

Multiple Myeloma Associated with Light-Chain Amyloidosis Manifesting as Gastric Retention: A Case Report and Review of the Literature

W Liu, X Zhou

ABSTRACT

We report a case of multiple myeloma associated with light-chain amyloidosis in a 62-year old woman. The patient came to hospital with the main complaint of epigastric pain and gastroscopy showed gastric retention. The patient had been diagnosed with multiple myeloma associated with light-chain amyloidosis after biopsy of the gastric mucosa and bone marrow aspirate. A review of the literature was also performed.

Keywords: Amyloidosis, gastric retention, multiple myeloma

Mieloma Múltiple Asociado con Amiloidosis de Cadenas Ligeras Manifestada como Retención Gástrica: Reporte de Caso y Revisión de la Literatura

W Liu, X Zhou

RESUMEN

Se reporta el caso de un mieloma múltiple asociado con amiloidosis de cadenas ligeras en una mujer de 62 años de edad. La paciente acudió al hospital aquejada principalmente por un dolor epigástrico y la gastroscopía mostró retención gástrica. A la paciente le había sido diagnosticado un mieloma múltiple asociado con una amiloidosis de cadenas ligeras luego de practicársele una biopsia de la mucosa gástrica y aspirado de la médula ósea. También se realizó una revisión de la literatura.

Palabras claves: amiloidosis, retención gástrica, mieloma múltiple

West Indian Med J 2011; 60 (6): 681

INTRODUCTION

Multiple myeloma is a form of cancer characterized by proliferation of plasma cells and monoclonal immunoglobulin in the bone marrow. Most patients suffer from bone damage and complications of such including bone pain, pathological fracture and hypercalcaemia, renal insufficiency and anaemia. Amyloidosis is a kind of conformational disease characterized by extracellular deposition of insoluble fibrillar protein, called amyloid, in various organs and tissues. To date, at least 24 different proteins have been recognized as causative agents of amyloid disease (1). All the deposits share a common core structure of β -pleated configuration and can produce apple-green birefringence under polarized light when stained with Congo red dye (2, 3).

From: Department of Digestive Diseases, First Affiliated Hospital of Chongqing Medical University 400016, Chongqing, China.

Correspondence: Dr X Zhou, Department of Digestive Diseases, First Affiliated Hospital of Chongqing Medical University, 400016, Chongqing, China. E-mail: chqxchzh@163.com

According to the distribution of amyloid deposits, amyloidosis can be classified as systemic or localized. Light-chain (AL) amyloidosis is the most common form of systemic amyloidosis with 12–15% of patients having multiple myeloma, but most are asymptomatic (4). There are less reports of multiple myeloma manifesting as gastric retention as a result of amyloidosis.

CASE REPORT

A 62-year old woman was admitted to hospital with the main complaint of upper abdominal pain with nausea and vomiting for three months. Gastroscopy from another hospital showed decreased gastric peristalsis and gastric retention. On admission, the patient displayed mucosal pallor and the skin of the peri-orbital, neck and abdomen was waxen yellow. There was mild pitting oedema of the lower extremities. Papular lesions were found in the peri-orbital and abdominal wall (Fig. A). Physical examination revealed tenderness of the upper abdomen. The rest of the examination was unremarkable.



Fig. A: The skin of the peri-orbital area turned waxen yellow and papules were found.

Laboratory data showed red blood cells $3.19 \times 10^{12}/L$, haemoglobin 98 g/L, white blood cell $8.6 \times 10^9/L$, platelet $269 \times 10^9/L$, albumin 27 g/L, total protein 45 g/L, alanine transaminase (ALT) 42 U/L, lactic dehydrogenase (LDH) 725 U/L, serum creatinine 108 mmol/L, urea 9.0 mmol/L, uric acid 471.7 mmol/L, potassium 2.8 mmol/L, serum sodium 132 mmol/L and serum calcium 2.1 mmol/L. The stool examination and occult blood test, rheumatoid factor, antistreptolysin O, C-reactive protein, ANA (antinuclear antibodies) and tumour markers were within normal. Endoscopy showed thickness of the gastric wall, narrow gastral cavity, distortion of the pylorus and there was no gastric peristalsis. The diagnosis of gastric antral cancer was made by endoscopy. Histopathological examination of the biopsy material showed massive eosinophilic amorphous material located in the submucosa (Fig. B) and stained

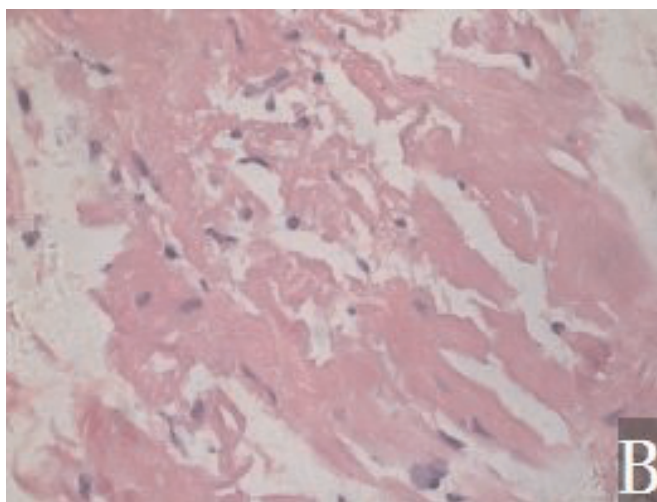


Fig. B: Histopathological examination of the biopsy material showed massive eosinophilic amorphous material located in the submucosa (HE \times 400).

characteristically positive with Congo-red, confirming amyloid deposition (Fig. C). The patient got nutritional

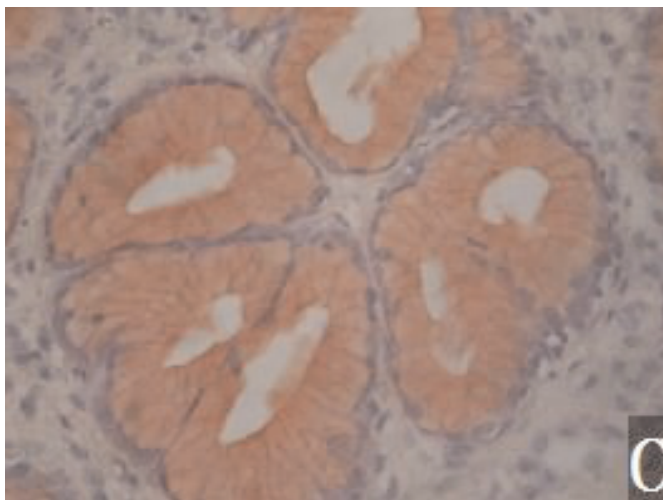


Fig. C: The amorphous material stained positively with Congo red. (Congo red staining \times 400).

support and antacid treatment. Gastroscopy was done a fortnight later and histopathological examination of the biopsy material showed amyloid deposition with chronic inflammation.

The diagnosis was then made of AL amyloidosis with skin and gastrointestinal involvement. The serum protein electrophoresis showed IgA, 0.16 g/L; IgM, 0.22 g/L and IgG, 4.76 g/L; κ light chain was 3.77 g/L, lambda light-chain was 7.68 g/L, the ratio was 0.49. β_2 -microglobulin:8604 mg/L; 24-hour urine protein was 306 mg/L. The patient had bone marrow aspiration which revealed marrow plasmacytosis (35% plasma cells) in accordance with multiple myeloma (Fig. D). We concluded that the patient suffered from multiple myeloma associated with AL amyloidosis.

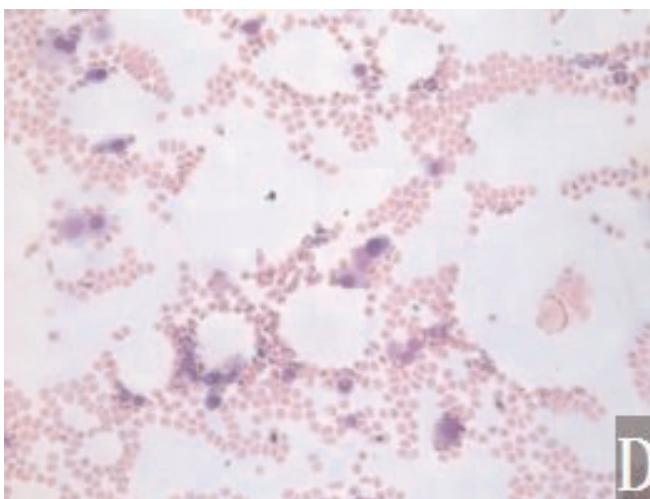


Fig. D: The sample of bone marrow aspiration revealed marrow plasmacytosis (35% plasma cells) [HE \times 400].

DISCUSSION

Multiple myeloma is a plasma cell dyscrasia characterized by monoclonal immunoglobulin production in the bone marrow. Most patients have bone pain, pathological fracture, hypercalcaemia, anaemia and renal insufficiency. Light-chain amyloidosis is a rare disease in which insoluble immunoglobulin light chain fragments are produced and polymerize into fibrils that deposit extracellularly, causing organ dysfunction and death. Twelve to fifteen per cent of myeloma patients have extracellular deposition of amyloid in tissues, resulting in amyloidosis. In these patients, symptoms frequently will manifest as nephrotic syndrome, congestive heart failure or restrictive cardiomyopathy, hepatomegaly, splenomegaly, carpal tunnel syndrome, macroglossia and waxy-looking papules (5).

Amyloid deposition in the gastrointestinal tract is also common but usually asymptomatic. Rarely is gastrointestinal amyloidosis the main symptom of multiple myeloma. The amyloid deposits in the gastrointestinal mucosa, muscles and blood vessels present as stasis syndrome: nausea, vomiting, dysphagia, gastroparesis, gastroesophageal reflux, loss of appetite, constipation, even chronic intestinal pseudo-obstruction because of gastrointestinal dysmotility, or recurrent gastrointestinal bleeding resulting from ulcers or erosions (6). When a lot of amyloid accumulations contribute to tumour-like amyloidoma, it is difficult to differentiate this from stomach cancer; mucosa biopsy with histology is the only way to differentiate. In the index patient, the diagnosis was difficult because symptoms were nonspecific whether for multiple myeloma or AL amyloidosis.

The presence of amyloidosis in multiple myeloma patients is usually associated with poor survival, and death usually occurs as a complication of amyloidosis affecting major organs, especially cardiac involvement (7). Some researchers revealed that the presence of amyloid deposits in patients with multiple myeloma is an independent adverse prognostic factor, and they suggest that the routine study of periumbilical fat-pad tissue should be mandatory in all patients with multiple myeloma (8).

The principles of treatment in systemic amyloidosis involves reducing amyloid formation by suppressing the synthesis of the fibril-precursor protein or promoting its clearance (9), coupled with appropriate supportive measures. Preservation or recovery of the function of amyloidotic organs is crucial. For localized amyloidosis, organ transplantation or resection is the best therapy (10, 11). High-dose melphalan chemotherapy and autologous peripheral blood stem cell transplantation (HDM/SCT) can prolong overall survival and get durable haematologic response in patients with multiple myeloma as well as those with AL amyloidosis who are eligible to receive it (12). However, due to amyloid-associated organ dysfunction, only selected patients may be eligible for HDM/SCT. In patients who are not eligible for peripheral blood stem cell transplant, melphalan plus dexamethasone can also produce long-term remissions in AL

amyloidosis (13). Other chemotherapeutic regimens such as CyBorD (cyclophosphamide, bortezomib and dexamethasone) or CTD (cyclophosphamide, thalidomide and dexamethasone) are also helpful (14, 15).

The index patient began to receive chemotherapy after the diagnosis of multiple myeloma. The chemotherapeutic regimen was cyclophosphamide 800 mg and vindesine 3 mg on the first day, plus pirarubicin (20 mg per day on days 1 to 2) and dexamethasone (20 mg per day on days 1 to 5). Unfortunately, because of chemotherapeutic toxicity, the patient suffered from serious gastrointestinal upset and myocardial injuries. On the third day of the chemotherapy, she had a cardiorespiratory arrest and developed grave metabolic acidosis. The hepatic and renal functions progressively declined. The patient died from multiple organ failure.

Although involvement of the gastrointestinal tract in primary amyloidosis is common, amyloid deposition on the stomach due to multiple myeloma is rare and indicates a poor prognosis. Due to the fact that endoscopic findings of gastrointestinal amyloidosis are identical to gastric cancer, gastrointestinal amyloidosis should be considered among the differential diagnosis of gastric cancer. When the diagnosis of amyloidosis is established, the second step, guided by clinical symptoms, is to identify the type of amyloidosis and to investigate other sites of amyloid deposition.

REFERENCES

1. Westermarck PE, Benson MD, Buxbaum JN, Cohen AS, Franjone B, Ikeda S et al. A primer of amyloid nomenclature. *Amyloid* 2007; **14**: 179–83.
2. Sunde M, Serpell LC, Bartlam M, Fraser PE, Pepys MB, Blake CCF. Common core structure of amyloid fibrils by synchrotron X-ray diffraction. *J Mol Biol* 1997; **273**: 729–39.
3. Gertz MA, Rajkumar SV. Primary systemic amyloidosis. *Current Treatment Options in Oncology* 2002; **3**: 261–71.
4. Bahlis NJ, Lazarus HM. Multiple myeloma-associated AL amyloidosis: is a distinctive therapeutic approach warranted? *Bone Marrow Transplant* 2006; **38**: 7–15.
5. Gertz MA, Comenzo R, Falk RH, Fermand JP, Hazenberg BP, Hawkins PN et al. Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): A consensus opinion from the 10th international symposium on amyloid and amyloidosis. *American Journal of Hematology* 2005; **79**: 319–28.
6. Petre S, Shah IA, Gilani N. Review article: gastrointestinal amyloidosis – clinical features, diagnosis and therapy. *Aliment Pharmacol Ther* 2008; **27**: 1006–16.
7. Madan S, Dispenzieri A, Lacy MQ, Buadi F, Hayman SR, Zeldenrust SR et al. Clinical features and treatment response of light chain (AL) amyloidosis diagnosed in patients with previous diagnosis of multiple myeloma. *Mayo Clin Proc* 2010; **85**: 232–8.
8. Vela-Ojeda J, García-Ruiz Esparza MA, Padilla-González Y, Sánchez-Cortés E, García-Chávez J, Montiel-Cervantes L et al. Multiple myeloma-associated amyloidosis is an independent high-risk prognostic factor. *Ann Hematol* 2009; **88**: 59–66.
9. Obici L, Perfetti V, Palladini G, Moratti R, Merlini G. Clinical aspects of systemic amyloid diseases. *Biochim Biophys Acta* 2005; **1753**: 11–22.
10. Monge M, Chauveau D, Cordonnier C, Noël LH, Presne C, Makdassi R et al. Localized amyloidosis of the genitourinary tract: Report of 5 new cases and review of the literature. *Medicine* 2011; **90**: 212–22.

11. Halwani O, Delgado DH. Cardiac amyloidosis: an approach to diagnosis and management. *Expert Rev Cardiovasc Ther* 2010; **8**: 1007–13.
12. Girnius S, Seldin M, Skinner M, Finn KT, Quillen K, Doros G et al. Short and long-term outcome of treatment with high-dose melphalan and stem cell transplantation for multiple myeloma-associated AL amyloidosis. *Ann Hematol* 2010; **89**: 579–84.
13. Palladini G, Russo P, Nuvolone M, Lavatelli F, Perfetti V, Obici L et al. Treatment with oral melphalan plus dexamethasone produces long-term remissions in AL amyloidosis. *Blood* 2007; **110**: 787–8.
14. Reeder CB, Reece DE, Kukreti V, Chen C, Trudel C, Hentz J et al. Cyclophosphamide, bortezomib and dexamethasone (CyBorD) induction for newly diagnosed multiple myeloma: High response rates in a phase II clinical trial. *Leukemia* 2009; **23**: 1337–41.
15. Dmoszynska A, Walter-Cronecka A, Hus I, Grzasko N, Manko J, Jedrzejczak WW et al. The efficacy and safety of the low-thalidomide dose CTD (cyclophosphamide, thalidomide, dexamethasone) regimen in patients with multiple myeloma—A report by the Polish Myeloma Study Group. *Leukemia Research* 2010; **34**: 1330–5.