AA-Amyloidosis Presenting with Chronic Diarrhea and Cardiac Manifestations

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SUMMARY

In secondary amyloidosis (AA type), clinically significant cardiac and gastrointestinal involvement are uncommon, in contrast to the primary type. We report a case presenting with chronic diarrhea and cardiac manifestations who was diagnosed as having AA-amyloidosis with unknown predisposing illness based on endomyocardial, rectal and subcutaneous fat tissue biopsies. (Jpn Heart J 35: 695–699, 1994)

Key words: AA-amyloidosis Restrictive cardiomyopathy Diarrhea Endomyocardial biopsy

AMYLOID heart disease gives rise to a wide spectrum of disorders ranging from cardiac amyloidosis, in which the heart is severely affected but other systems relatively spared, to so-called senile cardiac amyloidosis in which clinical features are usually absent but amyloid deposits are found at postmortem study. In other cases, the heart is involved in a multisystemic disorder.1,2,3)

Chronic diarrhea together with restrictive cardiomyopathy are not infrequent in the primary amyloidosis and these can alert one to the diagnosis of amyloidosis. Both findings are very rare in the secondary type.4,5) We present a case with AA-amyloidosis presenting as chronic diarrhea and restrictive cardiomyopathy confirmed by biopsy.

CASE REPORT

A 75-year-old woman was admitted to our hospital with complaints of diarrhea and abdominal pain of 1.5 years duration. She was healthy until 1.5 years ago when she started to pass 25–30 watery stools per day. She described no blood, bad odor or any other abnormality in the feces. She had no appetite and
lost 24 kg of weight in this period. There was no history of fever, nausea or vomiting. She had consulted a doctor when the diarrhea began. Her laboratory tests at that time were reported as normal and she was prescribed an antidiarrheal medication. She felt no better though she consulted the same doctor almost weekly thereafter with no improvement in her condition.

Her own and family history revealed no neuropathic chronic inflammatory disease, amyloidosis, rheumatic or infectious disease.

On physical examination at the time of admission she was a cachectic woman looking dehydrated and lethargic. Her temperature was 37°C, systemic blood pressure 120/60 mmHg and pulse 84/min. The neck veins were distended 11 cm above the heart; there were prominent V waves with a rapid Y descent. Her lung and heart sounds were normal. The liver was enlarged 4 cm below the right midcostal margin with a total height of 15 cm.

Laboratory tests revealed a 39% hematocrit, 11,400/mm leucocytes with a normal differential count and an erythrocyte sedimentation rate of 75 mm/hr. Renal and hepatic function tests were within normal ranges. Total protein was 5.9 gr/dl with albumin 2.8 gr/dl. Her stool test revealed (+) occult blood, no parasites, (+) triptic activity, (+) lipid with pH 6.0, no leucocytes on direct examination and no microorganisms detected in cultures. Urinalysis yielded leucocytes and urine culture yielded 200,000 E.coli. Myobacterium was not detected in urine cultures. There was proteinuria of 2 g/day. Serum protein and immunoelectrophoresis were normal. Bence Jones protein in 24 hour urine collection was absent and bone marrow was normal. No free light chains were detected in either the serum or urine.

An X-ray revealed fibrotic changes in the lung fields with blunted costophrenic sinuses; the cardiothoracic index was normal. Negative T waves, weak R progression in leads V₄, V₅, V₆ and low voltage were noted on the electrocardiogram. Corrected QT interval was 471 m sec. Gastrointestinal X-rays and endoscopies (panendoscopy, colonoscopy) were also normal. Rectoscopy revealed internal hemorrhoids. Abdominal ultrasonography revealed congestive hepatomegaly, but renal abnormalities were not reported. On echocardiographic examination, mild pericardial effusion, biatrial dilatation, normal-sized left ventricle, biventricular hypertrophy (interventricular septum thickness/left ventricular posterior wall thickness: 2, 1), mild mitral insufficiency and normal systolic, but abnormal diastolic left ventricular functions were detected (Figure 1). The left ventricular diastolic filling pattern showed a shortened deceleration time and increased E/A ratio on the Doppler echocardiographic study (restrictive pattern).

On right cardiac catheterization, the right ventricular pressure curve showed the characteristic dip-plateau of a restrictive cardiomyopathy (Table).

Left cardiac catheterization and coronary angiogram were not performed.
Figure 1. M-mode and 2-D echocardiograph of the case

### Table. Pressures (mmHg) during Right Cardiac Catheterization

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<thead>
<tr>
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<th>(a/v/m)</th>
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<tbody>
<tr>
<td>Pulmonary artery wedge</td>
<td>14/16/12</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>28/12/19</td>
<td></td>
</tr>
<tr>
<td>Right ventricle</td>
<td>31/12</td>
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<tr>
<td>Right atrium</td>
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Figure 2. Hematoxylin eosin (× 375). Homogenous eosinophilic material deposition in the walls of vessel and interstitium can be seen.
An endomyocardial biopsy specimen from the apex of the right ventricle via the femoral vein approach was obtained without difficulty. The biopsy specimen showed perivascular eosinophilic deposition in the interstitium. The alkaline Congo red stain and crystal violet stain were positive for amyloid in these depositions (Figure 2). Bleaching reaction was positive. Electron microscopy showed a fibrillar electron dense deposition in the walls or vessels and in the interstitium. Myocardial fibrils were normal (Figure 3).

Abdominal fat aspiration and rectal biopsy confirmed the diagnosis of secondary systemic amyloidosis.

**DISCUSSION**

Cardiac involvement is well known to occur in several types of amyloidosis. It has been reported that at autopsy, senile cardiac amyloidosis is present in 30–69 percent of patients older than 60 years, and affects only the heart.\(^6,7\)

Cardiac amyloid deposition is known to be present in 80–90 percent of primary and myeloma associated amyloidosis and 60 percent of secondary amyloidosis cases. Familial amyloidosis with neuropathy or nephropathy is only occasionally associated with overt cardiac involvement and then usually only late in the course of the disease. Cardiac amyloid infiltration is said to be predominantly in the interstitium in senile cardiac amyloidosis whereas it involves the intramyocardial vessels in other types of the disease.\(^3,6\)

Our patient with a 1.5 year history of chronic diarrhea was suspected at admission of having a gastrointestinal disease involving especially the ileum. Amyloidosis was not suspected because there was no positive history or predisposing illness. Abnormal clinical, ECG and echocardiographic findings strongly...
suggested cardiac amyloidosis. The question of primary amyloidosis was initially considered before we learned the results of the rectal and endomyocardial biopsies which revealed secondary systemic amyloidosis. Some cases of senile cardiac amyloidosis are asymptomatic while some may present with severe heart failure or fatal arrhythmias, but the disease affects only the heart. In our case, upper and lower gastrointestinal endoscopic and radiologic evaluations and biochemical and microbiological examinations of stool were negative. Therefore we believe that the diarrhea in our case was due to gastrointestinal amyloidosis proven by biopsy. Renal function tests were normal except for proteinuria. Urinary mycobacterial and fungal cultures were also negative. No renal abnormalities were reported on ultrasonographic examination. Although we did not perform a renal biopsy, we suggest that the proteinuria in our case was another manifestation of amyloidosis rather than chronic inflammatory renal disease. The renal, gastrointestinal and cardiac involvement suggests that our case had AA-amyloidosis with an unknown predisposing illness. Because there was no disease predisposing for secondary systemic amyloidosis in our case, we were unsure of the type of amyloidosis. However, the correlation between the nature of involvement and the type of amyloidosis is still unclear.

As a result, chronic diarrhea together with restrictive cardiomyopathy should alert one to the diagnosis of primary amyloidosis, but it should not be forgotten that both findings can be seen infrequently in secondary systemic amyloidosis.

REFERENCES