

CASE REPORT

Leukocyte chemotactic factor 2-related amyloidosis presenting with severe jaundice and hepatic encephalopathy

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Abstract

Amyloidosis is a well-known disease with various types and subtypes. One of the most recently identified types is leukocyte chemotactic factor 2 amyloidosis (LECT 2), which was found to be common in certain ethnic backgrounds. It is suggested that the diagnosis of this type is vital to prevent any therapy-related complications when it is erroneously diagnosed as AL amyloidosis. The clinical presentation is usually slowly progressive kidney disease and mild hepatic impairment. We report a case of LECT2 amyloidosis, which presented with severe painless cholestasis and hepatic encephalopathy alongside progressive kidney disease.

KEYWORDS

cholestasis, end-stage renal disease, Leukocyte chemotactic factor 2 amyloidosis

1 | INTRODUCTION

Leukocyte chemotactic factor 2 amyloidosis (ALect2) is a recently recognized type of amyloidosis. It commonly involves the kidneys presenting with proteinuria and slowly progressive renal disease. Rare involvement of the heart, relatively benign course, and specific ethnic distribution are special characteristics that differentiate ALect2 from other types of amyloidosis.¹

Most cases of ALect2 were diagnosed in patients with Hispanic descent. In addition, it was reported in Punjabi and native American ethnic groups.^{1,2}

Liver involvement is usually subclinical and underdiagnosed in ALect2, being more commonly detected in

autopsy studies. The manifestation of hepatic disease is usually mild hepatocellular injury or isolated elevation of alkaline phosphatase, and rarely, severe cholestasis.¹ Diagnosis of this disorder is usually made with special stains done on kidney or liver biopsies.³ The management of renal disease is usually conservative as there is no definitive treatment; however, it is important to identify this type of amyloidosis to avoid unnecessary and sometimes toxic treatment if it is erroneously diagnosed as AL or AA, which are more common subtypes of amyloidosis.³

We report a case of ALect2-related amyloidosis in a Punjabi-descent gentleman who presented with jaundice and hepatic encephalopathy and was eventually diagnosed with liver biopsy.

2 | CASE PRESENTATION

A 53-year-old Indian gentleman with history of hypothyroidism, systemic hypertension, and diabetes mellitus type II complicated by retinopathy and, presumably nephropathy under conservative management, presented to our hospital with chief complaint of jaundice. The patient noticed yellowish discoloration of his eyes and skin, which gradually progressed over a period of 1 week. Other complaints included generalized and intermittent pruritus which started one month before, and was more noticeable in the palms and soles, in addition to passing dark-colored urine.

There was no history of abdominal pain, nausea, vomiting, fever, weight loss, or altered bowel habits. The patient was a non-smoker with no history of alcohol consumption or use of any kind of recreational drugs.

There was no history of recent travel or change in dietary habits. He worked as a truck driver. Family history was negative. His home medications were sodium bicarbonate, linagliptin, levothyroxine, irbesartan, hydralazine, and furosemide.

Vital signs including blood pressure remained stable throughout the hospitalization course. Physical examination revealed generalized icterus in the skin and sclerae, with no appreciable organomegaly. Fine asterixis was noted in the hands upon outstretching them. His Glasgow-coma scale (GCS) was initially fluctuating in the range of 13–14/15, and he was noted to have a disturbed sleep cycle. His ammonia level was reported as 57 $\mu\text{mol/L}$ (reference range 10 to 35 $\mu\text{mol/L}$). Therefore, he was started

on regular lactulose oral solution to ensure 2–3 bowel motions per 24 h, which led to improvement in the GCS and sleep cycle and rapid decline in serum ammonia level to 28 $\mu\text{mol/L}$.

Laboratory workup revealed direct hyperbilirubinemia, in addition to elevated alkaline phosphatase and aminotransferases. The patient was admitted as a case of painless jaundice for investigation. Ultrasound of the abdomen and magnetic resonance cholangiopancreatography revealed cholecystolithiasis with unremarkable liver texture, and normal intra- and extrahepatic biliary ducts. Anti-smooth muscle, anti-mitochondrial, and anti-liver-kidney microsomal antibodies were negative. Furthermore, serology for Cytomegalovirus, Epstein-Barr virus, and hepatitis (A, B, and C) was negative. Acetaminophen and aspirin levels were undetectable in the serum. Urine dipstick was positive for +1 proteinuria and negative for hematuria.

As the patient's liver and kidney function tests were gradually worsening over the course of one week (Table 1), more invasive investigations were warranted. Endoscopic ultrasound was done, which revealed a lymph node with a size of 18 \times 15 mm at the porta hepatis; however, there was no evidence of any pancreatic masses. Fine needle aspiration biopsy of the lymph node showed reactive lymphocytosis otherwise not suggestive of a specific pathology.

As the endoscopic ultrasound was unrevealing, percutaneous ultrasound-guided liver biopsy was performed. Unfortunately, the liver biopsy was complicated by acute hemoperitoneum which necessitated admission into the medical intensive care unit and the initiation of hemodialysis due to acute worsening of his renal function.

TABLE 1 Laboratory investigations

	At Admission	After two weeks	After four weeks (Time of discharge)	Reference Range
Hb (gm/dL)	8.3	8	10.6 (post-transfusion)	13.5–17.5
Platelet (K/uL)	304	315	241	150–400
INR	1	1.6	1.1 (post-FFP administration)	0.8–1.1
Total Bilirubin ($\mu\text{mol/L}$)	116	357	650	2–17
Direct Bilirubin ($\mu\text{mol/L}$)	110	325	400	0–5.1
Alkaline phosphatase (U/L)	687	561	1644	40–130
Gamma glutamyl transferase (U/L)	478	398	N/A	10–71
ALT (U/L)	176	70	30	0–40
AST (U/L)	107	72	188	0–37
Lactic acid (mmol/L)	0.9	N/A	N/A	0.5–2.2
Albumin (gm/L)	32	22	15	35–52
Urea (mmol/L)	18.2	26.7	13	2.76–8.07
Creatinine ($\mu\text{mol/L}$)	269	372	226	70–115
eGFR (CKD-EPI Creatinine equation 2021- ml/min/1.73m ²)	24	16	29	More than 60 ml/min/1.73m ²

The liver biopsy revealed background cholestasis, in addition to prominent globular eosinophilic deposits in the portal tracts and the sinusoids. These deposits were positive for Congo red stain, displaying apple green birefringence. The findings were in keeping with globular hepatic amyloidosis, which was considered highly sensitive and specific for LECT2 amyloidosis⁴ (Figures 1 and 2). Mass spectrometry was not available.

After disclosure of the diagnosis to the patient and explanation of the nature of the disease and its progressive course, he chose to go back to his home country to spend more time with his family. He was discharged from our hospital after a four-week course in a stable condition. Unfortunately, we were not able to follow the patient after he traveled.

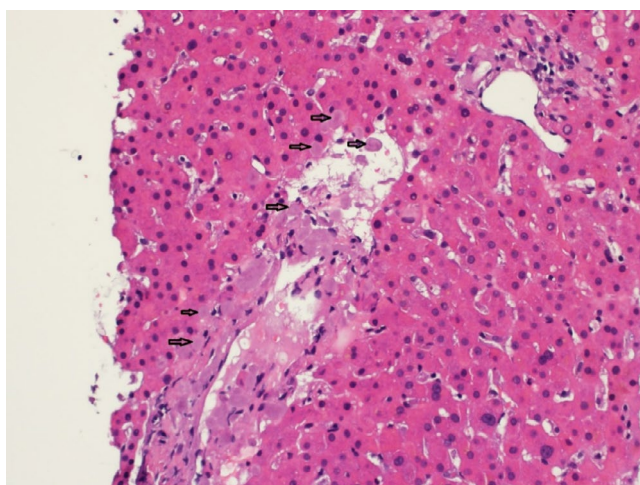


FIGURE 1 Liver biopsy showing prominent portal and sinusoidal globular eosinophilic deposits (black arrows) (H and E x 20)

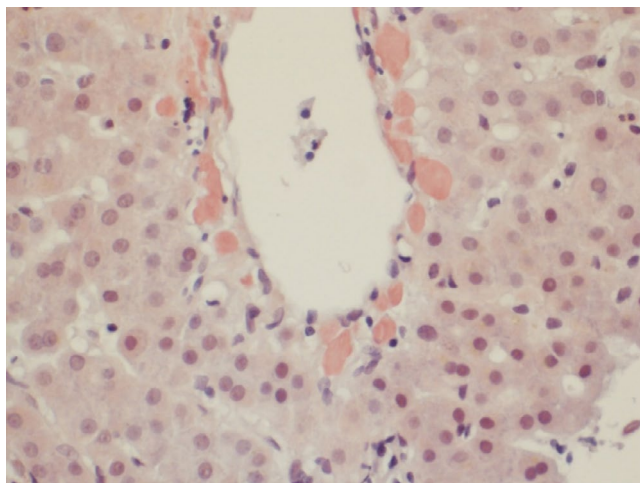


FIGURE 2 Globular deposits are positive for Congo Red

3 | DISCUSSION

Amyloid is a term that was first adopted in 1854 by Rudolph Virchow and first described by the German botanist Matthias Schleiden in 1838 as a plant starch, to refer to starch like bodies in the nervous system when exposed to iodine.^{5,6}

Amyloidosis is a spectrum of disorders that share the pathology of misfolded protein accumulation in various organs of the body, originating from diverse etiologies. There are 30 types of proteins, which were identified to cause amyloid formation and toxic effects to the tissues.³

The most common type of these proteins in the developed countries is derived from immunoglobulin light chain, namely AL. Other types of proteins include AA, transthyretin-derived amyloid, and B2-microglobuline, which is known to accumulate in patients with end-stage renal disease already established on hemodialysis. A minority of amyloidosis cases are hereditary in nature. Large case series showed that the most common types of amyloidosis in the United States of America are AL and AA; however, Lect2 amyloidosis is recently being more recognized especially in the Hispanic population. Studies performed outside the United States showed a relatively common occurrence of Lect2 amyloidosis in Egyptian, Sudanese, Pakistani-Kashmiri, and Punjabi-Indian populations.^{3,7,8}

Lect2 acts as a chemotactic factor for neutrophils and has a role in chondrocyte and osteoblast stimulation. It is mainly produced by the liver and is overexpressed in hepatocellular carcinoma and certain types of liver disease. It was suggested that Lect2 is an acute phase reactant produced as a response to hepatic inflammation and that it plays a role in hepatic regeneration.^{1,3}

Although some familial cases of Lect2 amyloidosis were described, it is not labeled as one of the hereditary forms of amyloidosis. The gene encoding for this protein is located on chromosome 5 (5q31.1-q32); however, abnormalities of chromosome 7 were also implicated in the pathogenesis of this disease. In a case series by Rezk et al., all cases except for one were found to be homozygous for the G allele while the remaining case was heterozygous.^{1,7}

Said et al. reported a case series of 72 patients with renal Alect2 who were mostly of Hispanic origin. The series showed that nephrotic-range proteinuria and significant hematuria were rare; however, up to one third of the patients developed end-stage renal disease in a duration of 26 months due to glomerular damage.⁸

Rezk et al. studied 24 patients with Lect2 amyloidosis and found that hepatic involvement was not associated with significant liver function impairment. In addition, none of the cases exhibited cardiac involvement, which might be the reason behind its benign course in most cases.¹

The diagnosis of LECT2 amyloidosis is usually made by kidney or liver biopsy, with specific staining techniques and spectrometry used for further confirmation. Unfortunately, there is no specific treatment for Lect2 amyloidosis and most of the time the treatment is supportive mainly directed at kidney disease.⁹

The importance of identifying this disease lies in avoiding modalities of treatment with potential toxicity when it is mistakenly diagnosed as AL amyloidosis. Common agents used for the treatment of AL amyloidosis are directed against plasma cell dyscrasia and include bortezomib and daratumumab.¹⁰ Multiple adverse events due to bortezomib were reported, and these include low platelet count, neuropathy, and ocular toxicity.¹¹ Daratumumab, on the contrary, has been associated with lymphopenia and increased predilection for opportunistic infections.¹²

Further studies are required to identify this disease and its management.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Almasri, Hussam: Manuscript writing, corresponding author; Razok, Almurtada: Manuscript writing; Badi, Ahmed: Manuscript review; Almohannadi, Muneera: Manuscript review; Lutf, Abdo: Clinical follow up; Petkar, Mahir: Pathology input; Elzouki, Abdel-Naser: Manuscript review and edit.

ETHICAL APPROVAL

Medical Research Canter, Hamad Medical Corporation, MRC-04-20-1037.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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REFERENCES

1. Rezk T, Gilbertson JA, Rowczenio D, et al. Diagnosis, pathogenesis and outcome in leucocyte chemotactic factor 2 (ALECT2) amyloidosis. *Nephrol Dial Transplant*. 2018;33(2):241-247.
2. Mereuta OM, Theis JD, Vrana JA, et al. Leukocyte cell-derived chemotaxin 2 (LECT2)-associated amyloidosis is a frequent cause of hepatic amyloidosis in the United States. *Blood*. 2014;123(10):1479-1482. doi:10.1182/blood-2013-07-517938
3. Picken MM. Alect2 amyloidosis: primum non nocere (first, do no harm). *Kidney Int*. 2014;86(2):229-232.
4. Chandan VS, Shah SS, Lam-Himlin DM, et al. Globular hepatic amyloid is highly sensitive and specific for LECT2 amyloidosis. *Am J Surg Pathol*. 2015;39(4):558-564.
5. Kyle RA. Amyloidosis: a convoluted story. *Br J Haematol*. 2001;114(3):529-538.
6. Sipe JD, Benson MD, Buxbaum JN, et al. Amyloid fibril protein nomenclature: 2012 recommendations from the nomenclature committee of the international society of amyloidosis. *Amyloid Int J Exp Clin Investig off J Int Soc Amyloidosis*. 2012;19(4):167-170.
7. Chakrabarti A, Samal P, Chakrabartty J. Amyloidosis: the newer discovered ALECT2 associated with der7q add(7). *J Clin Diagn Res JCDR*. 2016;10(9):ED04-ED05.
8. Said SM, Sethi S, Valeri AM, et al. Characterization and outcomes of renal leukocyte chemotactic factor 2-associated amyloidosis. *Kidney Int*. 2014;86(2):370-377.
9. Jiménez-Zepeda VH, Leung N. ALECT2 amyloidosis: a new type of systemic amyloid highly prevalent in the Hispanic population. *Rev Investig Clin Organo Hosp Enfermedades Nutr*. 2014;66(3):269-273.
10. Palladini G, Milani P, Merlini G. Management of AL amyloidosis in 2020. *Blood*. 2020;136(23):2620-2627.
11. Dennis M, Maoz A, Hughes D, Sancherawala V, Sloan JM, Sarosiek S. Bortezomib ocular toxicities: outcomes with ketotifen. *Am J Hematol*. 2019;94(3):E80-E82.
12. Cottini F, Huang Y, Williams N, et al. Real world experience of daratumumab: evaluating lymphopenia and adverse events in multiple myeloma patients. *Front Oncol*. 2020;10:575168.

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