CASE REPORT

DUODENAL BIOPSY: AN UNEXPECTED CONFIRMATORY TEST FOR A PATIENT WITH AL-AMYLOIDOSIS

Pirasath S, Kumanan T, Selvaratnam G, Sujanitha V and Dikowita DD

University Medical Unit, Teaching Hospital, Jaffna, Sri Lanka

Corresponding Author: Dr. S.Pirasath, University Medical Unit, Teaching Hospital, Jaffna, Sri Lanka.
Email: selladuraipirasath81@gmail.com ORCID iD https://orcid.org/0000-0002-4274-4919

Abstract: Systemic AL- amyloidosis is a disorder of protein folding in which there is extra-cellular accumulation as β pleated fibrillar deposits of monoclonal immunoglobulin light chain fragments. AL- amyloidosis is a rare clinical entity. A presentation with clinical and histological evidence of gastrointestinal amyloidosis is even rare. Here we report primary AL- amyloidosis secondary to lamda (λ) light chain myeloma in a middle-aged woman who presented with nephrotic syndrome and motor peripheral neuropathy.

Key words: Amyloidosis, Duodenum, Esophagogastroduodenoscopy

Introduction

Primary amyloid light chain (AL) amyloidosis is a rare variety of plasma cell dyscrasia, the diagnosis of which is often difficult to establish. There is extra cellular accumulation in β pleated fibrillar deposits of monoclonal immunoglobulin light chain fragments leading to organ failure. [1] Pathogenesis of amyloidosis involves extracellular deposition of insoluble protein fibrils in tissues, leading to insufficiency of affected organs. [2] Here we report a case of primary AL amyloidosis due to lambda light chain myeloma in a middle-aged woman who presented with nephrotic syndrome and motor peripheral neuropathy.

Case report

A 54-year-old woman presented with tiredness, exertional palpitations, dyspeptic symptoms and generalized body pains of 6-months duration. She had bronchial asthma and was on regular inhalers. Her systemic examination was normal with a pulse rate of 72/min and blood pressure of 130/80mmHg. She was treated with proton pump inhibitors. Her initial investigations revealed microcytic anaemia (Hemoglobin 10g/dL) and mildly elevated erythrocyte sedimentation rate (ESR- 54mm/1st hour). Her renal and liver profiles were normal. However, she had persistent generalized body aches, loss of appetite and weight loss of 5 kg within six months duration. One month later, she again presented with bilateral lower limb swelling, frothy urine, exertional shortness of breath and

Received:19/12/2019 **Accepted revised version: 17/06/2019** **Published: 30/06/2019**

abdominal distension. She also had arthralgia, bilateral numbness of hands and proximal myopathy. On examination, she had bilateral pitting ankle oedema. Her pulse rate was 92/min, low in volume and blood pressure was 100/80mmHg without a significant postural drop. Her jugular venous pressure (JVP) was not elevated. She had bilateral pleural effusions and moderate non tender hepatosplenomegaly. Her blood investigations revealed microcytic hypochromic anemia with normal other cell lines. Inflammatory markers were normal. The renal function was normal. Albuminiria (3+) detected on urine full report. A 24-hour urine for protein confirmed proteinuria of 1301 mg/day and the serum albumin-was 28g/dL. Her serum electrolytes including calcium, magnesium, and phosphate were well within normal limits. Chest X-ray showed bilateral moderate pleural effusion (Figure 1). Her pleural fluid analysis showed transudate pleural effusion with normal cell count, sugar and pH. Ultra sound scan of abdomen and chest showed moderate hepatosplenomegaly, moderate ascitis and bilateral pleural effusion. The ECG showed low voltage complexes and q waves in V1 to V3. A 2D echocardiography revealed significant LV hypertrophy with diastolic dysfunction with an EF>70% (Figure 2). She underwent an upper gastro intestinal endoscopy due to persistent microcytic anaemia and marked constitutional symptoms, It showed a yellowish coloured, 6mm raised lesion in anterior wall of the first part of the duodenum (D1). The duodenal biopsy revealed duodenal mucosa and submucosa consisting of islands of remarkable eosinophlic amorpous material around blood vessels and mild lymphocytic infiltrate, few foreign body giant cells in favouring the diagnosis of small bowel amyloidosis which was subsequently confirmed on Congo red stain.

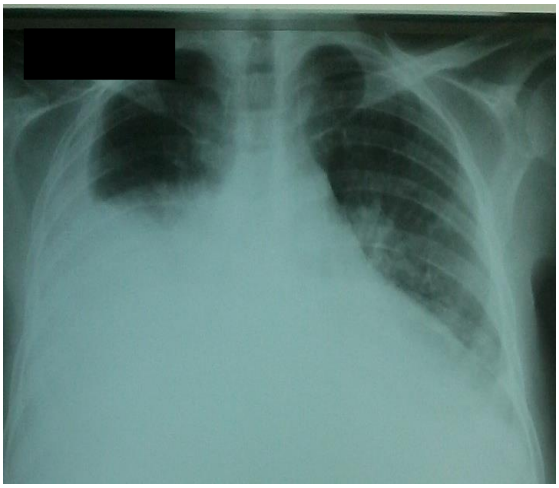

Figure 1: The Chest X-ray showed bilateral pleural effusion which is more marked on right side than left side.

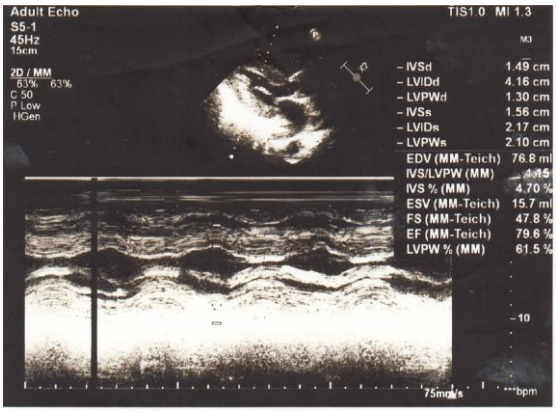

Figure 2: 2D Echocardiography showed moderate concentric left ventricular hypertrophy and diastolic dysfunction.

A myeloma screening including urine Bence -Jones protein skeletal survey, serum electrophoresis was negative. Nerve conduction tests showed motor axonal neuropathy of lower limbs and upper limbs and bilateral moderate carpal tunnel syndrome. The bone marrow biopsy showed normal erythropoietic, granulopoietic, megakaryopoietic cells, 8% lymphocytes, 10% plasma cells of marrow nucleated cells including few multinucleated cells. The serum free Kappa and free Lambda were 22.8mg/L (3.3-19.4mg/L) and 253.2mg/L (5.71-26.3mg/L) respectively and ratio of Kappa/Lambda was 0.08 (0.26-1.60). Serum immunofixation studies are

favoured a diagnosis of light chain myeloma in our patient.

She was diagnosed with light chain myeloma with cardiac, renal, gastrointestinal and nervous system involvement. An aggressive treatment approach to control the underlying plasma cell dyscrasia as well as supportive therapy were instituted. She was treated with high dose oral melphalan with dexamethasone along with a diuretics, human albumin, venous thromboembolism prophylactic therapy. Unfortunately she succumbed to the illness due to congestive cardiac failure.

Discussion

Systemic AL-amyloidosis is a disorder of protein folding in which there is extra cellular accumulation as β pleated fibrillar deposits of monoclonal immunoglobulin light chain fragments leading to organ failure [1]. AL- amyloidosis is a rare clinical entity. AA -amyloidosis, is composed of a non-immunoglobulin, amyloid A and is associated with various chronic inflammatory and infectious conditions [2]. AA -amyloid commonly affects the spleen, lymph nodes, kidney and liver[2]. The gastrointestinal amyloidosis may have a diagnostic challenge to clinicians. A presentation with clinical and histological evidence of gastrointestinal amyloidosis is even rare[3]. Cowan AJ et al. reported 76 patients (3.2%) having biopsy-proven amyloid involvement of the gastrointestinal tract among 2,334 patients with all types of amyloidosis over a period of over 13 years[2]. We report here a primary AL -amyloidosis secondary to lambda light chain myeloma in a 54-year-old woman who presented with nephrotic syndrome and motor neuropathy.

She initially presented with vague symptoms and subsequently developed multisystem involvement such as arthropathy, bilateral carpel tunnel syndrome, generalized oedema, nephrotic syndrome, cardiac and visceral involvement. These features were suggestive of generalized amyloid deposition in joints, heart, visceral organs and nervous system which can be well explained by primary amyloidosis[3] in this patient. The initial investigations to exclude plasma cell dyscrasia including, serum protein electrophoresis, Urine for Bence- Jones proteins as well as skeletal survey were negative. Bone marrow biopsy indicated 10% plasma cells. Since the bone marrow was inconclusive, further evaluation with serum light chain assay showed very clear peak of serum lambda light chain concentration with significantly low Kappa/Lambda light chain ratio confirming the diagnosis of primary AL Amyloidosis due to light chain myeloma in our patient.

Systemic AL -amyloidosis is a disease with considerable clinical heterogeneity due to multiple system involvement[4]. She had longstanding dyspeptic symptoms and hepatomegaly as initial presentation. It can easily be attributed to the amyloidosis involving the gastrointestinal system[2]. It may be caused by ischemia or infarction, by ulceration or an infiltrated lesion, or from generalized oozing without a particular source. Liver involvement is more common among patients with significant amyloid deposition[5]. Hepatomegaly may be explained by amyloid infiltration and due to venous congestion due to amyloid cardiomyopathy[4].

The accurate diagnosis by biochemical analyses is essential for management of Ig-related amyloidosis patients. Therefore, the characteristic deposition pattern of amyloidosis in routine histopathological examination of biopsy specimens, such as gastrointestinal biopsy, if present, may help in the selection of cases for further biochemical analyses[6]. The histopathological diagnosis from affected

organ especially rectal biopsy is essential for the diagnosis of AL amyloidosis. Endoscopic features of upper gastrointestinal tract are variable ranging from subtle erosive changes, mucosal friability and granularity to polypoidal protrusions[2] The Congo red staining with classical apple green birefringence under polarized light confirm deposition of amyloid fibrils[4].Duodenal biopsy confirmed the diagnosis of amyloidosis in our patient.

The serum free chain estimation gives a positive result in 98% of patients with AL amyloidosis[7]. It is not specific for AL amyloidosis as monoclonal free light chains are also found in Waldenstrom macroglobulinaemia and monoclonal gammopathy of undetermined significance (MGUS). Therefore difference between amyloidogenic and uninvolved FLC (dFLC) has being recognized as new estimate of light chains. Immunofixation studies are necessary in patients with negative serum and urine protein electrophoresis to determine level of paraprotein in AL -Amyloidosis[7].

The existing conventional chemotherapeutic regimes are associated with high treatment related morbidity. Therapy response can be monitored based on haematological and individual organ response. This patient was treated with high dose oral melphalan and dexamethasone therapy.

By reporting this case the authors emphasize the fact that a high degree of clinical suspicion is warranted for the early diagnosis of AL- amyloidosis with a predominantly gastrointestinal presentation. Although, amyloidosis is an extremely rare cause of long standing dyspepsia, Congo red staining for GI biopsies should be considered in the presence of histologically suspicious material or clinical suspicion of amyloidosis in patients with longstanding unexplained dyspeptic symptoms.

References

1. Ebert EC, Nagar M. Gastrointestinal manifestations of amyloidosis. Am J Gastroenterol. 2008; 103:776–87.
2. Cowan AJ, Skinner M, Seldin DC, et al. Amyloidosis of the gastrointestinal tract: a 13-year, single-center, referral experience.Haematologica. 2013;98:14 1-6. https://doi.org/10.3324/haematol.2012.068155
3. Menke DM, Kyle RA, Fleming CR, Wolfe JT, Kurtin PJ, Oldenburg WA. Symptomatic gastric amyloidosis in patients with primary systemic amyloidosis. Mayo Clin Proc. 1993;68:763–7.
4. Sattianayagam PT, Hawkins PN, Gillmore JD. Systemic amyloidosis and the gastrointestinal tract. Nat Rev Gastroenterol Hepatol. 2009;6:608–617. https://doi.org/10.1038/nrgastro.2009.147
5. Friedman S, Janowitz H. Systemic amyloidosis and the gastrointestinal tract. *Gastroenterol Clin North Am* 1998; **27**: 595–614. https://doi.org/10.1016/S0889-8553(05)70022-4
6. Ichimata S et al. Usefulness of gastroduodenal biopsy in the differential diagnosis of systemic AH amyloidosis from systemic AL amyloidosis, 2018:73(2);230-9. https://doi.org/10.1111/his.13631
7. M. A. Gertz, "Immunoglobulin light chain amyloidosis: 2011 update on diagnosis, risk-stratification, and management," American Journal of Hematology.2011;86: 180-6.https://doi.org/10.1002/ajh.21934