

CASE REPORT

A case of protein-losing gastroenteropathy caused by systemic AA amyloidosis secondary to undifferentiated carcinoma of unknown primary origin

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Abstract

We report the case of a 61-year-old woman with Kartagener syndrome who presented with a 3-month history of chronic watery diarrhoea and severe hypoalbuminaemia. Histopathological examination of duodenum and large intestine biopsies showed amyloid A (AA) amyloid deposition. Scintigraphy and alpha-1 anti-trypsin clearance evaluations revealed protein-losing gastroenteropathy. Computed tomography with contrast and positron emission tomography showed a pelvic mass with multiple para-aortic lymph node enlargement. We suspected protein-losing gastroenteropathy secondary to AA amyloid produced related to malignant tumours. Following tumour resection, histopathological examination of the lesion revealed undifferentiated carcinoma of unknown origin. Postoperatively, the patient's nutritional condition improved. There has been no recurrence of protein-losing gastroenteropathy 6 months postoperatively. This is the first report of protein-losing gastroenteropathy and AA amyloidosis secondary to undifferentiated carcinoma. Early recognition and intervention could increase the likelihood of amyloidosis remission.

INTRODUCTION

Protein-losing gastroenteropathy is a rare disease characterised by excessive protein loss into the gastrointestinal tract (1),

leading to hypoproteinemia, and is complicated by oedema and malnutrition, which can become life-threatening (2). Amyloid fibril deposition in various organs due to chronic inflammation, known as AA amyloidosis, can cause protein-

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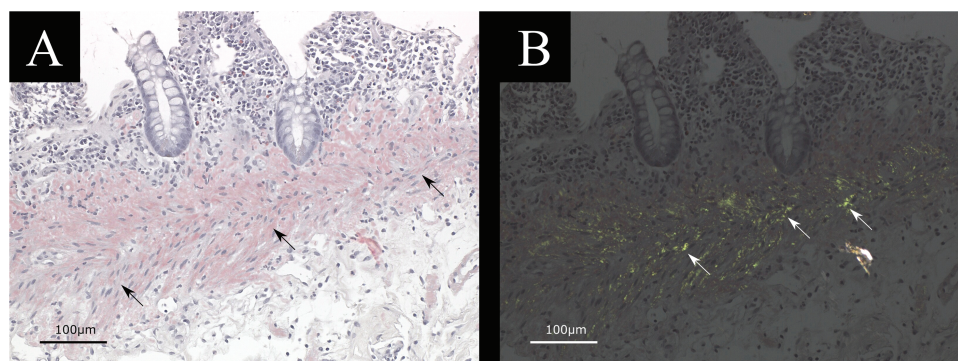


Figure 1: Staining with direct fast scarlet (A) and apple-green birefringence under polarised light (B) indicates amyloid deposit

losing gastroenteropathy (3). Several chronic inflammatory disorders cause protein-losing gastroenteropathy, including rheumatoid arthritis, inflammatory bowel disease and familial Mediterranean fever (1).

Undifferentiated carcinoma is an unusual type of cancer. To date, there has been no report of an association between undifferentiated carcinoma and protein-losing gastroenteropathy (4). Herein, we describe a case of protein-losing gastroenteropathy caused by AA amyloidosis secondary to undifferentiated carcinoma of unknown origin that resolved after tumour resection.

CASE REPORT

A 61-year-old woman with Kartagener syndrome attended our pulmonology clinic for a routine check-up with complaints of watery diarrhoea for 3 months and progressive bilateral lower leg swelling for 2 months. A month earlier, she had undergone gastrointestinal endoscopy without biopsy at a nearby clinic, but no abnormalities were detected. She did not take any medications and denied arthralgia, abdominal pain, rash and appetite loss. She had mild bronchiectasis due to Kartagener syndrome and had been evaluated annually for 3 years without symptoms.

On physical examination, she was alert and oriented. Her blood pressure was 105/66 mmHg, pulse rate 68 beats/minute, respiratory rate 16 breaths/minute, oxygen saturation 100% on room air and temperature 36.5°C. Abdominal examination revealed hyperactive bowel sounds and no pain on palpation. Laboratory findings showed severe inflammation and hypoproteinemia (white blood cell count, 6600/ μ L; neutrophils, 72.9%; C-reactive protein, 9.97 mg/dL; erythrocyte sedimentation rate, 60 mm/h; total protein, 5.7 g/ μ L; albumin, 1.5 g/ μ L). Her haemoglobin was 14.1 mg/ μ L. Urinalysis showed no proteinuria (including Bence Jones protein). Rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. The serum kappa/lambda free light chain ratio was 1.039 (normal). Serum and urine immunofixation electrophoresis showed no monoclonal band. A faecal sample showed occult blood and white blood cells. The *Clostridium difficile* toxin assay and stool culture were non-contributory. Echocardiography showed no abnormality.

Gastrointestinal endoscopy and colonoscopy were performed again to obtain diagnostic samples. Duodenum and large intestine biopsies showed remarkable amyloid deposition (Fig. 1), later confirmed as AA amyloidosis by immunohistological reactivity with anti-AA antibody. Bone marrow aspirate and biopsy did not show monoclonal plasmacytosis. Alpha-1 anti-

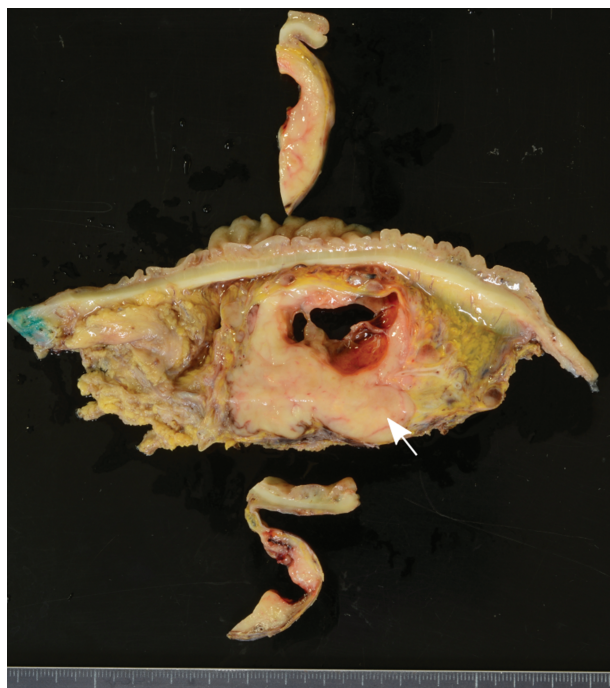


Figure 2: Laparoscopy revealed huge rectal mass in pelvis

trypsin clearance, which reflects the value of enteral protein loss, was 300 mL/day, and 99m Tc-diethylenetriaminepentaacetic acid human serum albumin scintigraphy showed protein leakage in the gastric body. Thus, we diagnosed protein-losing gastroenteropathy caused by AA amyloidosis. Repeat positron emission tomography and computed tomography (CT) with contrast showed a pelvic mass distant from the ovaries and intestines with a standardised uptake value of 22.9.

Upon hospitalisation, we initiated a low-fat, high-protein diet and administered supplemental parenteral nutrition including albumin through a central venous catheter. On hospital day 12, octreotide was started at 100 μ g/day to suppress her diarrhoea. We planned to improve her nutritional status and then perform elective surgery. Steroid therapy was suspended to avoid the risk of postoperative wound dehiscence. Despite multidisciplinary treatment, her hypoalbuminaemia worsened (albumin, 1.0 g/ μ L). Laparoscopic pelvic mass resection was then performed for diagnosis on hospital day 30. A huge rectal mesentery mass and all mesenteric lymph nodes were removed.

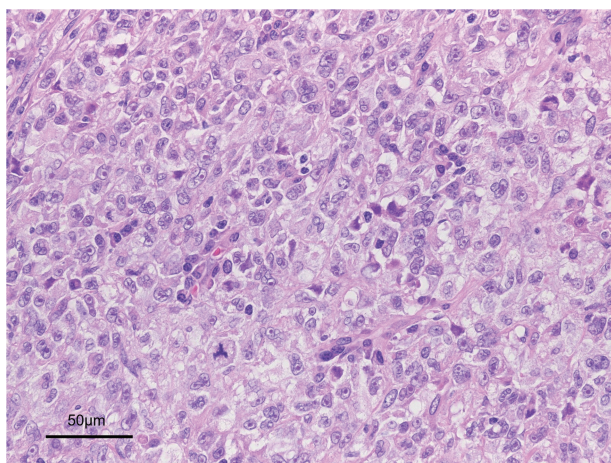


Figure 3: The pelvic tumours consist of anaplastic cells with large pleomorphic nuclei

The tumour was a well-demarcated mass measuring 60 × 50 mm (Fig. 2). Microscopically, the mass on mesentery comprised a solid sheet of anaplastic cells with prominent necrosis (Fig. 3). There was a compressed lymphoid structure at the periphery of the tumour, suggestive of lymph node metastases. On immunohistochemical analysis, the tumour was positive for pan-cytokeratin (AE1/AE3) and partially positive for hepatocyte paraffin 1 (Hep-Par1). However, it was negative for cytokeratin (CK) 7, CK20, calretinin, chromogranin A, synaptophysin, Melan-A, p40, S-100, cluster of differentiation (CD) 30, anaplastic lymphoma kinase and CD45. Considering the tumour location, morphological structure and immunohistochemical phenotype, we concluded that it was an undifferentiated carcinoma of unknown primary origin with multiple lymph node metastases.

After diagnosis, the follow-up plan was monthly observation with CT and PET-CT because all tumours were removed during surgery. Diarrhoea improved gradually. On hospital day 53, her albumin recovered to 2.5 g/μL; the central venous catheter was then removed. On hospital day 77, she was discharged home in good condition with monthly appointments. Her most recent CT and laboratory evaluations performed 6 months postoperatively showed no signs of carcinoma recurrence.

DISCUSSION

We present a rare case of protein-losing gastroenteropathy due to AA amyloidosis secondary to an undifferentiated pelvic carcinoma successfully treated by tumour resection. This case highlights two important clinical points.

Firstly, undifferentiated carcinoma can cause AA amyloidosis. Although Kartagener syndrome-related bronchiectasis with chronic inflammation could have caused her amyloidosis (5), abnormalities on her chest CT were subtle and unchanged during the 2-year follow-up that preceded the onset of diarrhoea. Further, her diarrhoea and hypoalbuminaemia improved dramatically after pelvic tumour resection. This disease response implies that the patient's amyloidosis was caused by the pelvic masses. To date, there have been case reports of AA amyloidosis caused by various cancers including hepatocellular adenoma and ovarian carcinoma (6, 7). However, this is the first case to show an association between amyloidosis and undifferentiated carcinoma.

Secondly, early investigation and intervention could lead to amyloidosis regression. Protein-losing gastroenteropathy should be included in the differential diagnosis of severe diarrhoea and hypoalbuminaemia. Tissue biopsy is crucial for amyloidosis diagnosis. Therefore, in cases of severe diarrhoea and hypoalbuminaemia, endoscopic examination with biopsy should be performed even if the physical examination reveals no abnormalities (8). Amyloidosis treatment comprises symptom management and treatment of underlying disorders (9). Herein, intractable diarrhoea did not respond to octreotide but resolved after tumour resection. Similarly, a previous case report indicated that intractable diarrhoea due to amyloidosis improved after resection of inflammatory hepatocellular adenoma (6). Early tumour resection could inhibit a chronic inflammatory state and provide definitive treatment for amyloidosis.

Thus, physicians must be aware that undifferentiated carcinoma is a cause of AA amyloidosis and protein-losing gastroenteropathy. Early investigation and intervention could help treat gastrointestinal amyloidosis.

FUNDING

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ETHICAL APPROVAL

Ethical approval is not required for a case report in Japan.

CONSENT

Written consent was obtained.

Conflict of interest statement. None declared.

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