Abstract:
Amyloidosis is a rare disease caused by extracellular deposits of fibrillar proteins in various organs. Gastrointestinal involvement can be seen in both primary and secondary amyloidosis. We present the case report of systemic amyloidosis presenting as long standing diarrhea.

Keyword: Primary and secondary Amyloidosis, Malabsorption

Introduction:
Amyloidosis is a generic term that refers to the extracellular tissue deposition of fibrils composed of low molecular weight subunits of a variety of misfolded proteins (1). These fibrils have predominantly a β-sheet configuration and can be identified both by their characteristic appearance on electron microscopy and their ability to bind Congo red leading to green birefringence under polarized light. Gastrointestinal involvement is more common in secondary amyloidosis than in primary. There is frequent delay in diagnosis because of the non-specific nature of symptoms.

Case Report:
A 42 year old lady presented with painless chronic diarrhoea of 4 years duration. She had loose stools 5-6 times a day, large in volume, watery in nature, postprandial in onset associated with borborygmi and ball rolling movements. She also had fecal incontinence and urgency of stools. She used to take codeine to control her diarrhea. There was no history of fever, blood in stools or abdominal pain. One year later she developed recurrent syncopal attacks and pain in the posterior surface of the left leg which was aggravated with coughing, sneezing and bending and associated with weakness in the left leg. Over the past 6 months, she had similar complaints in right lower limb followed by involvement of the upper limbs. There was no history of trauma to the back. She had anorexia and weight loss of 40 kg over this period. There was also history of exertional dyspnea and orthopnea. There was no history of extraintestinal manifestations of inflammatory bowel disease (IBD). There was no family history of IBD or malignancy.
She was evaluated multiple times elsewhere but her diagnostic work up was non-contributory. She had undergone prior colonoscopy which showed rectal and sigmoid aphthae with biopsy showing non-specific colitis on the basis of which she was started on mesalamine but had no relief. On examination, she appeared cachectic and thin built. Pallor and bilateral pedal edema were present. BMI was 17.06 kg/m², JVP was elevated. Abdominal examination was normal. Central nervous system: She had grade 4+ power in both upper limbs and grade 3 power in both lower limbs. Reflexes were sluggish in all four limbs. There was impaired sensation in bilateral L4-S2 distribution. Blood investigation showed hemoglobin of 9.8 gm/dl and serum albumin of 3.1 mg/dl. Urine protein 24 hr was 600 mg/400 ml volume. Urine for Bence Jones protein was negative. Serum electrophoresis did not show any evidence of plasma cell dyscrasia. CT abdomen was normal. Echocardiography showed restrictive cardiomyopathy with speckled appearance of myocardium suspicious of amyloidosis. Bone marrow aspiration showed cellular marrow with pink amorphous-gelatinous material and trilineage hematopoiesis. Gastroscopy and colonoscopy was deferred in view of her high cardiac risk. Rectal mucosal biopsy was consistent with amyloidosis. Subsequently her condition deteriorated and she was shifted to the high dependency unit and started on ionotropes. The family requested discharge at request as they did not opt for further management. Her final diagnosis at discharge was secondary amyloidosis.

DISCUSSION:

Amyloidosis should be considered in the differential diagnosis of chronic diarrhea seen in association with neuropathic and orthostatic symptoms (2). Systemic AL amyloidosis is the most common type associated with plasma cell dyscrasia which produces immunoglobulin light chain. The secondary amyloidosis is due to amyloid formed from serum amyloid A (AA), an acute-phase protein produced in response to inflammation. The most frequent type of familial amyloidosis is caused by mutant transthyretin (TTR) deposition. There are more than ten different types of amyloid described in the literature. AL (primary), AA (secondary or reactive), AF (familial) and beta-2 microglobulin associated amyloidosis (hemodialysis-related) account for 90% of all cases of amyloidosis producing gastrointestinal symptoms (3). Secondary amyloidosis is most commonly caused by rheumatoid arthritis, inflammatory bowel disease, tuberculosis and rarely familial Mediterranean fever. Gastrointestinal involvement is present in as many as 60% of patients with secondary amyloidosis (4) but has also been reported in primary amyloidosis with prevalence being about 1% (5). Constipation and mechanical obstruction are the usual presentation of primary amyloidosis while secondary amyloidosis presents with diarrhea and malabsorption (6) as seen in our patient. Mucosa predominant disease manifests as malabsorption whereas muscularis predominant disease presents as obstruction. Autonomic neuropathy which is generally characteristic of transthyretin amyloidosis may also affect gut function (7). Diarrhoea in amyloidosis can be due to number of reasons such as rapid transit, autonomic dysfunction, steatorrhea secondary to bile acid malabsorption (as consequence of bacterial overgrowth or rapid transit) and exocrine pancreatic insufficiency (due to ischaemia from amyloid deposition in the
arteries and arterioles or to infiltration of acinar tissue by amyloid). Diarrhoea usually does not respond to conventional therapies while somatostatin analogues or enterostomy have been efficacious in few case studies.(8,9) Since our patient’s diarrhea responded to antimotility agent-codeine, other therapies such as somatostatin was not considered. The diagnosis of amyloidosis should be considered in patients with unexplained symptoms simultaneously or sequentially developed like proteinuria, cardiomyopathy, neuropathy or hepatomegaly. Gastrointestinal involvement should be considered in patients presenting with diarrhoea, anorexia, and weight loss.
In all cases, the diagnosis is confirmed by demonstration of amyloid deposits in tissues by apple-green birefringence when stained with Congo red and viewed under polarizing microscopy. Tissue samples (such as abdominal fat, small intestinal mucosa, gums, gut, rectum and skin) may be taken by fine-needle aspiration or biopsy or surgery. Nevertheless, abdominal fat is the mostly used because it is positive for amyloid deposits in about 70% of patients with amyloidosis (10).
Immunofixation electrophoresis should be performed on the serum and urine because in AL amyloidosis, the concentration of the monoclonal light chain often is too low to be detected by simple protein electrophoresis (in contrast to multiple myeloma). In case of AL amyloidosis, confirmation of AL disease requires demonstration of a plasma cell dyscrasia by a bone marrow biopsy or by the presence of a monoclonal light chain in the serum or urine. In this patient we have excluded multiple myeloma by bone marrow and serum electrophoresis. In view of her moribund status, the relatives were not keen on further work up or specific management.

In summary, this case report of amyloidosis emphasizes the need for strong suspicion of this entity. In a retrospective study, the delay from onset of symptoms to diagnosis of amyloidosis was found to be between 7 to 24 months owing to both physician and patient factors [11]. Increasing medical awareness can prevent delay in diagnosis and treatment.

References:


