CLINICAL VIGNETTE

Amyloidosis with Gastrointestinal Involvement

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Case Report

A 56-year-old female with history of hypothyroidism, asthma, and a remote history of cervical cancer presented with progressive shortness of breath. She was in her usual state of health until 15 months ago. At that time she developed sudden onset shortness of breath, which was accompanied by abdominal and leg swelling. Since her initial presentation, her symptoms have progressively worsened. She underwent extensive cardiac and pulmonary evaluations at outside facilities without any apparent etiology of her symptoms. This evaluation included two negative chest x-rays and a trial of asthma inhalers without relief of her symptoms. One week prior to this current presentation she underwent a chest CT which reportedly revealed a pleural effusion and she was sent to an outside Emergency Department. Although the patient's shortness of breath had progressively worsened, the abdominal distention and discomfort had been relatively stable for the preceding few months. She reported normal formed bowel movements about twice each day. She denied seeing any blood in the stool. The patient underwent thoracentesis with removal of one liter of fluid. She then requested transfer to our facility for further evaluation.

On physical exam she had a temperature of 97.6 F, heart rate of 80 and blood pressure of 91/56. Positive findings on exam included decreased breath sounds bilaterally, tenderness in the epigastric area and right upper quadrant of the abdomen. There was also bilateral lower extremity edema.

She then underwent further diagnostic testing. CT scan of the abdomen and pelvis revealed heterogeneous enhancement of the liver, bilateral pleural effusions, ascites, and subcutaneous anasarca changes. A transthoracic echo showed small left ventricular size, moderate concentric left ventricular hypertrophy with EF>75%, grade III (restrictive) diastolic dysfunction. A 12-lead ECG showed low voltage. The combination of all of these findings was suspicious for amyloidosis. Serum protein electrophoresis showed a monoclonal peak at 0.2 g/dL. There was an abnormal free light chain assay with highly elevated lambda light chains and normal kappa light chains. The patient then underwent upper endoscopy, which showed diffusely erythematous gastric mucosa with superficial erosions. Multiple biopsies were obtained from the stomach and duodenum. She also underwent flexible sigmoidoscopy which was normal. Multiple biopsies were obtained from the sigmoid colon and rectum. All of the gastrointestinal biopsies showed submucosal amyloid deposition on Congo red staining. A bone marrow biopsy also confirmed amyloidosis. The patient was thought to have AL amyloidosis with involvement of the gastrointestinal tract, heart, and likely liver. She was referred for evaluation for chemotherapy and possible heart transplant.

Discussion

Amyloidosis refers to the deposition of low molecular weight subunits of various proteins into extracellular tissue. There are numerous different protein precursors which correspond with different types of amyloid diseases. The two most common types of amyloidosis are AL (primary) and AA (secondary). In AL amyloidosis the protein is from immunoglobulin light chain fragments. This can be seen as an isolated process or associated with multiple myeloma. AA amyloidosis can be seen in association with any chronic inflammatory condition. Examples of these conditions include inflammatory bowel disease, rheumatoid arthritis, spondyloarthropathy, or chronic infections[1]. In general the clinical manifestations of amyloidosis are determined by the type of protein, the amount of deposition, and the tissues that are involved (commonly heart, kidneys, liver). Typical signs or symptoms may include proteinuria, nephrotic syndrome, heart failure, arrhythmia, heart block, hepatomegaly, malabsorption, intestinal pseudo-obstruction [2-4].

The incidence of AL amyloidosis is about 6 to 10 cases per million person-years, in the United States[5]. This is a male predominant disease and the incidence

increases with age. As mentioned, AL amyloidosis can occur in the setting of multiple myeloma. Lytic bone lesions, hypercalcemia, or greater than 30% plasma cells are all suggestive of this combination[6]. The diagnostic evaluation should include serum and urine immunofixation and serum free light chain ratio analysis, as well as biopsy of either fat pad, bone marrow or other affected organ. The criteria that must be met for diagnosis of AL amyloidosis must include systemic/organ damage directly related to amyloid deposition, positive amyloid staining by Congo red, evidence of light chains by direct examination, and evidence of monoclonal plasma cell proliferative disorder[7,8].

Gastrointestinal involvement varies with the type of amyloidosis. It can be seen in up to 60% of patients with reactive amyloidosis[9]. Although gastrointestinal involvement is much less common with AL amyloidosis, hepatic involvement is quite common and is seen in up to 70% of patients. With AL amyloidosis the gastrointestinal deposition is usually in the muscularis mucosa, submucosa, and muscularis propria. The most common presentation is constipation related to mechanical or pseudo-obstruction. With AA amyloidosis the deposition is usually in the mucosa. The most common manifestations of this are mucosal friability, erosions, or diarrhea[10]. Another possible gastrointestinal manifestation of amyloidosis includes bleeding from mucosal lesions or vascular friability. Malabsorption can also be seen secondary to amyloid infiltration or small intestinal bacterial overgrowth. Abdominal pain can also occur.

With gastrointestinal amyloidosis, the radiographic findings and biopsies can be variable. Barium studies may show a course mucosal pattern in AA amyloidosis or thickened folds and polypoid protrusions with AL amyloidosis. CT findings may show bowel wall thickening or dilatation[11]. However, none of these findings are specific for amyloidosis. Biopsies should be stained with Congo red. When the gastrointestinal tract is involved, the yield of amyloid in biopsies depends on the area that is sampled. The highest yield is in the duodenum at nearly 100%, followed by the stomach and colon/rectum at >90%, followed by the esophagus at 70%[12].

This case illustrates the importance of being able to look at multi-systemic complaints and identifying a unifying diagnosis. This patient was having symptoms for over one year before a diagnosis was made. Once amyloidosis was considered, almost all of her diagnostic studies were consistent with and confirmed the diagnosis.

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Submitted on August 18, 2014