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AL Amyloidosis Presenting Terminal Heart Failure with Stomach Amyloidosis

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Radiographic abnormality of the stomach was presented in term of amyloid deposition in a 72 year-old Japanese female. Coarse mucosal folds in the stomach, and delay in the gastro-intestinal emptying of the barium were often suggestive of amyloidosis. High-risk factor for survival of AL amyloidosis such as congestive heart failure, urine light chain, hepatomegaly and multiple myeloma were adversely affecting survival AL patients in the literature. All of these were presented in this case who died in 4 months after the onset of clinical manifestations.

Key Words
Coarse mucosal foldings in the stomach,
Cardiac failure,
AL amyloidosis,
Poor prognosis.

INTRODUCTION

Amyloidosis is a systemic disorder, and one of the most complex disorders in clinical medicine (1). Clinical manifestations of amyloidosis are variable, and they depend on the distribution and extent of involvement of certain tissues and organs. Although amyloid infiltrations must eventually be determined histologically, careful examinations of the patients physically or by X-ray films (2～4) may provide some informations suggestive of amyloidosis.

In the present paper, we present some roentogenographic features of the stomach in correlation with histological finding in amyloidotic patient. It is also important for physicians to review high-risk factors for AL patients in terms of survival rate in clinical medicine (5).

CASE REPORT

C. Sug. 72 y.o. Japanese female, visited the hospital on December, 1972, because of dyspnea for the last 2 months. Her family history showed her younger brother's death of pulmonary tuberculosis at his age 33 and another brother's death of stomach cancer at his age 47. Past history showed renal disease during pregnancy at the age of 41, and later suffered from hypertension. She was admitted to the hospital after 2 months of therapy at out-patient clinic. On admission on March 2, 1973, she was found to be in distress, with dry skin and cervical vein engorgement and pitting edema in bilateral legs. Dry rales were audible in both lungs. Liver was enlarged 5 cm below the right costal margin with sharp

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Figure 1. Plasma cell proliferation in the bone marrow. HE stain x 400.

edge. Laboratory data on admission included a peripheral blood picture of white cell count 12,000/μl with stab 56%, segmented 33%, and lymphocyte 11%, red blood cell 316 X $10^4/\mu$l, hemoglobin 11.4 g/dl, hematocrit 34.5%, erythrocyte sedimentation rate 112 mm/hour, a sternal bone marrow aspirate consisting of erythroid 3%, graulopoiesis 28%, lymphocyte 5%, and plasma cells 64% out of nucleated cells (Figure 1), a serum total protein 8.9 g/dl consisting of albumin 3.1, α1-globulin 0.3, α2-globulin 0.6, β-globulin 0.5 and γ-globulin of monoclonal spike 4.4 g/dl which was immunologically identified as IgG (k), urinary protein including Bence Jones protein of kappa type, blood urea nitrogen 42 mg/dl, serum creatinine 1.9 mg/dl, serum calcium 8.3 mg/dl,

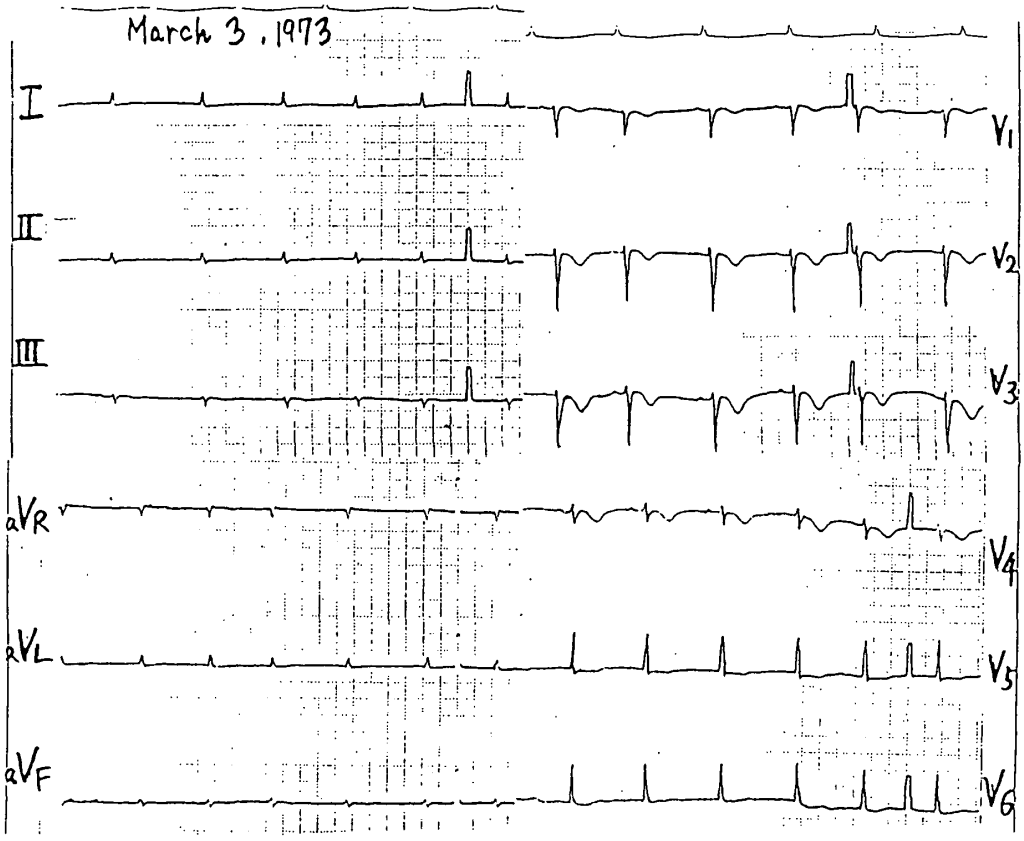
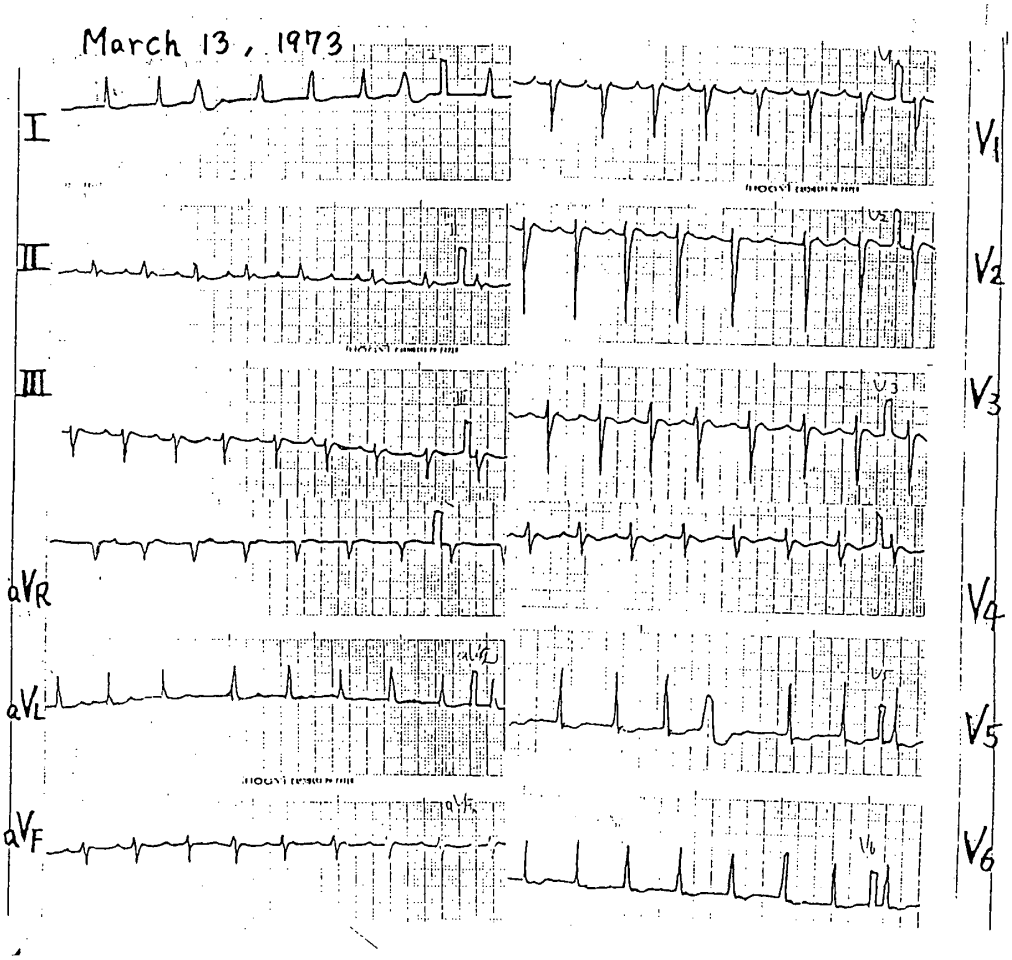


Figure 2. An electrocardiogram demonstrating low voltage in limb leads on admission on March, 3, 1973 (left). An ECG at the 11th hospital day, developing into a complete A-V block, transiently seen in limb leads from I to aVL, and, them recovering normal sinus rhythm from aVF to chest leads, with sporadic supra ventricular and ventricular premature contractious (right).

GOT 34 IU/l, GPT 12 IU/l, cholesterol 118 mg/dl, β-lipoprotein 290 mg/dl, triglyceride 100 mg/dl, fasting blood sugar 100 mg/dl, sodium 138 mEq/l, pottasium 3.9 mEq/l, and chloride 108 mEq/l. An electrocardiogram showed low voltage in limb leads, left axis deviation, ST depression in I and $V_{5,6}$, and inverted T waves in $V_{1\sim4}$, as shown in Figure 2. Chest X-ray showed a cardio-thoracic ratio of 62.0%. Bone X-ray survey realed osteoporisis with no evidence of osteolytic lesion. The fluoroscopic examination of this case disclosed some radiographic abnormalities. There were delay in gastric emptying, and noted presence of corse mucosal foldings. The stomach then appeared infiltrated in a manner similar to submucosal carcinoma, as shown in figure 2. As to therapy for cardiac insufficiency, a digitalization was started with digitalis C 0.4 mg intravenously 3 times within a days. Decreased in intensity of cervical venous engorgement and legs edema was seen only for the following 3 days. As she experienced oliguria on the 5th hospital day, she started to receive furosemide 40mg a day with some effects of urination. However, she had abdominal distension followed



by massive melena . An ECG at the 11th hospital day developed into transient complete A-V block (Figure 2). She died of cardiac arrest on 14th hospitalization day. Her clinical diagnosis was multiple myeloma and cardiac failure of unknown etiology. Her survival period of time after the onest of dyspnea was approximately 4 months.

Autopsy findings revealed systemic anyloidosis and myeloma. Amyloid was deposited diffusely in the antrum to pyrolus of the stmach. Histological evidence of amyloid infiltrations was shown in Figure 4, massively and diffusely in the submucosal and muscular layers of the stomach. Amyloid deposits were also found in the heart, lungs, rectum, liver (Fig. 5), spleen and kidneys. There were accessory findings including multiple ulcers in the rectum, myeloma kidneys, bronchopneumonia in both lungs, erosive atrophic gastritis, escophageal erosions, and infarction in the spleen.

DISCUSSION

This presentation gives us some clues to the diagnosis of systemic amyloidsis, knowing of the patients' terminal stage. On admission, the medical care had been needed to her cardiac insufficiency of unknown etiology. However, the patient had several findings suggestive of AL amyloidosis as follows: (a) serum IgG(k)-monoclonal immunoglobulin, (b) urinary Bence Jones protein, (c) plasma cell proliferations of 64% out of nucleated cells in the bone marrow, (d) low voltage in the limb leads in ECG, and (e) some unusual findings of fluoroscopic examination on the stomach. In case of usual hospitalization without emergent situation as this case, it is conceivable for physicians to reach a clinical diagnosis of AL amyloidosis and cardiac involvement.

As to cardiac failure which was considered to be the major cause of her death at the terminal stage, there is a significant observation by Kyle and his assocate (5). One hundred sixty-eight patients with primary systemic amyloidosis (AL) were identified. Median survival after diagnosis were 12 months and ranged from 4 months for patients presenting with congestive heart failure to 50 months for those presenting with peripheral neuropathy only. These were other groups including patients associated with orthostatic hypotension (12 months), nephrotic syndrome (16 months) and carpal tunnel syndrome (23 months). Utilizing the proportional-hazards model in a step-wise multivariate fashion to evaluate the simultaneous influence of putative risk factors as of diagnosis revealed that congestive heart failure, urine light chain, hepatomegaly, and multiple myeloma were the major factors adversely affecting survival during the first year after diagnosis. Serum creatinine, multiple myeloma, orthostatic hypotension, and monoclonal serum protein were the most important variables adversely affecting survival for patients surviving 1 year. These model proposed by Kyle et al (5) were categorize patients according to the variates in the models into low-, moderate-, and high-risk groups for the first year after diagnosis and separately for subsequent years. Knowing these risk factors, the present

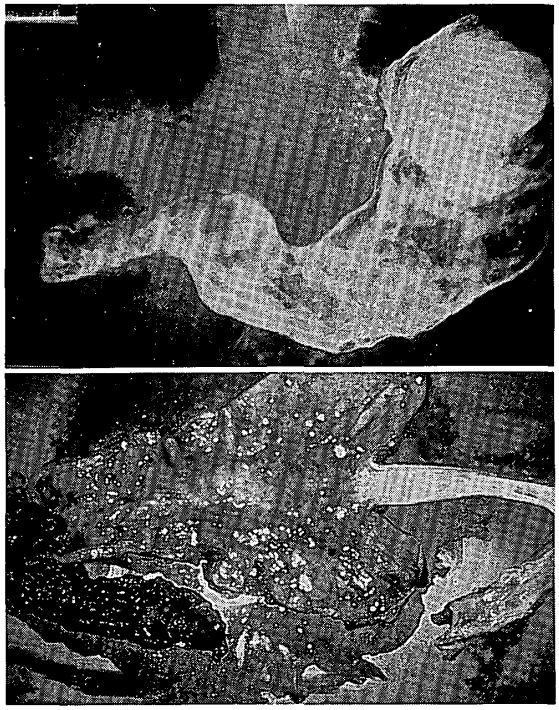


Figure 3. Coarse mucosal folds in the stomach. (Upper, Fluoroscopy and lower at autopsy).

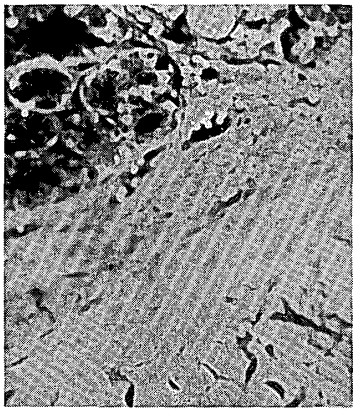


Figure 4. Diffuse amyloid infiltrations in the muscularis mucosa of the stomach. Congo-red stain, through fluorescence microscope. Original magnificantion x200.

case was just categorized into high-risk group. These variates on survival is important in stratification of the patient to prospective clinical medicine, although the present case was unfortunately failed to recover from distress situation.

These are growing accumulations of many radiographic features of amyloidosis, which contribute to the diagnosis. Amyloid is often found in the gastro-intestinal tract. The most frequent site of involment is the vasculature of the submucosa. The vessel walls are thickened and the lumen gradually reduced. Amyloid is also deposited within the muscularis mucosa. These changes may result atrophy, ulceration, infraction and even perforation (3), marked hemorrhage and malabsorption due to involved myoenteric neural plexus (3). The radiographic manifestations of histologically proven gastric amyloid are quite variable. Gastric emptying of the barium may delay, for up to 30 hours and suggest pyloric obstruction (3). The usual rugal folds are occasionally flattened, or stiffened. The irregularity of the gastric antrum can be mistaken for infiltrating scirrhous carcinoma or severe gastritis (2). A difference between AL and AA as to amyloid deposition (4) was demons-

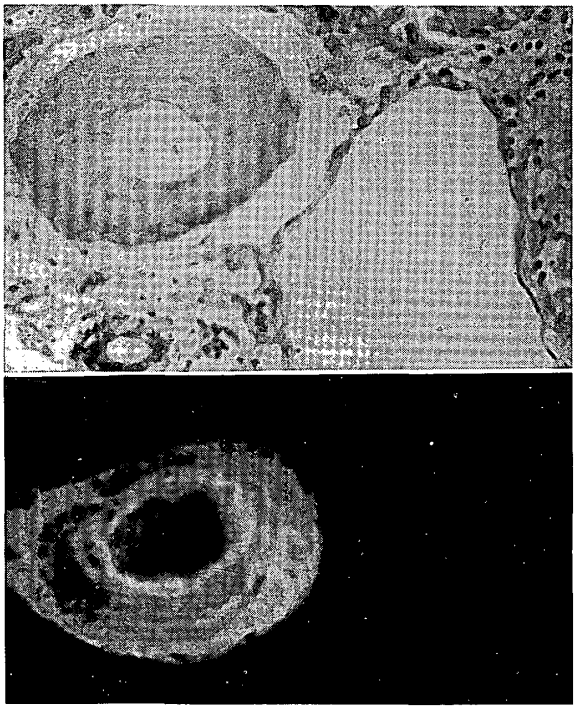


Figure 5. Perivascular amyloid deposits with HE stain x 400 (upper) and under polarization microscope x 400 (lower).

trated that parenchymal deposition was observed mainly in the muscularis mucosae and muscularis externa in the AL type, and lamina propria mucosae in the AA type. In AL, deposition in the lamina propria and musculàris mucosae was more frequent and marked in the stomach than in the rectum. Thus, gastric biopsy would be more valuable than rectal biopsy in the diagnosis of AL amyloid (4).

As discussed above, radiographic abnormalities followed by biopsy may contirbute to the suggestion and recognition of the presence of amyloid deposits in the clinical medicine. As to risk-factors for survival of patients with AL amyloidosis, the present case was found to have congestive heart failure, urinary light chain, hepatomegaly and multiple myeloma. All these four risk factor were recognized to be high-risk in the literature, resulting in the poor prognosis of this case.

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