

CASE REPORTS

Systemic amyloidosis as a cause of cerebral thrombo-embolic stroke: A case report

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ABSTRACT

Systemic amyloidosis is a rare clinical disorder and can lead to single organ or fatal multiple organ failure, heart and kidneys are the most affected organs. Currently, there are no relevant guidelines and recommendations about the treatment of systemic amyloidosis. Ischemic stroke is an uncommon complication of systemic amyloidosis and patients with systemic amyloidosis may carry a worse prognosis. We report a case of cerebral thrombo-embolism in a 40-year-old woman due to indicated systemic amyloidosis, she received intravenous rt-PA thrombolytic therapy in hyperacute phase of ischemic stroke and this case proved that intravenous rt-PA thrombolysis therapy may be an effective treatment for acute cerebral thrombo-embolic stroke patients with systemic amyloidosis.

Key Words: Ischemic stroke, Cardioembolism, Systemic amyloidosis

1. INTRODUCTION

Cardioembolism accounts for about 20% of ischemic stroke,^[1] the most common cause is atrial fibrillation,^[2] in addition, acute myocardial infarction, infective endocarditis, heart valve disease, atrial myxoma, congenital heart disease, cardiomyopathy can also cause cardioembolism. To date, patients with systemic amyloidosis and ischemic stroke have been sporadically reported, now we describe a case of cerebral thrombo-embolism in a 40-year-old woman due to systemic amyloidosis.

2. CASE PRESENTATION

A 40-year-old woman patient was admitted to our stroke unit due to a sudden attack of right-sided weakness and incapable of speech. She had a right limb dysfunction, stood instability and could not speech without definite causes in general activity 2 hours before admission all of a sudden.

The patient had a history of systemic amyloidosis 4 months ago, she was hospitalized at cardiac department in our hospital due to repeatedly bosom frowsty asthma, double lower limbs swelling and other symptoms of heart failure. The cardiac echocardiography demonstrated a thickening wall of the left ventricular (LV) and left ventricular diastolic dysfunction (see Figure 1), the further cardiac magnetic resonance imaging (CMRI) showed a characteristic pattern of subendocardial late gadolinium enhancement (see Figure 2) and abdominal tissue biopsy was performed to further define the diagnosis, it revealed collagen fibre hyperplasia and there were characteristic amyloid deposits that stained with Congo red, and crystal violet staining was negative (see Figure 3).

The vital signs on admission of the patient were as follows: body temperature: 36.8°C, pulse rate: 82 beats/min, breathing: 20 times per minute and blood pressure was 105/67

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mmHg in the right arm. The positive neurological signs were as follows: somnolence, motor and sensory aphasia, pupillary reaction to light were sluggish, the movement of eyes to the right direction were limited, central facial paralysis, right-sided paralysis (0/5) and positive babinski sign. The NIHSS score was 18.

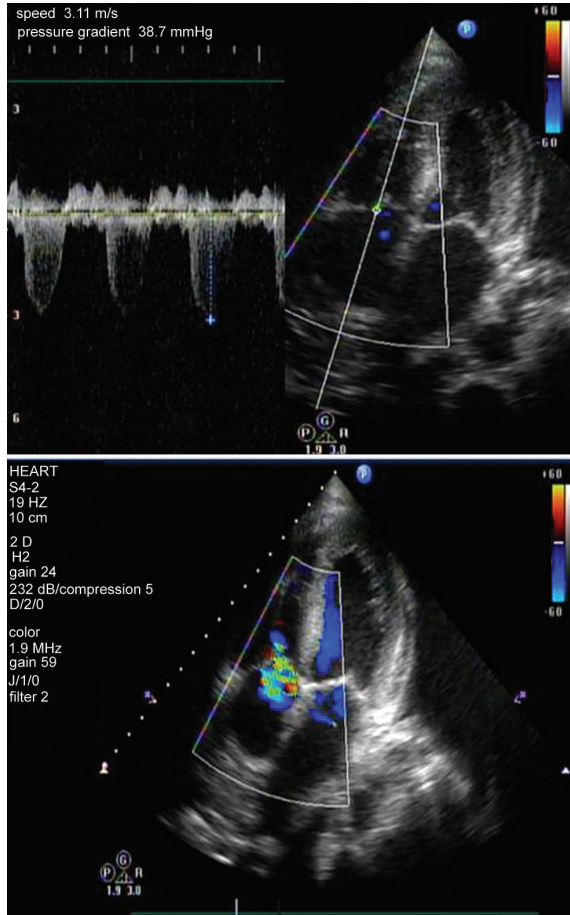


Figure 1. Cardiac echocardiography demonstrated a thickening wall of the left ventricular (LV) and left ventricular diastolic dysfunction

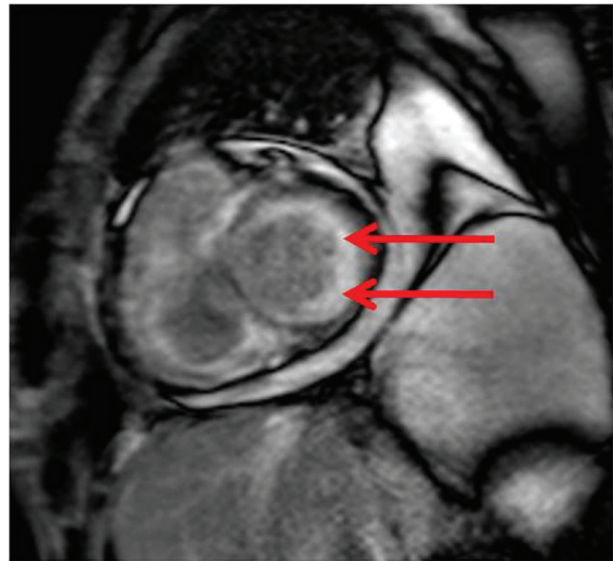


Figure 2. Cardiac MRI showed a characteristic pattern of subendocardial late gadolinium enhancement (arrow)

The patient's onset time was 20:00, an urgent computed tomography (CT) scan of the brain in the local hospital did not demonstrate any abnormalities, the blood routine, renal and coagulation functions were normal. Then she was transferred to our stroke unit at 22:00 for intravenous rt-PA thrombolytic therapy. The patient was in hyperacute phase of cerebral infarction without any contraindications, considering that this patient had basic diseases such as systemic amyloidosis and heart failure, the bleeding risk of thrombolysis was high, so low doses of rt-PA (0.6 mg/kg, total amount of 36 mg) was given for intravenous thrombolytic therapy after obtaining informed consent. The door to needle time (DNT) was 25 minutes and 1 hour after intravenous thrombolysis, the NIHSS score was 16.

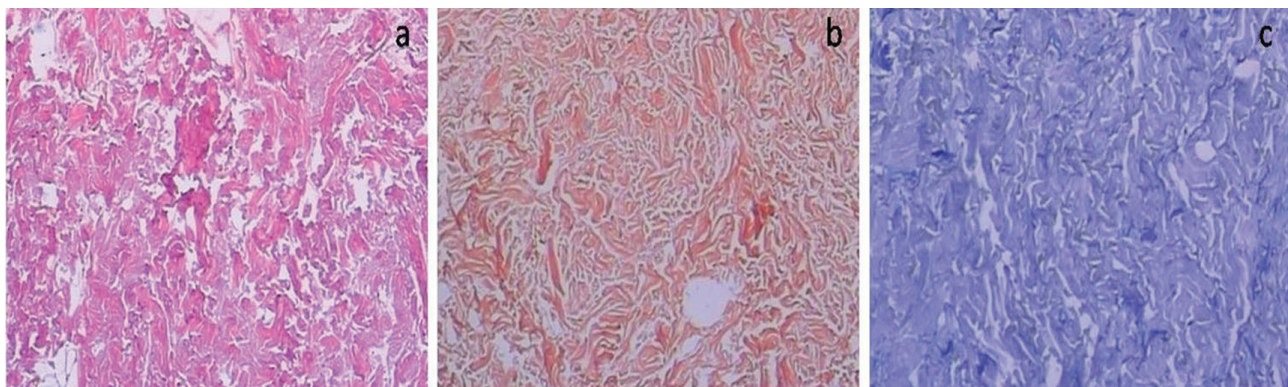


Figure 3. Abdominal tissue biopsy revealed collagen fibre hyperplasia (a) and there were characteristic amyloid deposits that stain with Congo red (b), and crystal violet staining was negative (c)

The further laboratory tests showed that the triglyceride (TG) level was 0.91 mmol/L, the total cholesterol (TC) level was 4.95 mmol/L, the high density lipoprotein cholesterol (HDL-C) level was 0.67 mmol/L and the low density lipoprotein cholesterol (LDL-C) level was 3.06 mmol/L. Other laboratory tests about liver function, electrolytes, homocysteine (HCY), fasting blood-glucose (FBG), c-reactive protein (CRP), cardiac enzymes were all normal except that the amino-terminal pro-brain natriuretic peptide (NT-proBNP) level was 2,893 pg/ml. There was no sign of hemorrhage on CT image at 24 hours after intravenous rt-PA thrombolytic therapy. The carotid artery ultrasonography was normal and there were no atherosclerotic plaques and stenoses of carotid arteries (see Figure 4). The further Magnetic Resonance Imaging and Angiography (MRI/MRA) scan revealed a new infarction lesion located in the left middle cerebral artery (MCA) distribution and the occlusion of the left middle cerebral artery was shown (see Figure 5). The dual antiplatelet agents (aspirin 100 mg and clopidogrel 75 mg daily) and

intensive statin therapy were given to this young patient. During hospitalization, diuretics were given to relieve the symptoms of congestive heart failure.

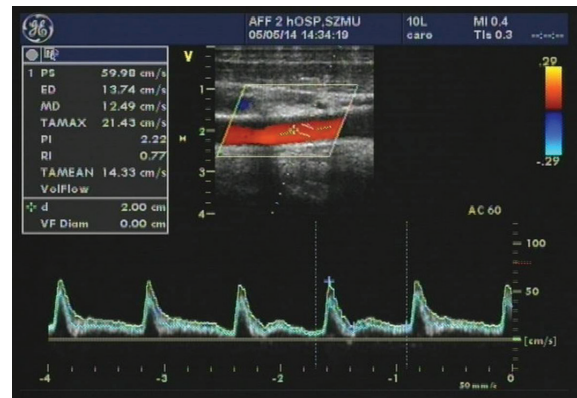


Figure 4. The carotid artery ultrasonography was normal and there were no atherosclerotic plaques and stenoses of carotid arteries

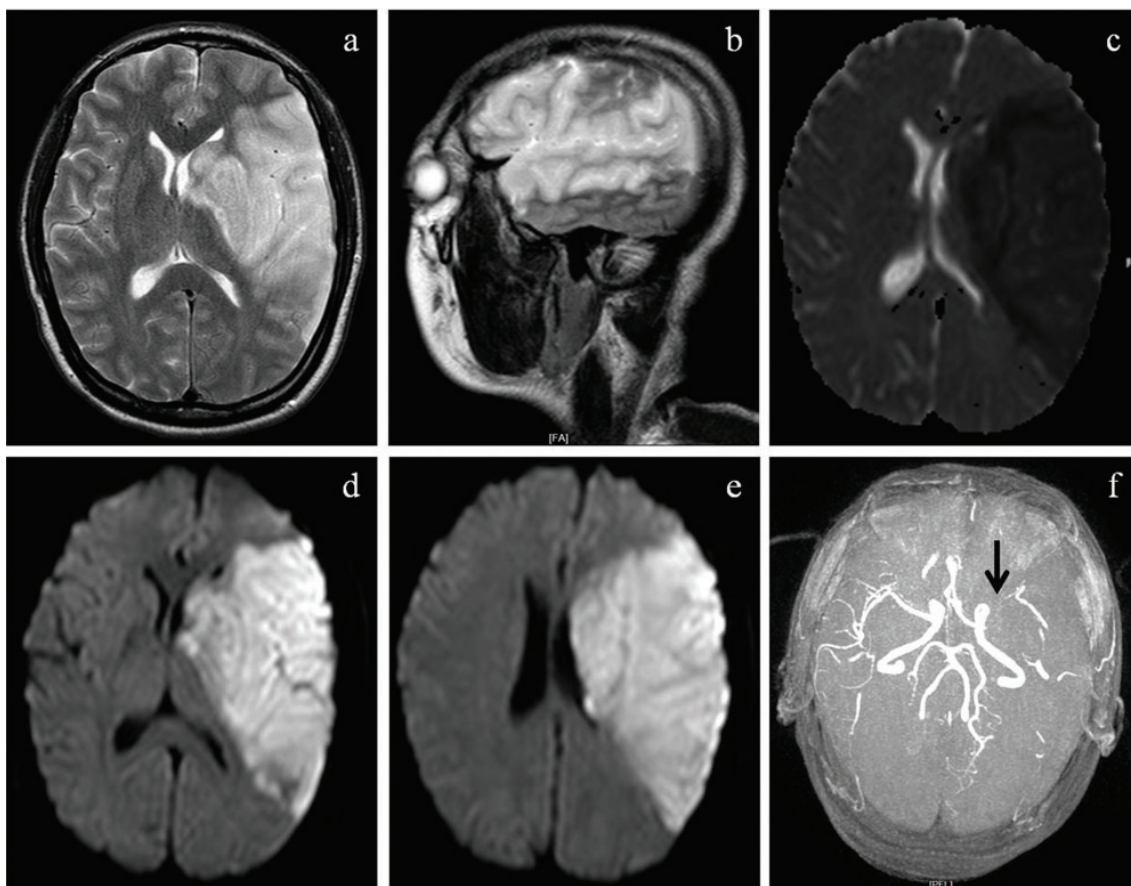


Figure 5. The Magnetic Resonance Imaging and Angiography (MRI/MRA) scan revealed a new infarction lesion located in the left middle cerebral artery (MCA) distribution, and the occlusion of the left middle cerebral artery was shown

After receiving treatment for 10 days during hospitalization, the patient's clinical symptom was improved and the NIHSS score was 13. Unfortunately, she died 5 months later after discharge from the hospital due to repeated heart failure.

3. DISCUSSION

Systemic amyloidosis is a rare clinical disease caused by extracellular tissue infiltration of misfolded, insoluble aggregated protein, which exhibits apple-green birefringence under polarized light when stained with Congo red dye.^[3] Deposition of amyloid can be localized or systemic. The systemic amyloidoses are generally classified into light chain or primary systemic amyloidosis (AL), hereditary (familial) amyloidosis, senile amyloidosis (wild-type ATTR), secondary amyloidosis (AA) and isolated atrial amyloidosis. The two most common types of systemic amyloidosis are AL and AA. Hereditary amyloidosis is an autosomal dominant disease caused by genetic mutations of some plasma proteins and has been more and more reported recently.^[4] The phenotypic features of hereditary amyloidosis may overlapped with those of AL and AA.

In all of the systemic amyloidoses, insoluble extracellular protein fibrils in β pleated sheets are deposited in tissues and, if unchecked, can lead to single organ or fatal multiple organ failure. Organ involvement can include heart, kidneys, liver, skin, blood vessels, central and peripheral nervous systems, lungs, intestines and eyes. Cardiac amyloidosis is a serious and progressive process and the most common clinical presentation is congestive heart failure because of restrictive cardiomyopathy and conduction abnormalities.^[5]

Electrocardiography (ECG), echocardiography, CMRI, radionuclide imaging and tissue biopsy have been used to the diagnosis of cardiac amyloidosis.

Almost all of the cardiac amyloidosis patients have ECG abnormalities, but the specificity is not high. A study performed at the Mayo Clinic^[6] confirmed that the two most common abnormalities were Low ECG voltage (presence of QRS voltage amplitudes ≥ 1 mV in all precordial leads or ≤ 0.5 mV in all limb leads) and a pseudoinfarction pattern (QS waves in consecutive leads), which were seen in roughly 50% of the patients included. Other ECG changes include cardiac arrhythmia and conduction delay, atrial fibrillation is the most common arrhythmia.^[7] The most common echocardiographic feature of cardiac amyloidosis is the thickened LV wall in the absence of hypertension^[8,9] and the most typical echocardiographic feature is the "granular sparkling" echogenicity of myocardium. One study demonstrated that the coincident findings of low voltage on electrocardiography and interventricular septal thickness of at least 19.8

mm on echocardiography are 72% sensitive and 91% specific for cardiac amyloidosis.^[10] In addition, CMRI showed a characteristic pattern of subendocardial late gadolinium enhancement coupled with abnormal myocardial and blood-pool gadolinium kinetics in cardiac amyloidosis.^[11] Biopsy is the gold standard for the diagnosis of cardiac amyloidosis. Congo red staining can identify amorphous pink deposits at light microscopy, which exhibit apple-green birefringence under the polarized microscopy.

In a necropsy series published, Roberts and Waller reported that 26% of patients with cardiac amyloidosis had one or more cardiac chambers thrombi.^[12] Cardioembolism might be related to haemodynamic stasis in the cardiac chambers, caused by atrial fibrillation or severe congestive heart failure. The haemodynamic stasis are prone to thrombus formation, with resultant embolic sequelae. So, haemodynamic stasis seems to play a leading role in the pathophysiology of cardioembolism.

In a retrospective study, 49 patients with confirmed AL and ischemic stroke were included in the study, ischemic stroke occurred in 13 patients (32.5%) as the initial presentation of AL.^[13] Systemic amyloidosis alone has a poor outcome and a superimposed cerebral embolism event is associated with a worse prognosis.

This patient was young and had no hypertension, diabetes mellitus, hyperlipidemia, smoking and other risk factors of atherosclerosis and the carotid artery ultrasonography was normal. The main clinical features of the patient included acute onset and the symptoms reached to peak after onset rapidly. Combined with abdominal tissue biopsy of this patient, the diagnosis of cardioembolism caused by systemic amyloidosis was certain.

The management of any forms of cardiac amyloidosis generally follows a two-fold strategy: reducing the amyloid fibrils formation and supportive treatment of cardiac related symptoms. The cornerstone of systemic treatment include high-dose melphalan with dexamethasone or high-dose melphalan with autologous stem cell transplantation (SCT).^[14] The treatment of heart failure contain diuresis, salt restriction, and maintaining hemodynamic stabilization. Loop diuretics, given at high dosage in patients with severe fluid retention, are the mainstay of treatment. Anticoagulation therapy is necessary in patients with atrial fibrillation and cordis mural thrombus. Pacemaker implantation may be indicated in patients who develop symptoms of bradycardia or conduction disorders.^[15]

For ischemic stroke patients with systemic amyloidosis, there is no specific treatment, the treatment is the same with other

cardioembolism patients. In our case, the patient underwent intravenous rt-PA thrombolysis therapy, dual antiplatelet and intensive statin therapy were given during hospitalization. After treatment, the clinical symptom relieved. It proves that rt-PA thrombolysis therapy is safe and effective for acute cardioembolism patients with systemic amyloidosis within the intravenous thrombolysis time window.

In summary, we describe an unusual cause of thromboembolic stroke, patients with systemic amyloidosis usually

have a worse prognosis, so when a patient is diagnosed with systemic amyloidosis, further genetic investigations to be performed if possible in order to avoid misdiagnosis and inappropriate treatment. It is necessary to maintain a high degree of clinical suspicion which may leave more options of effective treatment and may improve outcome.

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