Primary Systemic Amyloidosis - an Unusual Cause of Diarrhea

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The amyloidosis is a group of rare diseases caused by extracellular deposition of amyloid. It may affect multiple organs with protean manifestations, thus often causing delayed or incorrect diagnoses. We report a case of gastrointestinal involvement in primary systemic amyloidosis (PSA) in a patient complaining of diarrhea and weight loss. The diagnosis was confirmed by endoscopic biopsies of upper digestive tract and by multidisciplinary evaluation for systemic involvement.

Keywords: Amyloidosis, Chronic diarrhea, Red Congo stain, Immunohistochemistry

In patients with amyloidosis, recent data suggest an improved prognosis, with the median survival time increasing from six months to 18 months . Therapeutic success depends on an accurate and early diagnosis because prognosis worsens with the number and extent of organs involved. Amyloidosis mainly affects the heart, the kidneys and, commonly, the peripheral and autonomous nervous systems. However, gastrointestinal involvement, with symptoms such as chronic diarrhea, obstipation and steatorrhea, may also occur. The case described in the present article involved nonspecific but typical clinical manifestations of systemic amyloidosis and the appropriate diagnostic strategy is discussed.

Experimental part

A 78-year-old male with chronic kidney disease, recurrent pleural and pericardial effusion, chronic anemia, chronic cholestasis presented for diarrhea up to 4-5 stools/ day, related to meals, early satiety and weight loss, physical asthenia, peripheral paresthesiae, eye dryness, symptoms ongoing for the last 6 months.

Clinical examination

At physical examination the patient had a normal weight with a BMI of 20 kg/m^2, cutaneo-mucosal pallor, peripheral oedema, orthostatic hypotension, reduced right lower thoracic basis normal breath sounds , hepatomegaly with inferior liver margin at 4-5 cm under costal border.

Laboratory findings

Significant biochemical changes in blood test showed macrocytic anemie Hb 9.4 g/dL (11.6-16.8), MCV 102 fL (80-100), albumin 2.8 g/dL (3.5-5), creatinine 2.94 mg/dL (0.5-1.3), alkaline phosphatise 192 U/L (40-130), gamma glutamyl transferase 112 U/L (10-87), vitamin B12 90 pg/ mL (180-211), CRP 58 mg/L(<3). Stool tests were negative for Salmonella, Shigella, Yersinia and Clostrium difficile.

Paraclinical examination

Abdominal ultrasound showed an enlarged homogenous liver with a craniocaudal diameter of 210 mm. Upper digestive tract endoscopy revealed a pale stomach mucosa with prominent submucossal vessels and a jejunal mucosa with smooth tubular surface and flattened villi (Fig. 1).

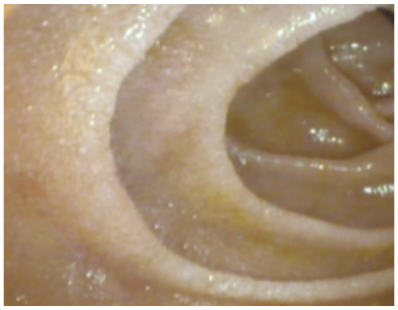

Fig. 1. Endoscopic aspect of jejunum. Flattened villi and smooth tubular surface

Histopathology examination

At thr histological examination of stomach and jejunum showed mucosa presenting vessels with thickened walls by deposition of positive Congo Red material, with green birefringence in the polarized light examination. Immunohistochemistry revealed vascular wall depositis positive for amyloid A with an intense reaction for lightweight kappa chains (Fig. 2, Fig. 3).

Further, the patient underwent investigations for the assessment of the systemic involvement. Schimmer test diagnosed Sicca syndrome with Schimmer test=1 mm lacrimal, electromyography was positive for moderate axonal sensorimotor polyneuropathy, cardiac ultraspund showed left ventricle wall hypertrophy with an interventricular septum of 14mm and the electro-cardiogram showed low QRS voltage, urinary test revealed a proteinuria of 0.24 g/24 h. Bone marrow aspirate showed normal cellularity, small interstitial and perivascular lymphocytic infiltrate and Congo red coloration negative, immunohistochemistry for CD 138 positive plasmocytes kappa/lambda was negative. The patient died soon after the initiation of dexamethasone due to complications caused by Clostridium difficile colitis and infectious pneumonia.

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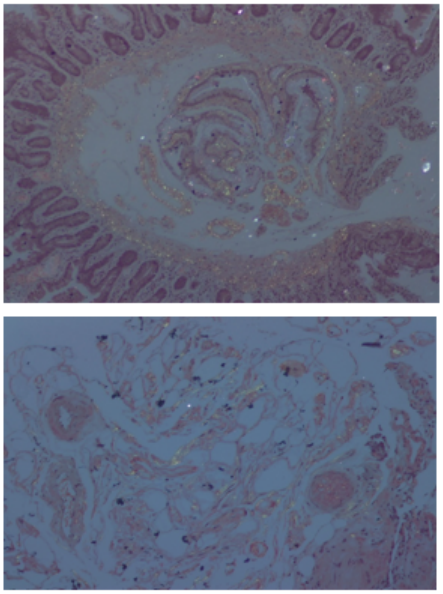

Fig 2., Fig 3. Jejunal biopsy with Congo Red stain showing green birefringence under polarized light compatible with amyloid deposits, 200x

Results and discussions

Immunoglobuline light chain amylodosis (AL) is the most common type of systemic amyloidosis with an incidence estimated yearly at nine cases /million in western countries [1]. AL amyloidosis is a plasma cell dyscrasia characterized by extracellular accumulation of beta-pleated fibrillar depositis of monocolonal light chain immunoglobulin.

Kidney involvement is the most common characterized by nephrotic syndrome [2]. At diagnosis our patient had no nephrotic range proteinuria. Heart involvement is represented by deposits of amyloid in the cardiac walls causing restrictive cardiopathy [3]. Peripheral nerve involvement includes sensorimotor peripheral and autonomic neuropathy that can manifest as gastroparesis, diarrhea or constipation or postural hypotension [4]. Hepatic involvement although common, clinical manifestations are mild. It is mostly characterized by hepatomegaly and abnormal liver function tests. Gastrointestinal involvement includes impaired intestinal transit, weight loss, dyspepsia, and gastrointestinal bleeding [5-9].

In our patient chronic diarrhea can be caused by mixed mechanisms: infiltrative by amyloid deposits in the intestine and neurological by peripheral neuropathy. Also intestine and gastric infiltration can explain hypoalbuminemia with no renal involvement and B12 deficit.

The diagnosis of AL amyloidosis is based by the detection of extracellular Congo red deposits by light chain microscopic examination that display apple green birefringence under polarized light. It is advisable that the biopsies to be obtained non-invasively from abdominal fat or minor salivary glands. If negative, it is to be considered biopsy from a clinically affected organ [2]. Once the tissue amyloid deposit was confirmed plasma cell dyscrasia must be confirmed by the predominace of gamma and kappa-producing plasma cells in the bone marrow aspirate although definitive results are obtained in less than 60% cases [10-13]. Treatment includes oral merphalan and prednisone or dexamethasone [14].

Conclusions

Gastrointestinal amyloidosis should be considered in patients with chronic diarrhea, especially if it is combined with weight loss, edema, anemia, low voltage in the ECG or other possible signs of a systemic amyloidosis and if more common diseases have been excluded. Besides chronic diarrhea, stasis symptoms such as vomiting, nausea, gastrointestinal reflux, early satiety can also occur in systemic amyloidosis. Early and accurate diagnosis and a prompt initiation of treatment are critical for the prognosis of light-chain amyloidosis. We hope that this report will help our peers keep vigilant of underlying diseases when similar clinical scenario occurs in order to make a prompt diagnosis and effective treatment.

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Manuscript received: 28.06.2019