Duodenal perforation in primary systemic amyloidosis

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Abstract

Spontaneous duodenal perforation in two patients with primary systemic amyloidosis associated with multiple myeloma is described. Bowel perforation is a rare and often fatal complication of amyloidosis, and duodenal perforation has not been previously described. Both patients survived the bowel perforation with conservative management. Bowel perforation should be suspected in patients with amyloidosis presenting with acute abdominal pain, and active non-surgical management can be associated with prolonged survival.

Acute abdominal complications of amyloidosis are uncommon. Gastrointestinal involvement in amyloidosis is often asymptomatic but perhaps universal if vigorously sought.\(^1\) Reported complications include gastrointestinal haemorrhage, malabsorption,\(^2\) and pseudo-obstruction.\(^4\) Other acute abdominal events include spontaneous rupture of the spleen and subcapsular haematoma of the liver.\(^5\) Bowel perforation is very rare and previous reports have suggested a poor prognosis.\(^6\) Two patients with primary systemic (immunoglobulin light chain derived, AL) amyloidosis complicated by spontaneous duodenal perforation are presented.

Case reports

PATIENT 1

A 65 year old man presented with anorexia, nausea, tiredness, and occasional vomiting for one week. He had been previously well, apart from hypertension treated with Atenolol and a long history of dyspepsia. A routine blood test two months previously had shown mild anaemia with a raised white blood count of \(15 \times 10^9/l\). A blood film showed atypical lymphoid and plasmacytoid cells. Subsequent investigation showed an immunoparesis and free kappa light chains in the serum and urine. His serum creatinine concentration was 0.13 mmol/l, 24 hour urine protein excretion was 5.1 g/l, and a bone marrow examination was requested but declined by the patient. No treatment had been given.

On examination he was clinically dehydrated. Respiratory and cardiovascular examinations were normal; the abdomen was soft with no tenderness. The haemoglobin concentration was 6.5 g/dl, white cell count 47.1 \(\times\) \(10^9/l\) with 30% plasmacytoid cells, serum creatinine 1.17 mmol/l, and serum calcium 2.6 mmol/l. His renal function did not improve with rehydration, he remained oliguric, and peritoneal dialysis was begun. The diagnosis was plasma cell leukaemia with renal failure and he was started on melphalan 0.2 mg/kg and prednisone 2 mg/kg for four days. Three days after treatment had begun he experienced epigastric pain of sudden onset. On examination he had marked upper abdominal tenderness with guarding. A plain abdominal radiograph showed free air under the diaphragm and the suspected perforated viscus was managed conservatively. One week later, abdominal computed tomography showed a large collection in the left subphrenic space and 100 ml of purulent material were aspirated by a percutaneous, transhepatic approach. A sinogram performed four days later showed a connection between the cavity and the duodenal cap. Upper gastrointestinal endoscopy showed some distortion of antral mucosal folds, the duodenal cap was deformed but no acute ulceration was seen. Biopsy specimens from the duodenal cap and distal duodenum showed a heavy submucosal infiltrate of amyloid (Fig 1).

The patient had a prompt response to chemotherapy, with rapid clearance of plasma cells from the peripheral blood and a gradual recovery of renal function. A barium meal four weeks after his initial presentation did not show any connection with the previous collection.

PATIENT 2

A 65 year old woman complained of loose bowel motions up to five times daily for the past nine months. Her appetite was decreased, but her...
weight was stable and she had no abdominal
pain. A barium enema had been normal. Three
weeks before admission she developed acute
onset of epigastric pain. The pain gradually
settled overnight but she continued to
experience more generalised abdominal dis-
comfort for one week. A small bowel enema
performed three weeks after her initial
symptoms showed an internal fistula between
the third part of the duodenum and an extra-
 luminal space (Fig 2).

Her past medical history was unremarkable
and she was taking no medication; her alcohol
intake was estimated at 80 g/day and she smoked
20 cigarettes daily. On examination she had no
signs of chronic liver disease. She was moderately
tender in the upper abdomen and her bowel
sounds were active. Computed tomography
showed the accumulation of barium to be
anterior to retroperitoneal structures. Upper
gastrointestinal endoscopy showed discrete
shallow ulcers in the antrum, and the duodenal
mucosa was oedematous and friable, although
the distal duodenum looked normal. Biopsy
specimens of the duodenal cap and distal duo-
denum showed extensive amyloid in the
submucosa. Subsequent investigations con-
firmed that she had multiple myeloma. There
were free kappa light chains in the urine and a

significant immunoparesis. She was treated
conservatively, with intravenous nutrition and
antibiotics, and gradually improved. A normal
diet was started four weeks later, after a barium
meal had shown no fistulous tract.

She has remained well for 36 months, although
further investigations performed when her
diarrhoea worsened showed that she had signifi-
cant steatorrhoea. A therapeutic trial with
tetracycline for presumed bacterial overgrowth
resulted in an improvement. She now has normal
bowel habit and her haemoglobin, renal function,
and serum albumin are normal.

Discussion

These two patients illustrate that a successful
outcome is possible after conservative treatment
of spontaneous perforation of the duodenum in
patients with gastrointestinal amyloidosis.
Perforation of the bowel is a rare complication
of amyloidosis and has usually been fatal. Five
patients have been described previously; three
with perforation of the small bowel and two with
perforation of the rectum and colon.14 Only
two patients survived the acute complications of
the perforation and long term survival has not
been previously reported.

Gastroduodenal amyloid is a relatively
frequent finding in patients with gastrointestinal
involvement, but is usually asymptomatic.11 The
most common complication is haemorrhage
from antral and duodenal ulceration. Occasion-
ally pyloric obstruction occurs either from
generalised thickening or a discrete mass which
may resemble gastric carcinoma on a barium
meal. Symptoms of epigastric discomfort sug-
gestting peptic ulceration have been ascribed to
gastroduodenal amyloidosis. However, the
patients have usually had a previous history of
duodenal ulcer disease.16 Spontaneous perfo-
ration of the duodenum as seen in our two
patients has not been previously reported.
Amyloidosis was the significant underlying
pathology in both our patients, however
additional factors were present. In the first
patient, there was a past history of dyspepsia,
and he may have had duodenal ulcer disease,
although the endoscopic appearances did not
show any deformity of the duodenal cap. Acute
renal failure and high dose steroids are both risk
factors for acute stress ulceration. The history in
our second patient strongly suggested that the
symptoms three weeks before admission were
due to spontaneous duodenal perforation. How-
ever, it is possible that a perforation was caused
by the nasojejunal tube used for the small bowel
enema.

Primary systemic amyloidosis is a dys-
proteinenaemia; up to 86% of patients will have
a monoclonal protein in the serum or urine, but
only 25% will have more than 10% plasma cells in
the bone marrow or have the criteria for the
diagnosis of multiple myeloma.17 This distinc-
tion is not always critical as the currently available
treatments for myeloma do not seem to reverse
the amyloid infiltration, except in some cases of
renal amyloidosis. The amyloid deposit is
composed of a beta pleated fibrillar protein
consisting of fragments of immunoglobulin light
Duodenal perforation in primary systemic amyloidosis

chains. There is a preponderance of lambda light chains; 62% lambda, 24% kappa, and 14% with no monoclonal protein in one series.17 The type of light chain does not influence the clinical presentation, with the exception that patients with kappa light chains are more likely to have nephrotic syndrome or renal insufficiency.

Non-operative management is probably preferable to laparotomy in patients with primary systemic amyloidosis as the prognosis is poor (mean survival of 20 months; five year survival 19-6%).1 Non-operative treatment of perforated duodenal ulcers has recently been compared with operative treatment in a randomised trial, and a similar mortality was shown for both groups.18 Despite the overall poor prognosis, particularly for those patients with associated myeloma, some patients can do remarkably well as illustrated by our second patient. A more favourable outcome is seen in those patients without cardiac and renal involvement. These two patients show the need for a more positive approach to the complications of amyloidosis as an extended survival is possible. Amyloidosis is all too often regarded as an irreversible condition with grave implications. While the reports of regression of amyloidosis with treatment of the underlying disease are few,14,15 the complications of amyloidosis should be actively managed.

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