Unusual presentation of more common disease/injury

Primary systemic amyloidosis presenting as idiopathic inflammatory colitis

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Summary

A 75-year old-female was referred with chest pain. She was fully investigated and it was felt that her symptoms were non-cardiac. Four months later, she was seen in gastroenterology outpatients with bloody diarrhoea and abdominal pain. Colonoscopy demonstrated inflammation up to the splenic flexure and histology confirmed inflammatory colitis. Later, she developed dyspepsia and weight loss. An oesophagogastroduodenoscopy (OGD) showed *Helicobacter pylori* negative erosive gastritis with a benign duodenal ulcer. Whole body CT scan was normal. Ten months later, she was admitted with dyspnoea due to severe heart failure. The admission ECG had significantly changed, now showing low voltage complexes and repeat echocardiography showed restrictive cardiomyopathy. Specific congo red staining on the biopsy specimens from the previous OGD and colonoscopy confirmed amyloid deposits. Further investigations detected an underlying light chain myeloma causing systemic (AL) amyloidosis. Unfortunately, her condition deteriorated rapidly and she died shortly afterwards.

BACKGROUND

From this case report, we want to highlight that primary AL amyloidosis of the gastrointestinal (GI) tract may mimic idiopathic inflammatory colitis. Several case reports are published of AL amyloidosis, presenting as ischaemic colitis, collagenous colitis, GI bleeding, intestinal obstruction and malignancy.^{1–6} There is only one case report in which it presented as inflammatory (ulcerative) colitis.⁷

Gastroenterologists should consider amyloidosis in the differential diagnosis of older patients presenting with diarrhoea, despite the endoscopy and histology suggesting idiopathic colitis.

Cardiologists should consider amyloidosis in patients with low voltage QRS pattern on 12-lead ECG and restrictive left ventricular function on echocardiography. This patient originally presented with non-cardiac chest pain and at the time the 12-lead ECG, echocardiogram and coronary angiogram done were all felt to be within normal limits.

This case report should increase the awareness of amyloidosis presenting as colitis and its characteristic endoscopic features and prompt specific staining requests for amyloid on histological specimens.

CASE PRESENTATION

A 75-year-old lady presented to the gastroenterology outpatient department with a 2-month history of loose stools associated with fresh blood and abdominal pain. She had no previous bowel conditions, recent treatment with antibiotics or travel abroad. Her general health was good and her weight was stable with a body mass index of 30 kg/m². She was taking regular atenolol 25 mg and simvastatin 20 mg, prescribed by her general practitioner for hypertension

and hypercholesterolaemia respectively. She did not use over the counter aspirin, non-steroid anti-inflammatory drugs or complementary medicines.

The only other significant medical history included normal investigations for chest pain 4 months earlier. Her cardiac risk factors included: hypercholesterolaemia, hypertension, previous smoking and a positive family history of premature coronary heart disease. There was no family history of inflammatory bowel disease or bowel cancer. She lived with her husband and was mobile and independent.

General physical and systemic examination was normal including a rectal examination and rigid sigmoidoscopy.

Following the consultation, she underwent a colonoscopy and biopsy which showed idiopathic inflammatory colitis. She was prescribed 5-aminosalicylates (5-ASA), which improved her symptoms. At follow-up, she was noted to have lost weight prompting further investigations including whole body CT scan, small bowel meal and follow through and upper GI endoscopy.

In February 2010, the patient was admitted with severe heart failure and bilateral pleural effusions, confirmed on chest x-ray.

INVESTIGATIONS

The initial cardiac investigations, done 4 months before presentation in gastroenterology outpatient were all normal and included: 12-lead ECG (figure 1A) with normal voltage QRS complexes. Echocardiography demonstrated normal left ventricular systolic function and selective coronary arteriography showed normal coronary arteries.

Routine blood tests done on first presentation in gastroenterology clinic, including full blood count, urea,

Figure 1 (A–D) ECG, ECHO.

electrolytes, creatinine, liver function tests and inflammatory markers (erythrocyte sedimentation rate and C reactive protein) were normal. A urine dipstick showed few leucocytes but no proteinuria.

An outpatient colonoscopy, which was performed 5 months after her initial presentation with chest pain and 10 months before her final presentation with heart failure, showed moderately severe colitis up to splenic flexure. Further advancement of the scope was abandoned due to severity of inflammation (figure 2A,B). The mucosa was uniformly inflamed and oedematous with contact bleeding and there were several aphthous ulcers in the sigmoid colon. On retrospective review of the images taken during the colonoscopy, there appeared to be a small submucosal haematoma in the sigmoid colon. Histology confirmed the diagnosis of acute focally active chronic inflammatory colitis with rectal sparing.

A CT scan of her chest, abdomen and pelvis was reported as showing featureless, thickened sigmoid colon with no other abnormalities to account for the weight loss. A subsequent small bowel meal was also reported normal. Upper GI endoscopy revealed *Helicobacter pylori* negative erosive gastritis and a small benign duodenal ulcer (figure 2C). The gastric and duodenal biopsies excluded Crohn's disease and other conditions such as coeliac disease.

Later on, when she presented with heart failure, the admission ECG had significantly changed with 1st degree heart block, low voltage QRS complexes and right axis deviation (figure 1B). Repeat echocardiogram now showed thickened left ventricular muscle with mildly impaired systolic contraction but a markedly restrictive filling pattern on Doppler ultrasound: an E:A ratio of 2.4 and a MV deceleration time of 165 ms (figure 1C,D). A bright speckled echogenic appearance was noted, mainly affecting the interventricular septum. CT angiography did not show any significant coronary artery disease. These findings

were consistent with a severe restrictive cardiomyopathy and were considered highly suspicious for amyloidosis.

At this stage, review of all previous histology was requested, specifically looking for amyloid deposition. Congo red staining of all the histology specimens from the previous colonoscopy 10 months earlier and oesophagogastroduodenoscopy 3 months earlier was carried out. These clearly demonstrated typical birefringence pattern under polarised light consistent with the diagnosis of amyloid deposits (figure 3). Urine sample was positive for Bence-Jones proteins and plasma protein electrophoresis confirmed κ light chains at a concentration of 383 mg/l and κ/λ ratio of 45.3 units, consistent with the diagnosis of underlying myeloma. A bone marrow biopsy confirmed plasma cell dyscrasia and a skeletal survey showed a single myeloma deposit in the left upper femoral shaft.

DIFFERENTIAL DIAGNOSIS

This patient had clinical and endoscopic features of inflammatory bowel disease and the differential diagnosis at that time included: infective, ischaemic and drug related colitis and other rare conditions such as tuberculosis, lymphoma and amyloidosis. The secondary presentation of heart failure due to restrictive cardiomyopathy was suspicious of cardiac amyloidosis but the differential diagnosis includes sarcoidosis, haemochromatosis and malignant infiltrative disorders.

TREATMENT

This patient was initially treated for idiopathic inflammatory colitis with 5-ASA to which she responded and did not need oral steroids. At follow-up, she underwent further investigations for weight loss and dyspepsia and was given a proton pump inhibitor in the form of omeprazole 20 mg once daily.

Figure 2 (A–C) Endoscopy.

When she was admitted as an emergency with new onset heart failure, she was treated with intravenous frusemide 40 mg twice daily and later oral bumetanide 1 mg once daily. She also received an ACE inhibitor in the form of enalapril 2.5 mg once daily. During this admission, she developed recurrent severe diarrhoea and was started on intravenous hydrocortisone 100 mg four times a day, which improved her diarrhoea symptoms.

A multidisciplinary team with involvement of cardiology, gastroenterology, pathology and haematology were involved in her management. Once the diagnosis of myeloma and amyloidosis was established, she was treated with dexamethasone 20 mg once daily, thalidomide 50 mg once daily and anticoagulated with warfarin.

OUTCOME AND FOLLOW-UP

Unfortunately, she responded poorly to treatment of heart failure and conventional treatment for multiple myeloma. The cardiac involvement resulted in progressive heart failure and hypotension. After consultation with the patient and family, further active treatment was withdrawn and she was transferred to a hospice for palliative care where she died shortly afterwards.

DISCUSSION

Amyloidosis is defined as an extracellular deposit of protein fibrils with a β sheet fibrillar structure and characteristic

properties after staining with congo red dye. It is a rare disease with reported incidence of 1–5 cases per 100 000. Deposition of amyloid throughout the body, termed systemic amyloidosis, causes multi organ failure and carries a poor prognosis. The mortality is mainly caused by cardiac and renal complications. Primary (AL) or light chain (L) associated AL amyloidosis is the most common form with generalised deposition of excess light chains.

The published literature (Embase, MEDLINE), reports several cases of primary (AL) amyloidosis presenting as: ischaemic colitis, collagenous colitis, acute GI bleeding, intestinal obstruction and malignancy.^{1–6} Only one case report exists, where AL amyloidosis presented as inflammatory (ulcerative) colitis.⁷ The aim of reporting this case report is to improve awareness of the non-specific GI presentation of primary (AL) amyloidosis which can mimic colitis, so that an early diagnosis and appropriate treatment of the underlying plasma cell dyscrasia can be given and improve outcome.

Primary (AL) amyloidosis is commonly associated with plasma cell dyscrasia of which 15% have multiple myeloma.^{8–10} Secondary (AA) amyloidosis with acute phase reactant serum amyloid A protein (A) is associated with infectious, inflammatory or less commonly, neoplastic disorders. With the widespread use of antibiotics and anti-inflammatory medications, the predominant type of amyloid in the western world has shifted from secondary

Figure 3 (A–C) Histopathology.

(AA) amyloidosis to primary (AL) amyloidosis. Other recognised types of amyloid include: patients undergoing long-term haemodialysis with deposits of β 2-microglobulin^{11 12}; hereditary amyloidosis (an autosomal dominant inheritance of amyloidogenic proteins) and Senile amyloidosis is found in 10–36% of patients over 80 years old and occasionally in younger individuals.^{9 10}

In primary (AL) type amyloidosis GI tract involvement is nearly universal; and 30–60% of these patients develop common GI symptoms. Untreated AL amyloidosis carries a median 1-year survival of approximately 50%, which makes early diagnosis and treatment important.

Presentations are often non-specific and include GI bleeding, gut dysmotility leading to pseudo-obstruction, vomiting, dysphagia and malabsorption due to secondary bacterial overgrowth. Most of these symptoms result from infiltrative and ischaemic changes caused by accumulation of amyloid in confined tissue spaces in bowel and blood vessel walls. More rarely massive amyloid deposition can cause pseudotumours known as amyloidomas that can cause bowel obstruction.

Similar to the clinical presentation, the endoscopic findings are non-specific in AL amyloidosis. Findings described include: macroglossia; atonia/achalsia in oesophagus and thickened folds; erosions, friability, ulcerations and polyps in stomach and small bowel.^{13–17} Colonic findings are described as typical feature of idiopathic colitis including: mucosal oedema, loss of haustrations, luminal narrowing or thick folds; ulceration and mucosal nodularity with specific submucosal haematomas.^{2 7–10} This

patient had what looks like a small but characteristic submucosal haematoma, which was not recognised by the endoscopist, while other endoscopic findings were non-specific (figure 2A–C).

A high degree of clinical suspicion is needed to make an early diagnosis of amyloidosis in order to prevent multi-system damage.^{9 10} This patient presented with typical non-specific symptoms and responded to standard treatment of idiopathic inflammatory colitis. It was only when she represented with heart failure and repeat cardiac investigations suggested restrictive cardiomyopathy that amyloidosis was considered.

The goal of treatment in AL amyloidosis is to suppress the synthesis of immunoglobulin light chains by controlling the underlying plasma cell disorder with chemotherapy. Recently, high-dose chemotherapy with haematopoietic stem cell transplantation is being performed in AL amyloidosis, with encouraging results but this is limited to patients with good performance status and who have only limited cardiac involvement.^{18 19} Patients need maximum supportive treatment to prevent multi-organ damage and complications associated with immunosuppression.

Our patient was unfortunately not considered fit for a bone marrow transplant because she presented with advanced systemic (AL) primary amyloidosis with significant cardiac involvement and poor performance status.¹⁸ The underlying myeloma was treated with dexamethasone and thalidomide, but due to widespread disease and systemic involvement she failed to respond to the conventional treatment, developing progressive heart failure and death.

Learning points

- ▶ Acute inflammatory colitis is a rare presentation of primary (AL) amyloidosis and should be considered in the differential diagnosis of patients with colitis especially in older people. The specific endoscopic features can be hard to differentiate for other forms of colitis but the condition is easily diagnosed with congo red staining of biopsies.
- ▶ Early diagnosis of primary (AL) amyloidosis is important to prevent complications as only fit patients without significant cardiac involvement can be considered for bone marrow transplantation.
- ▶ One should always consider the possibility of underlying amyloidosis in a patient presenting with heart failure and GI symptoms.

Competing interests None.

Patient consent Obtained.

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