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SYSTEMIC AMYLOIDOSIS INVOLVING DUODENUM AND LIVER – POOR OUTCOME

Histopathology

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ABSTRACT

Amyloidosis involving the liver and gastrointestinal tract had a very unusual presentation. We present a case of small bowel diarrhea and unexplained weight loss in an elderly male patient, further workup reveals amyloid deposit in the liver and duodenum, which was confirmed under a polarised microscope. So, in the unusual presentation of patients who may need a workup for amyloidosis, the physicians may keep a biopsy in mind.

KEYWORDS

Amyloidosis, Hepatic, Duodenal.

INTRODUCTION:

Amyloidosis is a group of rare disorders resulting from extracellular accumulation of insoluble fibrillary amyloid protein leading to end-organ dysfunction [1,2]. It is classified as systemic or localised according to deposition of amyloid protein and acquired or hereditary according to aetiology [3]. The gold standard for diagnosis is tissue biopsy demonstrating amyloid material followed by Congo Red staining and apple-green birefringence of the deposit under a polarized microscope. Kidney, subcutaneous fat, liver, bone marrow and gastrointestinal tract are the common biopsy sites for diagnosis in systemic amyloidosis. Direct biopsy of affected organ showed 100% sensitivity for diagnosis. Immunohistochemistry can be routinely used for typing of amyloid protein, since treatment is type specific [3].

Case history:

A 51 years old male presented with a chief complaint of large volume watery loose stools associated with abdominal bloating sensation and loss of appetite for 20 days. The patient had significant unintentional weight loss of around 8 kg within this period. He was known hypertensive on theraphy for last 5 years. He denied any history of alcohol use. On examination, patient had mild hepatomegaly and spleen was not palpable. Routine investigations revealed mild direct hyperbilirubinemia (total bilirubin of 1.68 mg/dl & direct fraction of 1.24 mg/dl), mild transaminitis (AST: 83 U/L, ALT: 27 U/L) raised serum alkaline phosphatase (830 U/L) and gamma glutamyl transpeptidase (799 U/L), hypoalbuminemia (2.3 gm/dl) with unremarkable hemogram and renal function test. Stool examination for routine microscopic examination revealed plenty of pus cells without any organism and stool for Clostridium difficile toxin assay was negative. Esophagogastroduodenoscopy (EGD) showed erosive antral gastropathy with duodenal erosions. Duodenal biopsy taken for histopthological examination. It revealed glassy pink material deposited in lamina propria with associated mild chronic inflammation(Fig1). Subsequently, colonoscopy revealed a few diminuted polyps over ascending colon and multiple discrete small ulcers with surrounding edematous mucosa from rectum to ascending colon. Histopathological examination of colonic mucosal tissue depicted features of infective colitis. Meanwhile, he was treated with hydration (initially with oral rehydration solution and later with IV fluids) empirical antibiotics (initially with ciprofloxacin + metronidazole and later with rifaximin) which led to mild transient relief of symptoms initially. However, after one week of hospitalization, he developed progressive breathlessness due to rapidly developing bilateral pleural effusion. Contrast enhanced CT scan of abdomen revealed mild hepatomegaly with volume redistribution (suggestive of chronic liver disease), minimal ascites and gross bilateral pleural effusion. Pleural fluid analysis revealed features of transudative effusion. Blood NT pro-BNP was very high i.e.30000pg/ml. However, 2D echocardiography was unremarkable. PET CT scan of whole body was done to rule out any malignancy, which did not reveal any lesion with abnormal hypermetabolism. Hence, transjugular liver biopsy was also performed to rule out any infiltrative systemic disease. Liver biopsy revealed normal lobular architecture and bile ductules. Extensive deposition of homogenous glassy pink material in perisinoidal space with focal destruction of hepatocytes and mild chronic inflammation in portal tracts and bile plugging (Fig-2). On Masson trichrome stain the acellular material appeared bluish. This deposit in both the tissues was Congo red positive and showed apple-green birefringence under polarised light (Fig-3&Fig-4).

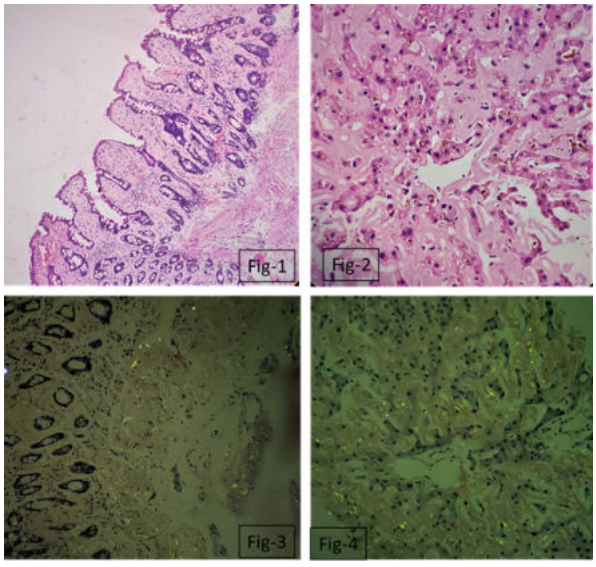

Fig -1: H&E 100X,Duodenum showing glassy pink material in lamina propria and submucosa. **Fig-2:** H&E 200X,Liver showing glassy pink material in perisinusoidal spaces and focal bile plugging. **Fig -3:** Congo red stain 200X showed apple-green birefringence under polarised light in liver. **Fig -4:** Congo red stain 200X showed apple-green birefringence under polarised light in duodenum

Hence, a diagnosis of hepatic and duodenal amyloidosis was made. However, biopsy from colon didn't show amyloid deposit. Meanwhile patient's general condition started to worsen gradually and he developed multiorgan failure (shock, respiratory failure) in the third week of hospitalization and managed with inotrope infusion and mechanical ventilation. Further workup like serum/urine protein electrophoresis, serum levels of light chain or bone marrow

examination couldn't be done because the patient died within 24 hours of diagnosis.

DISCUSSION:

Amyloidosis is a rare disease characterized by the deposition of insoluble, fibril-forming amyloid proteins in the extracellular space of organs, which can result in end-organ dysfunction. [1, 2] The amyloid proteins can deposit in various organs such as the heart, kidney, peripheral nerves, and liver [3]. Liver involvement in amyloidosis usually presents with nonspecific clinical symptoms such as weight loss and fatigue and hepatic amyloidosis is associated with a poor prognosis [4].

In a cohort of 98 cases of hepatic amyloidosis patients described by Park et al [5] most patients presented with vague, nonspecific symptoms such as weight loss and fatigue, were noted to have hepatomegaly on physical examination, and had elevated alkaline phosphatase levels on presentation. Amyloidosis involving liver had very nonspecific clinical symptom, so, initial diagnosis taking liver biopsy is critical [5]. Prognosis was very poor with 8.5 months median survival rate [5]. We reported a case of hepatic and duodenal amyloidosis in our institution with only 1month history of symptoms and patient succumbed next day of diagnosis. The case presented with large volume stool and significant weight loss, mild hepatomegaly and increased alkaline phosphatase. The present case had also presented with unexplained weight loss, mild hepatomegaly and markedly raised alkaline phosphatase at later stages like Park et al in his study.

Gastrointestinal amyloidosis is defined as signs and symptoms of gastro intestinal tract along with direct biopsy conformation of the disease [6]. Gastrointestinal involvement of amyloidosis mostly presented with diarrhoea. Etiologies can be due to small intestinal bacterial overgrowth, rapid intestinal transit of digested products and secretions related to autonomic neuropathy and bile salt malabsorption.[1]

The patient had very poor outcome may be explained due to advanced disease during diagnosis. The hepatic amyloidosis along with involvement of small intestinal amyloidosis is very rare with poor prognosis. As the case has high level of NT pro BNP around 30,000ng/L may be suffered from cardiac amyloidosis. Our case died of sudden cardiac arrest like a cohort study done with 230 patients of AL amyloidosis 4 cases died with same cause [7]. Overall poor outcome of amyloidosis involving liver should need prompt diagnosis and comprehensive management of this difficult case. Further investigation and prognostication for primarily liver AL amyloidosis are warranted to improve outcomes for this patient population.

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