



Amyloidosis and liver. Review.

Paul Carrier^{1,2*} , Marilynne Debette-Gratien^{1,2} , Julie Abraham³ , Anne Cypierre⁴ , Jean-François Cadranel⁵ , Arnaud Jaccard^{3*} , Véronique Loustaud-Ratti^{1,2} 

¹Service d'Hépatogastroentérologie, CHU Dupuytren, 87042 Limoges, France

²Unité INSERM U-1248, Pharmacologie & Transplantation, Faculté de Médecine et de Pharmacie, Limoges University, 87042 Limoges, France

³Service d'Hématologie clinique et de thérapie cellulaire, Centre national de référence Amylose AL et autres maladies de dépôts d'immunoglobulines monoclonales, CHU Limoges, 87042 Limoges, France

⁴Service de Maladies infectieuses, CHU Limoges, 87042 Limoges, France

⁵Service d'Hépatogastroentérologie, d'Addictologie et de Nutrition, Groupe hospitalier public du Sud de l'Oise, Centre hospitalier Creil, 60100 Creil, France

***Correspondence:** Paul Carrier, Service d'Hépatogastroentérologie, CHU Dupuytren, 2, avenue Martin Luther King, 87042 Limoges, France. paul.carrier@chu-limoges.fr; Arnaud Jaccard, Service d'Hématologie clinique et de thérapie cellulaire, Centre national de référence Amylose AL et autres maladies de dépôts d'immunoglobulines monoclonales, CHU Limoges, 2, avenue Martin Luther King, 87042 Limoges, France. arnaud.jaccard@unilim.fr

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Abstract

Amyloidosis is a rare disease, corresponding to a deposition of proteins in various tissues. Amyloid light-chain (AL) amyloidosis can involve the liver in 17% to 45% of patients. Diagnosis of liver disease is based on specific criteria, coupling alkaline phosphatases and hepatomegaly. Liver stiffness is altered in cases of heart involvement, and overall, in cases of liver involvement. Liver biopsy is generally avoided due to an important bleeding risk. Treatment is essentially based on stem cell transplantation and chemotherapy, with large progress during the last decade. Liver involvement recovery is generally diagnosed with a reduction in alkaline phosphatases and in liver size.

Keywords

Amyloidosis, liver stiffness, liver involvement

Introduction

Amyloidosis is a rare and heterogeneous disease characterized by the deposition of beta-fibrillar proteins in various tissues. It was first described by Rudolf Virchow in 1853 [1]. Sixty forms of amyloidosis have been identified, 27 of which are potentially associated with human diseases. The clinical presentation can be systemic or, in some cases, restricted to a single organ.



The liver is primarily affected in amyloid light-chain (AL) amyloidosis, the most common form, which results from the deposition of monoclonal immunoglobulin light chains [2]. Amyloid A (AA) amyloidosis, typically associated with chronic inflammatory conditions, is caused by the deposition of serum AA (SAA) protein. While it can lead to gastrointestinal manifestations, the liver is usually spared. Finally, in hereditary transthyretin amyloidosis (ATTR), the liver is not directly affected by the disease but is the site of transthyretin production.

Epidemiology

Amyloidosis is a rare disease with a prevalence ranging between 1/17,000 and 1/50,000 in Europe and the USA [3]. AL amyloidosis accounts for approximately 80% of cases [4]. The disease is most diagnosed between the ages of 50 and 70, with fewer than 10% of cases occurring before the age of 50. In the study of Kyle et al. [5], men were involved in 54% of cases. Among AL amyloidosis cases, 75% to 80% involve lambda light chains, while the remaining 20% to 25% involve kappa light chains [6]. Overall, the incidence of amyloidosis appears to be increasing [7].

Pathophysiology

The hallmark of amyloidosis is the abnormal folding of soluble precursor proteins [8].

AL amyloidosis is considered a multi-organ disease, with the heart, spleen, peripheral nervous system, kidneys, and gastrointestinal tract being the most frequently affected. It results from the abnormal production of light chains by clonal plasma cells, typically in elderly patients. These light chains are thermodynamically and kinetically unstable, leading to self-aggregation into misfolded oligomers. These oligomers subsequently form cross-beta amyloid fibrils, which are 8–10 nm in diameter as observed by electron microscopy [9]. These fibrils exert toxic effects on organs by interacting with serum amyloid P component (SAP) and glycosaminoglycans [10]. Their accumulation disrupts tissue architecture, leading to organ dysfunction through both a mass effect and a proteotoxic mechanism involving precursor protein oligomers [11]. In the liver, amyloid proteins accumulate in the space around hepatocytes, especially in sinusoids and portal areas, leading to distortion and compression of hepatocytes. Sinusoidal deposition can compress the hepatocytes, leading to hepatocellular atrophy and can efface the overall architecture. These modifications can lead to liver congestion, giving an increase in liver stiffness. In cardiac involvement, activation of the p38 MAP kinase pathway has been associated with increased cell apoptosis and elevated pro-BNP (pro-brain natriuretic peptide) levels.

A genetic influence is observed in approximately 50% of cases, with a chromosomal translocation t(11;14) involving the immunoglobulin heavy-chain locus (IgH) and the oncogene cyclin D1 [12]. In 10% of cases, diploidy, a common feature in multiple myeloma, is reported [13]. Additionally, mutations in the *IGLV* gene family may contribute to amyloid fibril formation.

There are no well-defined risk factors for AL amyloidosis, except for monoclonal gammopathy of undetermined significance (MGUS), which confers a relative risk of 8.8. AL amyloidosis is diagnosed in 10% to 15% of multiple myeloma patients, and Congo red-positive deposits in subcutaneous fat aspirates or bone marrow are observed in 38% of these patients [14]. Agent Orange, an herbicide used during the Vietnam War, was suspected to increase the risk of amyloidosis, but this association has not been confirmed [15].

Liver involvement

Liver involvement is described in 17% to 45% of patients diagnosed with AL amyloidosis [3, 16, 17]. Specific data concerning age and gender are limited concerning liver involvement, just a Chinese study suggests a ratio of male-female near 3:1 [18]. The fact that patients with AL amyloidosis are old can impact liver function and protein homeostasis, which may influence amyloid deposition.

Autopsy studies report a prevalence of 80% [6]. Isolated liver involvement is rare, occurring in only 1% of cases, while in 5% of patients, the liver is the dominant affected organ. Without treatment, the median survival in cases of hepatic amyloidosis is approximately 8.5 months [19]. Two-thirds of patients with liver involvement also present with cardiac or renal amyloidosis, which has a greater impact on survival.

The classical clinical presentation includes hepatomegaly, typically exceeding 15 cm on imaging, and an elevation of alkaline phosphatase levels above 1.5 times the upper normal limit [20]. However, diagnosis can be challenging in cases of isolated hepatomegaly or isolated elevation of alkaline phosphatase [21–23]. Other, less common presentations include cholangitis, portal hypertension, or, in rare cases, spontaneous hemorrhagic rupture [24–26]. There is evidence that amyloidosis can compromise liver vascular integrity, leading to fragility and hemorrhage. Also, it can lead to ascites formation.

Amyloidosis is often not considered initially, with the correct diagnosis suspected in only 26% of cases before liver biopsy. Furthermore, transaminases (AST and ALT) are not considered sensitive markers for liver amyloidosis, in contrast to alkaline phosphatase. There is no strong evidence that particular liver diseases increase the risk of AL amyloidosis.

Liver biopsy carries a high risk of bleeding and is generally contraindicated or avoided due to factor X deficiency, loss of von Willebrand factor, and amyloid deposition within the walls of blood vessels, all of which increase hemorrhagic risk [27, 28].

Imaging techniques such as ultrasound and computed tomography (CT) scan are not specific but are useful for differential diagnosis and follow-up (Figure 1). In 1988, ¹²³I-labeled SAP scintigraphy was introduced as a non-invasive method for detecting amyloid deposits in the liver, kidneys, adrenal glands, and spleen [29]. Lovat et al. [30] demonstrated that SAP scintigraphy is highly specific and sensitive, but its availability is limited, and the cost is high.

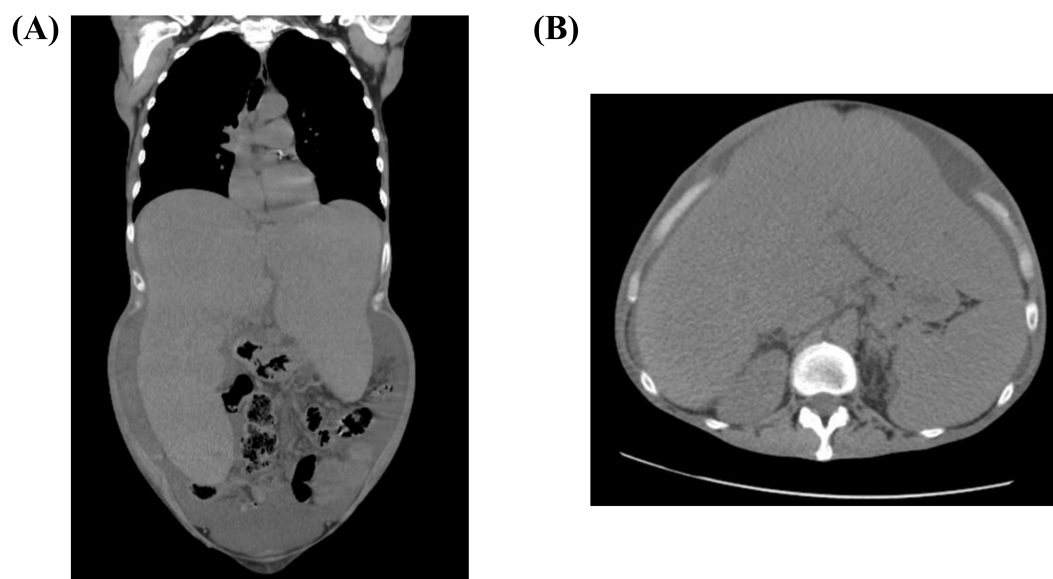


Figure 1. CT-scan showing an important liver size increase. Patient deceased from her liver involvement. (A) Sagittal section; (B) axial section

Given that amyloid fibril deposition increases liver stiffness, non-invasive elastography methods have been explored [24, 31, 32]. The first study, conducted at our hospital in 2011 on 41 patients, showed a significant increase in liver stiffness in amyloidosis: the median stiffness was 27.4 kPa in liver amyloidosis (with or without cardiac involvement), 10.4 kPa in cardiac amyloidosis (with or without liver involvement), compared to 4.8 kPa in controls, 6.8 kPa in HCV patients, 11 kPa in patients with cardiac disease, and 6.1 kPa in AL amyloidosis without cardiac or hepatic involvement [33]. Extreme values (up to 75 kPa, the maximum measurable stiffness) were also observed. We proposed a threshold of 17.3 kPa for liver amyloidosis with good specificity. However, liver stiffness can also be elevated in isolated cardiac

involvement (4–38 kPa), making interpretation more complex in these patients. A German study by Brunger et al. [34], conducted on 70 AL amyloidosis patients, identified a threshold of 14.4 kPa, with 50% sensitivity and 74% specificity, using SAP scintigraphy as the gold standard. Notably, their median alkaline phosphatase level was 88 IU/L (range 70–135), differing from standard reference values. These findings were confirmed in the French national registry, which also observed a trend toward increased liver stiffness via FibroScan [35]. The values are near, but the samples were different. Also, further studies are warranted, and we would probably keep a value around 15–17 kPa as a good criterion for liver involvement. Recent studies and case reports have explored MRI and shear wave elastography, but sample sizes remain limited [36, 37].

In suspected liver amyloidosis, the diagnostic approach should include exclusion of other causes of cholestasis or hepatomegaly, confirmation of amyloidosis, and consideration of transient elastography or advanced imaging techniques. All is summarized in Table 1 and Figure 2.

Table 1. Liver involvement in AL amyloidosis: clinical features, complications, and outcomes

Clinical aspect	Findings/characteristics
Prevalence of liver involvement	Observed in approximately 70% of symptomatic AL amyloidosis patients
Diagnosis criteria	Hepatomegaly, elevated alkaline phosphatase above 1.5N
Specific complications	Portal hypertension, ascites, hepatic failure, and rare spontaneous hepatic rupture
Investigations	Liver stiffness measurement (≥ 14.4 –17.3 kPa) Liver biopsy, carefully, showing amyloid deposits
Prognosis	Generally good with recent treatments High mortality with cardiac and hepatic failure
Treatment	Essentially, anti-plasma cell chemotherapy (e.g., daratumumab), emerging CAR-T cells, siRNA, and autologous transplant

AL: amyloid light-chain; CAR-T: chimeric antigen receptor T; N: normal limit; siRNA: small interfering ribonucleic acid

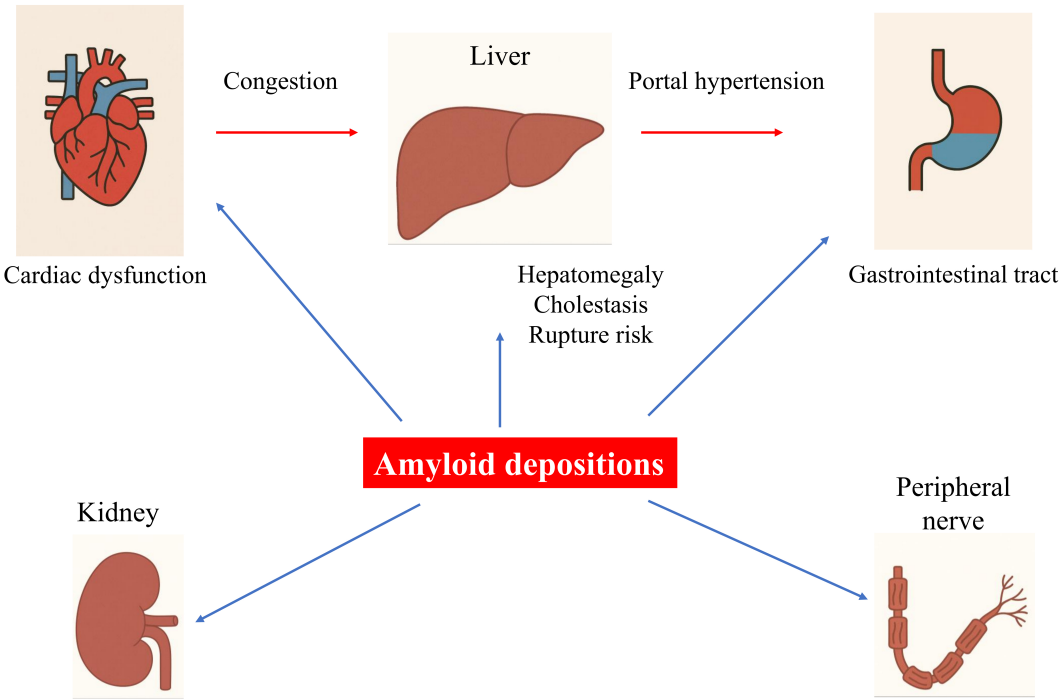


Figure 2. Schematic diagram showing the involvement of different organs in AL, with major highlights in liver-related complications. AL: amyloid light-chain

Amyloidosis diagnosis

The diagnosis of amyloidosis is primarily based on clinical examination, as symptoms are often non-specific. Common manifestations include heart failure, periorbital purpura, edema, macroglossia, and hepatomegaly.

Regarding organ involvement, based on both biological and clinical criteria (note: items in *italics* are considered defining criteria) [8, 20]:

- Cardiac involvement is defined by an *NT (N-terminal)-proBNP level greater than 332 ng/L* (in the absence of renal failure or atrial fibrillation) or *a diastolic septal thickness over 12 mm* without another cause. Clinically, patients may have signs of right heart decompensation, hypotension, dyspnea, or peripheral edema.
- Kidney involvement is characterized by *a 24-hour proteinuria ≥ 0.5 g/day*, predominantly albumin. This may lead to nephrotic syndrome, renal insufficiency, and clinically significant edema.
- Neurologic involvement may be peripheral or autonomic. *Peripheral neuropathy* typically presents as a sensorimotor neuropathy of the lower limbs. *Autonomic dysfunction* includes impaired gastric emptying, intestinal pseudo-obstruction, voiding difficulties unrelated to direct infiltration, orthostatic hypotension, and erectile dysfunction.
- Pulmonary involvement may be histologically proven in patients with respiratory symptoms. Clinical manifestations include interstitial lung disease or pleural effusions.

Initial laboratory tests include serum free light chain (FLC) assay, serum protein electrophoresis, and proteinuria detection. Bone marrow examination is recommended to assess for associated multiple myeloma [8].

The gold standard for diagnosis remains histological examination of affected tissues, demonstrating beta-fibrillar protein deposits, particularly with Congo red staining [38]. Amyloid fibrils appear as amorphous, eosinophilic deposits on hematoxylin-eosin staining, with characteristic apple-green birefringence under polarized light using Congo red. Further characterization of amyloid deposits is performed using direct immunofluorescence or immunohistochemistry with specific antibodies (Figure 3). When deposits are sparse and difficult to detect with Congo red, electron microscopy may be utilized. More advanced techniques such as mass spectrometry, DNA analysis, and protein sequencing are also available [39].

Biopsies are usually performed on subcutaneous fat (approximately 70% sensitivity) or minor salivary glands (60% sensitivity) [40, 41]. In some cases, samples may be obtained from the gastrointestinal tract, kidneys, myocardium, or peripheral nerves. Given the high bleeding risk, these sites are preferred over liver biopsy [2]. The combination of abdominal fat and bone marrow biopsy confirms AL amyloidosis in 83% of patients [41].

Due to its prognostic significance, cardiac involvement must be assessed in all patients, as it occurs in approximately 80% of cases. Evaluation includes NT-proBNP measurement, electrocardiography, transthoracic echocardiography with an experienced cardiologist, and, if needed, cardiac MRI. Key findings include low-voltage ECG (electrocardiogram), elevated NT-proBNP, myocardial thickening (especially of the interventricular septum), and characteristic features on MRI. 99mTc-phosphate scintigraphy helps distinguish ATTR amyloidosis from AL amyloidosis. NT-proBNP monitoring is also crucial for assessing treatment response. From a hepatogastroenterology perspective, identifying cardiac involvement is important to assess hepatic congestion. Distinguishing between primary liver amyloidosis and secondary hepatic congestion can be challenging. A French study of 200 prospectively enrolled patients with cardiac amyloidosis found that 49% had elevated liver enzymes (> 1.5 times the upper limit of normal). Liver abnormalities included hepatomegaly (40% of cases), hepatic vein dilation (38%), increased hepatic uptake on scintigraphy (liver/mediastinum ratio = 0.7 vs. 0.6, $p < 0.001$), and sinusoidal dilation on histology (56%). Notably, bilirubin levels had prognostic value, with a threshold of 5 $\mu\text{mol/L}$ associated with reduced 3-year survival (28% vs. 65%) [42].

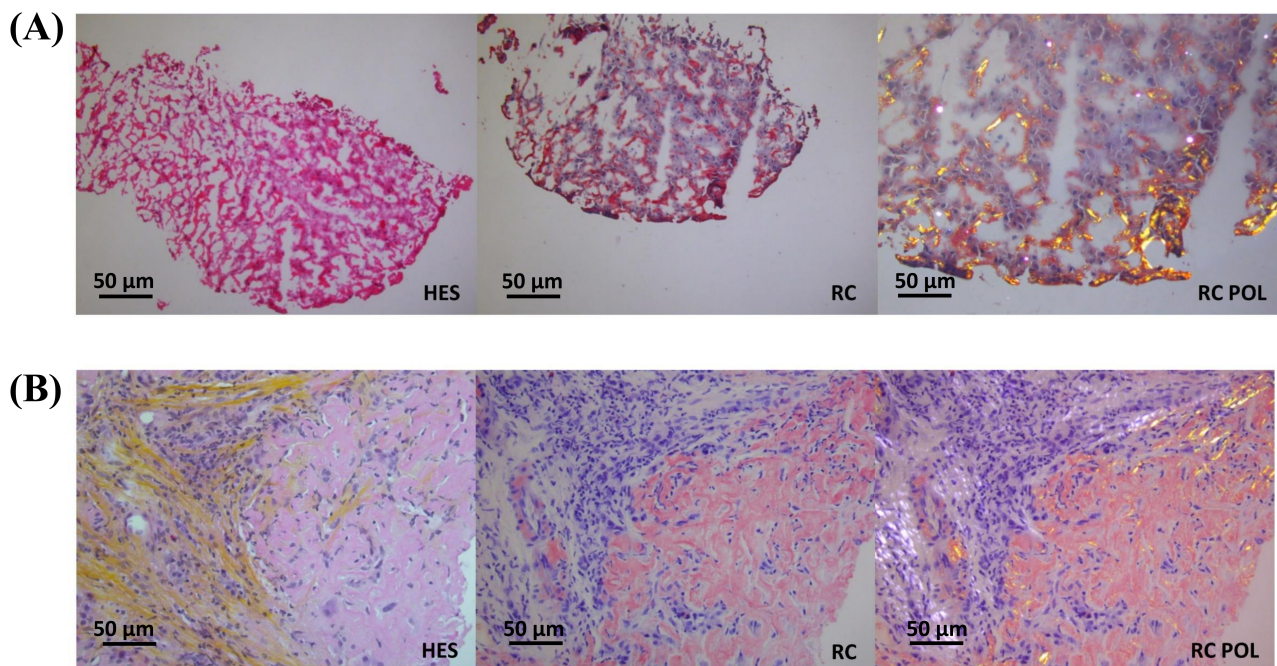


Figure 3. Liver biopsy from amyloid light-chain (AL) amyloidosis. RC (Congo red) staining is characteristic of hepatic amyloidosis. HES (hematein-eosin-saffron), RC, and RC POL (RC in polarized light) staining show significant extracellular deposition, including the RC staining, without and with (for birefringence) POL, showing amyloid deposits. (A) Frozen section staining. Original magnification: $\times 400$. (B) Staining on deparaffinized sections. Original magnification: $\times 400$. Sourced from the [CNR Limoges/Poitiers](#) database

Gastrointestinal symptoms frequently accompany liver involvement. While symptoms occur in 20% of patients, histological evidence of amyloid deposits is found in 80% of gastrointestinal biopsy samples. Presentations range from diarrhea, weight loss, and abdominal pain to constipation, gastroparesis, perforation, or intestinal obstruction. Treatment relies on conventional antidiarrheal agents such as opium tincture, loperamide, and octreotide [43], as well as evaluation for small intestinal bacterial overgrowth. AL amyloidosis patients are often malnourished, requiring nutritional support.

Other organs may also be involved, including the kidneys and peripheral nerves, while rare cases of amyloid deposition have been reported in the bones, skin, larynx, and adrenal glands [39]. The brain is uniquely spared. Laboratory findings such as plasma cell dyscrasia (elevated immunoglobulin-secreting plasma cells) and isolated factor X deficiency may provide additional diagnostic clues.

Treatment

Prognosis and evolution

Prognosis often depends on the extent of organ involvement and the delay in diagnosis [44]. In liver amyloidosis, a high bilirubin concentration is generally associated with an increased mortality risk [2, 45].

Over the last decades, significant improvements in treatment and prognosis have been observed. Overall survival has increased from 15% in the 1980s to 58% in the 2010s, even before the latest advancements in specific treatments, including protocols based on cyclophosphamide-bortezomib-dexamethasone combined with daratumumab [46].

For specific liver involvement, response criteria are determined by a reduction in alkaline phosphatase levels of more than 50% and a decrease in liver size of at least 2 cm [20, 47]. These criteria, proposed by the Amyloidosis Forum Multi-Organ System Working Group, require further validation in clinical settings [3, 48]. In some cases, the treatment response can be rapid and clinically remarkable. Additionally, a decrease in liver stiffness may be considered a criterion for liver response (personal data).

Improvement depends on response criteria, with response typically occurring within 6 to 12 months but sometimes taking over 24 months [47, 49]. The estimated time for a full liver clinical response is 39 months [47].

General management

Treatment is classically based on three principles: rapid and significant reduction in amyloidogenic protein production, individualized management based on organ involvement and treatment risks, targeting specific organ involvement [8]. Management is coordinated by hematologists, potentially within clinical trials, and follows risk stratification according to the Mayo Clinic standard classification system. This system categorizes patients into low, medium, or high risk based on the following parameters: NT-proBNP less than 5,000 ng/L, troponin less than 0.06 ng/mL, glomerular filtration rate greater than 50 mL/min per 1.73 m², age less than 65 years, performance status 0 to 2, NYHA class less than III, ejection fraction greater than 45%, systolic blood pressure greater than 90 mmHg at rest and carbon monoxide diffusing capacity (CMDC) greater than 90% [50]. Autologous stem cell transplantation with melphalan is generally preferred for low-risk patients. Depending on disease severity, a regimen of cyclophosphamide, bortezomib (a proteasome inhibitor), and dexamethasone may be used as a first-line treatment, eventually with daratumumab [40, 51]. Other treatments can be suggested in case of failure, such as melphalan, proteasome inhibitors, anti-CD-38 monoclonal antibodies, and immunomodulatory agents [8]. Also, antifibril monoclonal antibodies are an emergent class.

The goal of treatment is to reduce or stop monoclonal protein production, allowing progressive elimination of amyloid deposits from affected organs.

Monitoring is based on the reduction of FLC production. Predictors of survival include: iFLC (involved FLC) value of less than 20 mg per liter and a dFLC (uninvolved FLC) value less than 10 mg per liter, predicting survival. This treatment achieves a high hematologic response rate, with 78% of patients showing at least a good partial response and 50–55% exhibiting organ response 18 months after initiation. If unsuccessful, alternative treatments are available [52, 53]. New therapeutic approaches, such as chimeric antigen receptor T (CAR-T) cells and specific antibodies, are under investigation for refractory cases. Chemotherapy can pose specific liver toxicity risks, and stem cell transplantation may lead to conditions like sinusoidal obstruction syndrome. Even in cases of good hematologic response, measurable residual disease may persist, potentially contributing to residual organ dysfunction [54].

Specific liver-related complication management

There is no specific treatment aimed at liver amyloidosis involvement. Nevertheless, in case of fluid retention, most often due to heart failure, salt restriction and diuretics are prescribed. In case of portal hypertension rather rare in this situation, specific management is necessary, including diuretics, beta-blockers, and ligation in case of esophagus varices, such as in cirrhosis [55]. Also, data in the literature report a 72% improvement rate of liver involvement criteria in case of standard treatment [56].

ATTR amyloidosis

ATTR amyloidosis results from transthyretin, a serum transporter primarily for holo-retinol-binding protein and, to a lesser extent, thyroxine [57]. It predominantly affects men over 70 years, leading primarily to cardiomyopathy. In hereditary forms, symptoms appear earlier and manifest as systemic disease, including polyneuropathy and autonomic dysfunction [58].

Although ATTR amyloidosis does not directly involve the liver, it can influence liver stiffness as a secondary effect of cardiac disease. A recent French study reported that 36% of patients with ATTR cardiac amyloidosis exhibit liver stiffness > 10 kPa, which correlates with advanced cardiomyopathy and increased hospitalization risk for heart failure in wild-type ATTR patients [59].

Because the liver is the primary site of transthyretin production, liver transplantation was historically considered to slow disease progression. More than 2,000 patients with ATTR amyloidosis have undergone liver transplantation in a domino program, where they receive a liver from a deceased donor and their explanted liver is transplanted into patients with end-stage liver disease (cirrhosis, hepatocellular carcinoma) [60].

Recent advancements in pharmacotherapy, including tafamidis, inotersen, and patisiran (an interfering RNA), have transformed disease prognosis, reducing the need for liver transplantation [61, 62]. Patients who receive a liver graft from ATTR amyloidosis donors remain at risk of transthyretin-related symptoms, but these usually occur late and can be managed with early screening and intervention [63].

Conclusions

Amyloidosis is a rare systemic disease that often involves multiple organs. While diagnosis is primarily managed by hematologists, hepatologists should recognize liver-related presentations, such as elevated cholestatic enzymes and hepatomegaly. Liver stiffness is frequently increased in cases of liver and/or cardiac involvement, but its precise role in diagnosis and prognosis warrants further study.

Abbreviations

AA: amyloid A

AL: amyloid light-chain

ATTR: transthyretin amyloidosis

FLC: free light chain

NT: N-terminal

pro-BNP: pro-brain natriuretic peptide

SAP: serum amyloid P component

Declarations

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Author contributions

PC: Conceptualization, Investigation, Writing—original draft. MDG, JA, AC, JFC, AJ, and VLR: Writing—review & editing. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

Jean-François Cadranel, who is the Guest Editor and Editorial Board Member of Exploration of Digestive Diseases, had no involvement in the decision-making or the review process of this manuscript. Other authors declare that they have no conflicts of interest.

Ethical approval

No ethical approval is required, as data were obtained from routine diagnostic procedures.

Consent to participate

No informed consent for participation is required, as data were obtained from routine diagnostic procedures.

Consent to publication

No informed consent for publication is required, as data were obtained from routine diagnostic procedures and do not contain patient-identifying information.

Availability of data and materials

The pathological images presented in this study are derived from the internal archives of Centre Hospitalier Universitaire de Limoges and are not publicly available. Requests for accessing the datasets should be directed to the corresponding author.

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References

1. Dahiya DS, Kichloo A, Singh J, Albosta M, Wani F. Gastrointestinal amyloidosis: A focused review. *World J Gastrointest Endosc.* 2021;13:1–12. [DOI] [PubMed] [PMC]
2. Carrier P, Loustaud-Ratti V, Jaccard A, Debette-Gratien M, Cypierre A, Cadranet JF. Hepatic amyloidosis. What should the hepato-gastroenterologist know? *Hépatogastro Oncol Dig.* 2024;31:392–7. French. [DOI]
3. Mauermann ML, Clarke JO, Litchy WJ, Obici L, Lousada I, Gertz MA, et al.; Amyloidosis Forum Working Group Participants. Peripheral Nervous, Hepatic, and Gastrointestinal Endpoints for AL Amyloidosis Clinical Trials: Report from the Amyloidosis Forum Multi-organ System Working Group. *Adv Ther.* 2023;40:4695–710. [DOI] [PubMed] [PMC]
4. Jaccard A, Desport E, Mohty D, Bridoux F. Amylose AL [AL amyloidosis]. *Rev Med Interne.* 2015;36:89–97. French. [DOI] [PubMed]
5. Kyle RA, Larson DR, Kurtin PJ, Kumar S, Cerhan JR, Therneau TM, et al. Incidence of AL Amyloidosis in Olmsted County, Minnesota, 1990 through 2015. *Mayo Clin Proc.* 2019;94:465–71. [DOI] [PubMed] [PMC]
6. Dias E, Cardoso H, Marques M, Liberal R, Lopes S, Pereira P, et al. Hepatic amyloidosis: a prevalence study and clinical characterization of a rare and severe disease. *Rev Esp Enferm Dig.* 2023;115:16–21. [DOI] [PubMed]
7. Quock TP, Yan T, Chang E, Guthrie S, Broder MS. Epidemiology of AL amyloidosis: a real-world study using US claims data. *Blood Adv.* 2018;2:1046–53. [DOI] [PubMed] [PMC]
8. Sanchorawala V. Systemic Light Chain Amyloidosis. *N Engl J Med.* 2024;390:2295–307. [DOI] [PubMed]
9. Falk RH, Comenzo RL, Skinner M. The Systemic Amyloidoses. *N Engl J Med.* 1997;337:898–909. [DOI] [PubMed]
10. Hipp MS, Park SH, Hartl FU. Proteostasis impairment in protein-misfolding and -aggregation diseases. *Trends Cell Biol.* 2014;24:506–14. [DOI] [PubMed]
11. Morgan GJ, Wall JS. The Process of Amyloid Formation due to Monoclonal Immunoglobulins. *Hematol Oncol Clin North Am.* 2020;34:1041–54. [DOI] [PubMed]
12. Bochtler T, Hegenbart U, Kunz C, Granzow M, Benner A, Seckinger A, et al. Translocation t(11;14) Is Associated With Adverse Outcome in Patients With Newly Diagnosed AL Amyloidosis When Treated With Bortezomib-Based Regimens. *J Clin Oncol.* 2015;33:1371–8. [DOI] [PubMed]

13. Bochtler T, Hegenbart U, Heiss C, Benner A, Moos M, Seckinger A, et al. Hyperdiploidy is less frequent in AL amyloidosis compared with monoclonal gammopathy of undetermined significance and inversely associated with translocation t(11;14). *Blood*. 2011;117:3809–15. [DOI] [PubMed]
14. Madan S, Dispenzieri A, Lacy MQ, Buadi F, Hayman SR, Zeldenrust SR, et al. Clinical Features and Treatment Response of Light Chain (AL) Amyloidosis Diagnosed in Patients With Previous Diagnosis of Multiple Myeloma. *Mayo Clin Proc*. 2010;85:232–8. [DOI] [PubMed] [PMC]
15. Munshi NC. Association of Agent Orange With Plasma Cell Disorder: Further Evidence. *JAMA Oncol*. 2015;1:1035–6. [DOI] [PubMed]
16. The Inaugural Amyloidosis Forum Panelists, Lousada I. The Amyloidosis Forum: a public private partnership to advance drug development in AL amyloidosis. *Orphanet J Rare Dis*. 2020;15:268. [DOI] [PubMed] [PMC]
17. Rutten KHG, Raymakers RAP, Hazenberg BPC, Nienhuis HLA, Vellenga E, Minnema MC. Haematological response and overall survival in two consecutive Dutch patient cohorts with AL amyloidosis diagnosed between 2008 and 2016. *Amyloid*. 2018;25:227–33. [DOI] [PubMed]
18. Zhao L, Ren G, Guo J, Chen W, Xu W, Huang X. The clinical features and outcomes of systemic light chain amyloidosis with hepatic involvement. *Ann Med*. 2022;54:1226–32. [DOI] [PubMed] [PMC]
19. Park MA, Mueller PS, Kyle RA, Larson DR, Plevak MF, Gertz MA. Primary (AL) Hepatic Amyloidosis: Clinical Features and Natural History in 98 Patients. *Medicine (Baltimore)*. 2003;82:291–8. [DOI] [PubMed]
20. Gertz MA, Comenzo R, Falk RH, Fermand JP, Hazenberg BP, Hawkins PN, et al. Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): A consensus opinion from the 10th International Symposium on Amyloid and Amyloidosis, Tours, France, 18–22 April 2004. *Am J Hematol*. 2005;79:319–28. [DOI] [PubMed]
21. Gertz MA, Kyle RA. Hepatic Amyloidosis: Clinical Appraisal in 77 Patients. *Hepatology*. 1997;25:118–21. [DOI] [PubMed]
22. LEVINE RA. Amyloid disease of the liver. Correlation of clinical, functional and morphologic features in forty-seven patients. *Am J Med*. 1962;33:349–57. [DOI] [PubMed]
23. Levy M, Polliack A, Lender M, Eliakim M. The Liver in Amyloidosis. *Digestion*. 1974;10:40–51. [DOI] [PubMed]
24. D’Alitto F, Scherz A, Margini C, Von Tengg-Kobligk H, Montani M, Pabst T, et al. Portal Hypertension and a Stiff Liver. *Cureus*. 2018;10:e2768. [DOI] [PubMed] [PMC]
25. Sarsik B, Sen S, Kirdok FS, Akarca US, Toz H, Yilmaz F. Hepatic amyloidosis: Morphologic spectrum of histopathological changes in AA and nonAA amyloidosis. *Pathol Res Pract*. 2012;208:713–8. [DOI] [PubMed]
26. Ades CJ, Strutton GM, Walker NI, Furnival CM, Whiting G. Spontaneous Rupture of the Liver Associated with Amyloidosis. *J Clin Gastroenterol*. 1989;11:85–7. [DOI] [PubMed]
27. Sucker C, Hetzel GR, Grabensee B, Stocksclaeder M, Scharf RE. Amyloidosis and Bleeding: Pathophysiology, Diagnosis, and Therapy. *Am J Kidney Dis*. 2006;47:947–55. [DOI] [PubMed]
28. Vrana JA, Theis JD, Dasari S, Mereuta OM, Dispenzieri A, Zeldenrust SR, et al. Clinical diagnosis and typing of systemic amyloidosis in subcutaneous fat aspirates by mass spectrometry-based proteomics. *Haematologica*. 2014;99:1239–47. [DOI] [PubMed] [PMC]
29. Hazenberg BPC, van Rijswijk MH, Piers DA, Lub-de Hooge MN, Vellenga E, Haagsma EB, et al. Diagnostic Performance of ¹²³I-Labeled Serum Amyloid P Component Scintigraphy in Patients with Amyloidosis. *Am J Med*. 2006;119:355.e15–24. [DOI] [PubMed]
30. Lovat LB, Persey MR, Madhoo S, Pepys MB, Hawkins PN. The liver in systemic amyloidosis: insights from ¹²³I serum amyloid P component scintigraphy in 484 patients. *Gut*. 1998;42:727–34. [DOI] [PubMed] [PMC]
31. Mueller S, Sandrin L. Liver stiffness: a novel parameter for the diagnosis of liver disease. *Hepat Med*. 2010;2:49–67. [DOI] [PubMed] [PMC]

32. Lanzi A, Gianstefani A, Mirarchi MG, Pini P, Conti F, Bolondi L. Liver AL amyloidosis as a possible cause of high liver stiffness values. *Eur J Gastroenterol Hepatol*. 2010;22:895–7. [DOI] [PubMed]
33. Loustaud-Ratti VR, Cypierre A, Rousseau A, Yagoubi F, Abraham J, Fauchais A, et al. Non-invasive detection of hepatic amyloidosis: FibroScan, a new tool. *Amyloid*. 2011;18:19–24. [DOI] [PubMed]
34. Brunger AF, Tingen HSA, Bijzet J, van Rheenen R, Blokzijl H, Roeloffzen WWH, et al. Diagnostic performance of liver stiffness as marker of liver involvement in systemic immunoglobulin light chain (AL) amyloidosis. *Ann Hematol*. 2025;104:653–63. [DOI] [PubMed] [PMC]
35. French National Society of Gastroenterology (SNFGE); French National Association Continuing Training in Hepato-Gastroenterology (FMC-HGE). Francophone Days of Hepato-Gastroenterology and Digestive Oncology. 2023 Mar 16–19; Paris, France. Available from: https://www.jfhod.com/sites/www.jfhod.com/files/2023-01/JFHOD23_programme_sp.pdf
36. Trifanov DS, Dhyani M, Bledsoe JR, Misdraji J, Bhan AK, Chung RT, et al. Amyloidosis of the liver on shear wave elastography: case report and review of literature. *Abdom Imaging*. 2015;40:3078–83. [DOI] [PubMed]
37. Bayramoglu Z, Akyol Sari ZN, Koker O, Adaletli I, Eker Omeroglu R. Shear wave elastography evaluation of liver, pancreas, spleen and kidneys in patients with familial mediterranean fever and amyloidosis. *Br J Radiol*. 2021;94:20210237. [DOI] [PubMed] [PMC]
38. Yakupova EI, Bobyleva LG, Vikhlyantsev IM, Bobylev AG. Congo Red and amyloids: history and relationship. *Biosci Rep*. 2019;39:BSR20181415. [DOI] [PubMed] [PMC]
39. Gillmore JD, Wechalekar A, Bird J, Cavenagh J, Hawkins S, Kazmi M, et al.; BCSH Committee. Guidelines on the diagnosis and investigation of AL amyloidosis. *Br J Haematol*. 2015;168:207–18. [DOI] [PubMed]
40. Bustamante JG, Zaidi SRH. Amyloidosis. 2023 Jul 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. [PubMed]
41. Muchtar E, Dispenzieri A, Lacy MQ, Buadi FK, Kapoor P, Hayman SR, et al. Overuse of organ biopsies in immunoglobulin light chain amyloidosis (AL): the consequence of failure of early recognition. *Ann Med*. 2017;49:545–51. [DOI] [PubMed]
42. 91st AFEF Scientific Days. 23rd Continuing Medical Education Day in Hepatology. 2022 Oct 5–8; Dijon, France. Available from: https://afef.asso.fr/wp-content/uploads/2023/06/22AFEF_Abstract-book_Communications-affichees.pdf
43. Shin JK, Jung YH, Bae MN, Baek IW, Kim KJ, Cho CS. Successful treatment of protein-losing enteropathy due to AA amyloidosis with octreotide in a patient with rheumatoid arthritis. *Mod Rheumatol*. 2013;23:406–11. [DOI] [PubMed]
44. Muchtar E, Dispenzieri A, Magen H, Grogan M, Mauermann M, McPhail ED, et al. Systemic amyloidosis from A (AA) to T (ATTR): a review. *J Intern Med*. 2021;289:268–92. [DOI] [PubMed]
45. Peters RA, Koukoulis G, Gimson A, Portmann B, Westaby D, Williams R. Primary amyloidosis and severe intrahepatic cholestatic jaundice. *Gut*. 1994;35:1322–5. [DOI] [PubMed] [PMC]
46. Writing Committee; Kittleson MM, Ruberg FL, Ambardekar AV, Brannagan TH, Cheng RK, et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81:1076–126. [DOI] [PubMed]
47. Muchtar E, Dispenzieri A, Leung N, Lacy MQ, Buadi FK, Dingli D, et al. Depth of organ response in AL amyloidosis is associated with improved survival: new proposed organ response criteria. *Amyloid*. 2019;26:101–2. [DOI] [PubMed]
48. Brunger AF, van Rheenen R, Gans ROB, Hazenberg BPC, Nienhuis HLA. How well does liver span as part of the consensus criteria for liver involvement in AL amyloidosis perform? *Amyloid*. 2023;30:437–9. [DOI] [PubMed]

49. Szalat R, Sarosiek S, Havasi A, Brauneis D, Sloan JM, Sanchorawala V. Organ responses after highdose melphalan and stemcell transplantation in AL amyloidosis. *Leukemia*. 2021;35:916–9. [DOI] [PubMed]
50. Muchtar E, Dispenzieri A, Gertz MA, Kumar SK, Buadi FK, Leung N, et al. Treatment of AL Amyloidosis: Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Statement 2020 Update. *Mayo Clin Proc*. 2021;96:1546–77. [DOI] [PubMed]
51. Jaccard A, Moreau P, Leblond V, Leleu X, Benboubker L, Hermine O, et al.; the Myélome Autogreffe (MAG) and Intergroupe Francophone du Myélome (IFM) Intergroup. High-Dose Melphalan versus Melphalan plus Dexamethasone for AL Amyloidosis. *N Engl J Med*. 2007;357:1083–93. [DOI] [PubMed]
52. Manwani R, Cohen O, Sharpley F, Mahmood S, Sachchithanantham S, Foard D, et al. A prospective observational study of 915 patients with systemic AL amyloidosis treated with upfront bortezomib. *Blood*. 2019;134:2271–80. [DOI] [PubMed]
53. Sarosiek S, Zheng L, Sloan JM, Quillen K, Brauneis D, Sanchorawala V. Comparing measures of hematologic response after high-dose melphalan and stem cell transplantation in AL amyloidosis. *Blood Cancer J*. 2020;10:88. [DOI] [PubMed] [PMC]
54. Staron A, Burks EJ, Lee JC, Sarosiek S, Sloan JM, Sanchorawala V. Assessment of minimal residual disease using multiparametric flow cytometry in patients with AL amyloidosis. *Blood Adv*. 2020;4:880–4. [DOI] [PubMed] [PMC]
55. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol*. 2018;69:406–60. [DOI] [PubMed]
56. Rees MJ, Toumeh N, Dispenzieri A, Gertz M, Yohannan B, Atallah-Yunes SA, et al. Hepatic involvement in light chain amyloidosis: analysis of 130 patients and predictors of hepatic response and survival. *Amyloid*. 2025;32:267–75. [DOI] [PubMed]
57. Purkey HE, Dorrell MI, Kelly JW. Evaluating the binding selectivity of transthyretin amyloid fibril inhibitors in blood plasma. *Proc Natl Acad Sci U S A*. 2001;98:5566–71. [DOI] [PubMed] [PMC]
58. Adams D, Sekijima Y, Conceição I, Waddington-Cruz M, Polydefkis M, Echaniz-Laguna A, et al. Hereditary transthyretin amyloid neuropathies: advances in pathophysiology, biomarkers, and treatment. *Lancet Neurol*. 2023;22:1061–74. [DOI] [PubMed]
59. Lointier E, Cariou E, Beneyto M, Fournier P, Lavie-Badie Y, Eyharts D, et al.; Toulouse Amyloidosis Research Network collaborators. Prevalence, clinical significance and prognosis value of liver stiffness measurement anomalies in transthyretin cardiac amyloidosis. *Int J Cardiol*. 2024;416:132485. [DOI] [PubMed]
60. Ericzon BG, Wilczek HE, Larsson M, Wijayatunga P, Stangou A, Pena JR, et al. Liver Transplantation for Hereditary Transthyretin Amyloidosis: After 20 Years Still the Best Therapeutic Alternative? *Transplantation*. 2015;99:1847–54. [DOI] [PubMed]
61. Maurer MS, Schwartz JH, Gundapaneni B, Elliott PM, Merlini G, Waddington-Cruz M, et al.; ATTR-ACT Study Investigators. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. *N Engl J Med*. 2018;379:1007–16. [DOI] [PubMed]
62. Maurer MS, Kale P, Fontana M, Berk JL, Grogan M, Gustafsson F, et al.; APOLLO-B Trial Investigators. Patisiran Treatment in Patients with Transthyretin Cardiac Amyloidosis. *N Engl J Med*. 2023;389:1553–65. [DOI] [PubMed] [PMC]
63. Antonini TM, Lozeron P, Lacroix C, Mincheva Z, Durrbach A, Slama M, et al. Reversibility of Acquired Amyloid Polyneuropathy After Liver Retransplantation. *Am J Transplant*. 2013;13:2734–8. [DOI] [PubMed]