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A rare case of Amyloidosis presenting as ascites -Case report

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ABSTRACT
BACKGROUND:Amyloidosis is term for a group of protein misfolding disorders characterized by extracellular eposition of insoluble polymeric protein fibrils in tissues and organs.Major types of amyloidosis include L,AA,ATTR,etc.The clinical spectrum can vary depending upon the type of amyloid and the distribution of deposition making the diagnosis sometime challenging as the patients may present with symptoms that could closely mimic many other conditions.
CASE SUMMARY:CASE- A 52 year old female presented with complaints of abdominal distention for 1 month. It was insidious in onset,generalized and progressive in nature. It was associated with fatigue and dyspnea on exertion. She also had significant loss of weight and appetite since last 1 year. She had no history suggestive of renal or cardiac involvement. There was no h/o fever or jaundice. She has history of backache and polyarthralgia since2 year and visited multiple local hospital for same. She was evaluated and definite diagnosis couldn't be made.On examination, she was thin and emaciated,mild pallor and Patchy hyperpigmented skin changes was present in face.Abdomen was distended,tense and non tender, fluid thrill was present. Liver was palpable 10 cm below costal margin and liver span was increased. No other mass was palpable.In view of loss of weight,polyarthralgia,emaciation,ascites and massive hepatomegaly, possible differentials such aslymphoma,HCC,Sarcoidosis and amyloidosis were initially considered.On Routine blood investigation,there was mild anemia,high ESR,AG reversal, elevated SGOT/SGPT and elevated ALP and elevated GGT.USG abdomen showed massive hepatomegaly and gross ascites, no e/o portal hypertension. Her RFT,Urine routine,CXR was within normal limit.Viral markers were negative.Ascitic fluid study showed high SAAG. Echocardiography showed- No RWMA,good LV systolic function, Conc LVH,RV Dysfunction,no PAH. Serum protein electrophoresis –showed an abnormal M band in gamma region.S. AFP, S. ACE were negative.Patient was reexamined,found to have sensory polyneuropathy in both lower limb clinically which was confirmed by Nerve Conduction velocity(Axonal type of neuropathy). Patient was then provisionally diagnosed as Probable POEMS syndrome (polyneuropathy,organomegaly, M band,skin changes).Once ascites reduced, Liver biopsy was done under high risk.Bone marrow biopsy was also done after repeated counselling. She was discharged and kept under follow up. Later, Liver biopsy result was consistent with amyloidosis.Once Amyloidosis is diagnosed,the next challenge was whether amyloidosisexplains all the findings?Is it localised or generalised?Which organs are involved?What is the Type of Amyloidosis.?Bone marrow biopsy result showed features consistent with plasma cell myeloma. Serum free light chain assay showed increase in lambda chain. In view of high index of suspicion, a repeat echo was done which showed possible cardiac amyloidosis.
Patient was diagnosed as AL type Systemic amyloidosis involving liver,cardiac,neuropathy causingascites without renal involvement and was finally initiated on treatment.
CONCLUSION:This a rare case of AL type of systemic amyloidosis primarily involving Liver with unexplained ascites which otherwise predominantly involve heart and kidney.This case highlights the challenges in coming to the diagnosis and management of amyloidosis.From this case and available literature,hepatic amyloidosis should be suspected in patients who present with hepatomegaly but without abnormal focal lesions in imaging, with increased ALP,GGT along with constitutional symptoms such as unexplained fatigue,ascites and weight loss.

Keywords: Amyloidosis, Hepatomegaly

I. INTRODUCTION

Amyloidosis is term for a group of protein misfolding disorders characterized by extracellular deposition of insoluble polymeric protein fibrils in tissues and organs.Amyloidosis can be inherited or acquired. Both localised and systemic illness are possible. Amyloid can build up in the liver, spleen, kidney, heart, nerves, and blood vessels, leading to a variety of clinical syndromes such as cardiomyopathy, hepatomegaly, proteinuria, macroglossia, autonomic dysfunction, ecchymoses,

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neuropathy, renal failure, hypertension, as well as abnormalities of the cornea and vitreous.(1)Major types of amyloidosis include AL, AA, ATTR,etc. Diagnosis of amyloidosis can be difficult as patients with this disorder may present with symptoms that could closely mimic many other conditions.

Patient Information
52 year
Female
Panamana,Palakkad
Housewife

History
Chief complaints
Abdominal distension x 1 month
History of Present Illness

Patient was apparently in her usual health when she started having abdominal distension since 1 month which was gradual in onset, generalized and progressive in nature. It was associated with fatigue and dyspnea on exertion(MMRC grade 2). She had history of loss of appetite and significant loss of weight. She is since then unable to her routine activities without help.

No history of frothing of urine or decrease urine output,facial puffiness or pedal edema. No h/o orthopnea or PND. No h/o pain abdomen,vomiting,loose stools or dysphagia.No h/o of exertional chest pain or cough. No history of Fever, evening rise of temperature. No history yellowish discoloration of urine,eyes,skin. No h/o travel,contact with animals.

Past History
Low Backache and Polyarthalgia X 2 years
H/o Significant loss of weight and appetite. Visited multiple local hospital and definite diagnosis couldn't be made and lost follow up.
No history of DM, Hypertension, CKD,Malignancies, TB,CLD, CAD,Thyroid Disease

Personal history
Non vegetarian diet
Normal bowel and bladder habit
Married, Two children
Menopause at age of 45 years
No significant family history

II. PHYSICAL EXAMINATION

GENERAL EXAMINATION
Conscious,Oriented
Thin,Emaciated
Vitals : Afebrile BP : 110/70 mm Hg, PR-82/min regular, RR 20/min
Mild Pallor, No Icterus, clubbing, Cyanosis, lymphadenopathy, Pedal edema Patchy hyperpigmented skin changes in face

Systemic Examination
Per Abdomen:
Distented,Tense,Ascitespresent, Fluid Thrill+
Liver Palpable – 10 cm below costal margin, smooth, regular, nontender, no bruit
Liver span increased
Spleen not palpable
No other mass palpable
CVS –JVP normal,First and second heart sound heard,no murmur
Chest- Bilateral normal vesicular breath sound
CNS : Higher Mental function- within normal limit,move all 4 limbs

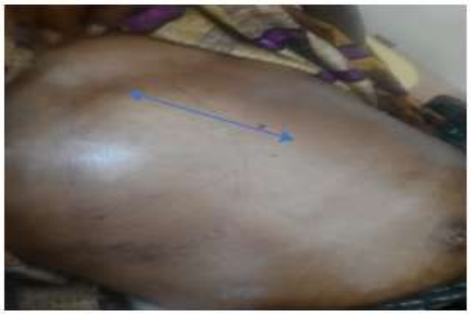

Fig 1: Hepatomegaly

DIFFERENTIALS

1.NEOPLASTIC- Lymphoma,HCC.
2. CLD with Hepatomegaly, HCC
3.INFILTRATIVE – Sarcoidosis, Amyloidosis

Diagnostic Assessment
Initial investigations

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RBS	163
RFT	29/0.9
TP/A	7.5/2.5
TB/D	0.9/0.5
OT/PT/ALP	79/65/622
Na/k	130/4.2
URE	Alb +
INR/APTT	1.08/29.4

Hb	12
TC	13000
DC	P86L9
Platelet	4.6
MCV	85
ESR	76
Screening	Negative
TFT	N
CXR PAV	No significant finding
ECG	SR

ASCITIC FLUID STUDY
Total count – 60
Polymorphs 10% Lymphocyte 90%
Protein 3.1
Alb 1.3
Saag 1.2 (high)
ADA –Neg
CBNAAT, C/s – Neg

P. Smear – Normocytic Normochromic anemia, Poikilocytosis.Increased rouleax formation
Previous old reports (2021)
S. protein electrophoresis : ? M band in B gamma region
BONE MARROW BIOPSY
Trilineage hematopoiesis with eosinophilia

Cardiology consulted- Echocardiography was taken- No RWMA,good LV systolic function, Conc LVH,RV Dysfunction,no PAH
X Ray Skull and pelvis- No lytic lesions

Investigation	Finding	Comment
AFP	Normal	
USG Abdomen	Hepatomegaly,gross ascites	
MRI Liver	Hepatomegaly,gross ascites	HCC ruled out
ANA IF,RA factor	Negative	Autoimmune/connective tissue Ruled out
RepeatHb	9.6	
S. ceruloplasmin	Normal	

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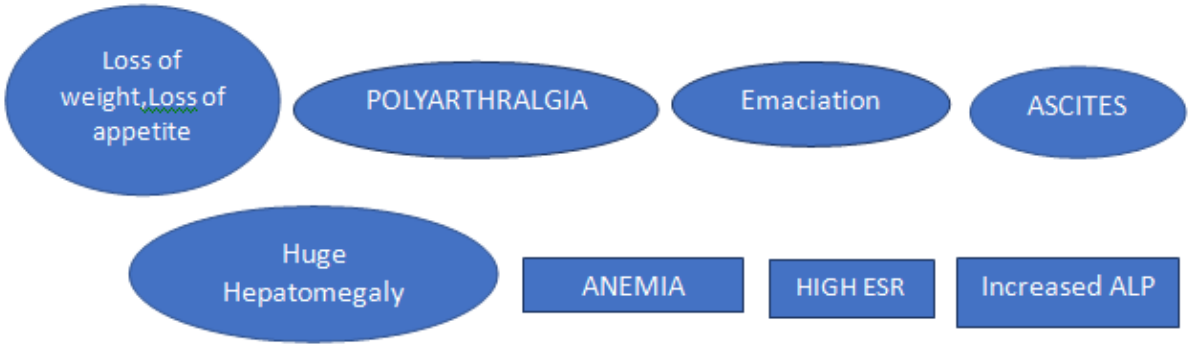
Reassessment
Loss of Position sense and vibration sense

Touch and temperature Intact
Diagnostic differentials



DIFFERENTIALS

POEMS Syndrome

(Polyarthralgaia, h/o bone pain, Loss of weight and appetite, sensory neuropathy, ascites, Anemia, High ESR, Increased ALP)

Planned for

1.Skeletal Survey CT chest and abdomen to look for Sclerotic bone lesions

2.NCS

3. Protein electrophoresis

SARCOIDOSIS

Planned for
S.ACE

Opthalmology consulted to look foruveitis and KF ring

Planned for liver biopsy once ascites settles in view of high risk of bleeding

Opthalmologist consulted – **No uveitis**
S. protein electrophoresis – **an abnormal monoclonal band seen in gamma region suggestive of M band.**
GGT -187 high
Corrected s. Calcium- 10.2
NCS- **reduced CMAP from both tibial, peroneal and ulnar nerves**.
LIVER BIOPSY REPORT

S. ACE – neg (Sarcoidosis ruled out)
SFLC – **lambda free light chain Increased-** 148(5.71-26.30).
Kappa/lamda ratio -0.249(0.26-1.65)
Liver biopsy was done under high risk
Bone marrow done after repeated counselling

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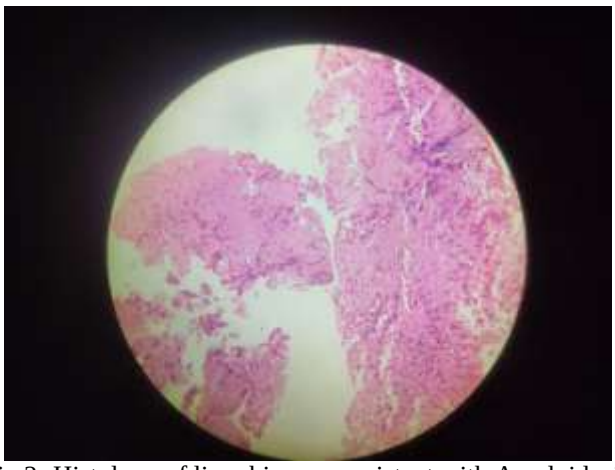

Fig 2- Histology of liver biopsy consistent with Amyloidosis

Extracellular,homogenous,Pink Eosinophilic hyaline material deposits in background In H &E stain consistent with Amyloidosis of Liver

Challenges
If Amyloidosis, Can it explain all the findings?
Is it localised or Generalised?
Which organs are involved?
What is the Type of Amyloidosis?

Bone marrow biopsy result

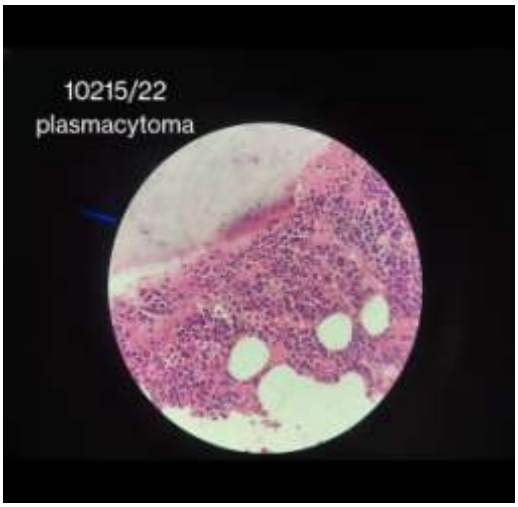

Fig 3- Bone marrow biopsy showing plasma cell myeloma

Consistent with plasma cell myeloma

IHC for CD138 showing strong membranous positivity in 60 % of cells

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Follow up and reassessment
Repeat Echo(advanced)- Possible cardiac amyloidosis- significant LVH, RVH, IAS hypertrophy, diastolic dysfunction.

CT chest and abdomen
Bilateral symmetrical calcific foci in ischiogluteal bursa,greater trochanter region and shoulder joint
Calcific foci in b/l gluteal region
No lytic or sclerotic lesion.

POEMS cannot be ruled out as VEGF couldn't be done.

Final diagnosis
Systemic Amyloidosis (AL Amyloidosis)
Involving Liver, Cardiac, Neuropathy
Multiple myeloma
No involvement of Kidney
? POEMS syndrome

III. DISCUSSION

The clinical spectrum can vary depending upon the type of amyloid and the distribution of deposition making the diagnosis sometime challenging as the patients may present with symptoms that could closely mimic many other conditions.

The majority of cases of amyloidosis are systemic, however 10–20% of them might be localised.The average age of presentation is between 55 and 60 years old, and men are afflicted more than women. Despite the fact that patients with amyloidosis frequently have hepatic involvement, the clinical symptoms of hepatic involvement are frequently minimal. Rarely may involvement cause symptoms such rupture, portal hypertension, or hepatic failure. In patients with hepatic amyloidosis, hepatomegaly and a borderline abnormal liver function test are the most typical symptoms. Non-specific radiological signs of hepatic involvement. The amyloid deposit occasionally contained amorphous or erratic calcifications. Since CT findings are vague, biopsy confirmation is necessary for a final diagnosis.(2)Around 70%-80% of the cases have associated nephrotic syndrome, congestive cardiac failure, orthostatic hypotension or peripheral neuropathy.(3)

Chemotherapy is the main form of treatment for AL amyloidosis, and it aims to kill the underlying plasma cell or B-cell clone. The current regimen consists of an alkylating agent (melphalan or cyclophosphamide), dexamethasone, and a proteasome inhibitor, commonly bortezomib. About 25% of AL amyloidosis patients are eligible for autologous stem cell transplantation, which is frequently paired with chemotherapy. (4)

Prognosis of AL amyloidosis depends on the organ systems affected but is often poor when the heart is involved.(4)

This is a atypical rare case of amyloidosis as patient presented with unexplained ascites with wasting which is usually not a common presenting complaint especially in a predominant hepatic involvement.

What is the likely cause of ascites in this patient?
Rare in Hepatic Amyloidosis
Ways in which Amyloidosis can cause ascites include-
Cardiomyopathy
? Peritoneal amyloidosis
Anasarca due to hypoproteinemia
Renal Involvement –Nephrotic syndrome

What are the causes of High ALP in myeloma
Usually low in myeloma unless there is a pathological fracture.
What is the source of high ALP? Liver or bone??

Hepatic Amyloidosis- Increased ALP, increased GGT
Why previous Bone marrow was inconclusive?
Early Changes?
MGUS?

Why calcifications in this patient?
Secondary calcification of amyloid deposits have been reported.

IV. CONCLUSION

This a rare case of AL type of systemic amyloidosis primarily involving Liver with unexplained ascites, Al Amyloidosis otherwise mostpredominantly involve heart and kidney. This case highlights the challenges in coming to the diagnosis and management of amyloidosis. From this case and available literature, hepatic amyloidosis should be suspected in patients who present with hepatomegaly without specific finding in imaging, with increased ALP, GGT along with constitutional symptoms such as unexplained fatigue,weight loss and ascites.

List of abbreviation
ATTR : Amyloid transthyretin
AL: Amyloid Light chain
ALP: Alkaline phosphatase
PND: paroxysmal nocturnal dyspnea
DM : Diabetes mellitus

CKD : chronic kidney disease
GGT : gamma glutamyl transferase
LVH : Left Ventricular hypertrophy
IAS : Inter atrial septum
ACE : Angiotensin converting enzyme
SFLC : serum free light chain assay
HCC: Hepatocellular carcinoma
TC: Total count
DC: differential count
TP/A- total protein/albumin
OT/PT- SGOT/SGPT
AFP- Alpha fetoprotein
MMRC – Modified Medical Research Council

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2.	Liver Biopsy consistent with amyloidosis liver
3.	Bone marrow biopsy consistent with plasma cell myeloma

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