100 mmHg, and the terminal B-type natriuretic peptide precursor level was 1391 ng/L < 1800 ng/L, which met one risk factor and was finally diagnosed as PSA stage IIIb.

Although biopsies of abdominal wall fat, gingiva, tongue, and rectal mucosa have a high positive rate (72% to 100%), there is still a lack of effective screening tools [4,19]. The sensitivity of traditional serum and urine immunoelectrophoresis to detect monoclonal proteins is limited, but combined with free light chain detection, it can significantly improve the diagnostic accuracy [20]. Changes in light chain difference are widely used to early judge treatment response and predict patient prognosis [12]. The levels of λ light chains in the serum and urine of this patient were significantly increased, indicating that the deposition of monoclonal immunoglobulin light chains from abnormal plasma cell clones is the main pathological mechanism of the disease. Congo red staining further confirmed the presence of amyloid, which was consistent with the above laboratory test results. From the perspective of treatment response, partial remission is reflected in the reduction of light chain difference. This shows that the treatment inhibited the

proliferation of abnormal plasma cell clones and the further deposition of amyloid to a certain extent.

The treatment goals of PSA are to quickly clear toxic protein precursors, reduce amyloid protein deposition, restore hematological indicators (such as free light chains reaching normal levels), and improve organ function. For patients who are initially treated, it is necessary to evaluate whether they are suitable for autologous peripheral blood stem cell transplantation (ASCT). For patients who are not suitable for transplantation, a combination chemotherapy regimen with bortezomib as the core is recommended. Currently, the bortezomib + cyclophosphamide + dexamethasone (CyBorD regimen) has a high complete remission rate in improving hematological indicators and organ function [21]. In addition, the combination of daratumumab and CyBorD can significantly improve the complete remission rate and major organ response rate, becoming a first-line chemotherapy regimen [21]. Organ transplantation is only suitable for specific patient groups [22]. The patient in this case was in poor general condition and was considered to be temporarily unsuitable for ASCT after evaluation. He was given D-CyBorD chemotherapy, and the efficacy was evaluated to achieve partial remission. In summary, PSA is a rare disease with diverse clinical manifestations and is easy to misdiagnose. In this case, the patient showed prominent manifestations in the upper gastrointestinal tract and multiple organ damage. After a clear diagnosis, he was given D-CyBorD chemotherapy, and the efficacy was evaluated as partial relief. However, the patient's multiple organ involvement was not fundamentally improved, and the prognosis was extremely poor. Therefore, early correct diagnosis and timely treatment are of great significance to improving the prognosis of PSA patients. This case uses the D-CyBorD regimen (daratumumab, bortezomib, cyclophosphamide, dexamethasone) based on the patient's advanced disease stage (Mayo IIIb) and ineligibility for autologous stem cell transplantation (ASCT). ASCT is beneficial for some early-stage patients with preserved organ function, but the treatment-related mortality is significantly higher in patients with advanced multi-organ involvement (approximately 15%–20%). Only 20%–30% of AL amyloidosis patients are eligible for ASCT, mainly due to cardiac or renal insufficiency. In contrast, the D-CyBorD regimen, through the synergistic action of daratumumab targeting CD38 and bortezomib as a proteasome inhibitor, can rapidly suppress plasma cell clones. The response rate (≥80% partial remission) is significantly higher than monotherapy and is more suitable for patients with impaired organ function.

Although D-CyBorD significantly reduces free light chains (by 97%), its immunosuppressive effects and side effects of corticosteroids may accelerate the patient's clinical deterioration, leading to recurrent infections. Retrospective studies show that 30%–40% of patients receiving D-CyBorD treatment need to adjust doses or delay chemotherapy due to severe infections, significantly impacting treatment continuity and survival outcomes. Despite the reduction in dexamethasone (from 20 mg to 5 mg), its inhibitory effect on mucosal repair may increase the risk of gastrointestinal bleeding, especially in patients with hypoalbuminemia. The recurrent vomiting of blood after chemotherapy in this case may be due to persistent amyloid deposits damaging blood vessel structures, compounded by the inhibitory effect of dexamethasone on mucosal repair.

Amyloid deposition not only disrupts organ function through biochemical and structural damage but also profoundly alters the mechanical properties of affected tissues. In cardiac amyloidosis, amyloid fibrils infiltrate the myocardial interstitium, replacing normal contractile elements and increasing myocardial stiffness. This pathological remodeling leads to restrictive cardiomyopathy, characterized by impaired ventricular filling and reduced cardiac output. Studies using echocardiographic strain imaging and cardiac magnetic resonance (CMR) have demonstrated that amyloid-infiltrated myocardium exhibits significantly elevated stiffness parameters, such as reduced global longitudinal strain (GLS) and increased extracellular volume (ECV) fraction. For instance, a study by Bravo et al. reported that myocardial amyloid deposition correlates with a 1- to 2-fold increase in tissue stiffness compared to healthy myocardium, as measured by shear wave elastography [23]. These biomechanical alterations exacerbate diastolic dysfunction and contribute to the high mortality associated with cardiac amyloidosis.

Gastrointestinal bleeding in this case likely resulted from amyloid deposition, which compromised the structural integrity of mucosal and submucosal blood vessels. Amyloid fibrils infiltrate the extracellular matrix of vessel walls, replacing collagen and elastin fibers, reducing vascular elasticity and tensile strength. This pathological remodeling leads to vessel fragility, microaneurysm formation, and impaired angiogenesis, increasing the risk of mucosal ulceration and hemorrhage. Histopathological studies have shown that amyloid-laden vessels exhibit thinning of the endothelial layer and loss of pericyte support, making them more prone to rupture under physiological stress. In the duodenum, where the patient exhibited erosions, amyloid infiltration likely worsened mucosal vulnerability, contributing to the massive hematemesis. The recurrence of bleeding after chemotherapy may also reflect the dual role of dexamethasone in the treatment regimen. While dexamethasone suppresses plasma cell proliferation and light chain production, its glucocorticoid effects inhibit prostaglandin synthesis and mucosal repair, delaying ulcer healing. Despite a dose reduction from 20 mg to 5 mg, cumulative dexamethasone exposure could have impaired gastric epithelial regeneration and collagen deposition at ulcer sites, creating a microenvironment prone to rebleeding. Retrospective studies in AL amyloidosis patients have reported a 15%–20% incidence of glucocorticoid-associated gastrointestinal complications, particularly in those with pre-existing mucosal damage. This underscores the need for cautious steroid dosing and prophylactic measures, such as proton pump inhibitors, in patients with amyloid-related gastrointestinal involvement.

4. Conclusion

This case of primary systemic amyloidosis, initially presenting with hematemesis, underscores the critical interplay between amyloid pathology, biomechanical tissue alterations, and clinical outcomes. The diagnosis was confirmed through gastroscopy, bone marrow biopsy, and Congo red staining, revealing widespread amyloid deposition. While chemotherapy (D-CyBorD) achieved partial hematologic remission, the patient's irreversible multi-organ dysfunction highlights the profound impact of amyloid-induced biomechanical changes on disease

progression.

Amyloid deposition disrupts organ function not only through biochemical toxicity but also by fundamentally altering tissue mechanical properties. In the heart, myocardial infiltration increases stiffness, leading to restrictive cardiomyopathy and diastolic dysfunction. Similarly, renal glomerular amyloidosis elevates basement membrane rigidity, impairing filtration mechanics and accelerating proteinuria. These biomechanical disruptions—measurable via advanced imaging techniques like cardiac magnetic resonance (CMR) and transient elastography—are key drivers of organ failure and poor prognosis.

The case emphasizes that current therapies targeting plasma cell clones, though effective in reducing amyloid production, often fail to reverse pre-existing biomechanical damage. This gap underscores the need for innovative strategies addressing both biochemical and mechanical facets of amyloidosis. Future research should prioritize the development of non-invasive biomechanical biomarkers, focusing on tools such as shear wave elastography and atomic force microscopy. These advanced technologies would enable the real-time quantification of tissue stiffness, offering valuable insights into the mechanical properties of tissues without the need for invasive procedures. Such advancements could significantly improve early diagnosis, monitoring, and treatment of various diseases, particularly those associated with tissue fibrosis or abnormal protein deposition, by providing more accurate and accessible measures of tissue health.

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