Acute ischemic stroke patient with cardiac involvement of light chain amyloidosis

Esra Demir¹, Hesna Bektas¹, Oguzhan Kursun²

¹Department of Neurology, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Turkey
²Clinic of Neurology, Ankara City Hospital, Ankara, Turkey

Copyright © 2020 by authors and Annals of Medical Research Publishing Inc.

Abstract
Light chain amyloidosis is one of the clonal plasma cell disorders characterized by the accumulation of misfolded light chain in tissues and organs. It may affect many organs and tissues like kidney, heart, nervous system, intestinal systems. Symptoms may mimic several diseases. The natural history of the disease, involvement of other organs and treatment options vary significantly based on the origin of the protein. In amyloid light-chain (AL) amyloidosis, amyloid protein is derived from immunoglobulin light chains and most often involves the kidneys and the heart. Cardiac amyloidosis is important in terms of causing intracardiac thrombus and increases the risk of thromboembolic complications as stroke. We discussed a 55-year-old patient with known cardiac involvement of systemic amyloidosis who presented to an emergency department with loss of consciousness and progressive left-sided weakness and had the diagnosis of acute ischemic stroke.

Keywords: Acute ischemic stroke; cardiac amyloidosis; light chain amyloidosis

INTRODUCTION
The cerebrovascular system is the most affected area of systemic diseases such as hypertension, diabetes, hyperlipidemia and heart diseases. Less common causes of cerebrovascular diseases include arterial dissections, fibromuscular dysplasia, Moyamoya disease, paraneoplastic strokes, amyloidosis and paraproteinemias (1). Amyloidosis can accumulate in many different organs and tissues and has a poor prognosis. Although stroke is an infrequent case in amyloidosis, it occurs in the highest prevalence in patients especially, with cardiac involvement (2). In this case report, we present an acute ischemic stroke patient due to the cardiac involvement of systemic amyloidosis.

CASE REPORT
A 55-year-old female patient was admitted to the emergency department with a sudden loss of consciousness and progressive weakness on the left side at home. On her examination, consciousness was drowsy and had a partial cooperation with verbal stimuli. In her neurological examination, sensorimotor aphasia left homonymous hemianopia, forced gaze deviation to the right side, hemiplegia on the left upper and lower extremities were detected. The patient was admitted to the emergency department in three-and-a-half hours window and her NIHSS (National Institutes Of Health Stroke Scale Scores) score was 16. Brain computed tomography (CT) and CT angiography were reported as ‘ Bilateral anterior cerebral artery (ACA) and left middle cerebral artery (MCA) were patent with extracranial and intracranial sections of the left external and internal carotid arteries (ICA) and weak opacity compared to symmetry in the traceable extracranial and intracranial segments of the right internal carotid artery was seen. ICA and right MCA M1 (sphenoidal or horizontal segment) occlusion was seen in the segment (Figure 1). The patient underwent mechanical thrombectomy because of the right MCA occlusion. There were no significant differences in the neurological examination of the patient after procedure who had full recanalization in the right MCA M1 segment, and the control brain BT was taken after 24 hours from the procedure. Hemorrhagic transformation of the infarcted area was seen (Figure 2). The patient was followed up in the neurology intensive care unit.

She had a history of cardiovascular system diseases like hypertension, heart failure, and newly diagnosed cardiac amyloidosis. Transthoracic echocardiography was
performed to the patient in the name of her cardiological complaints and was evaluated as hypertrophy and hypokinesia in the left ventricle and myocardium, systolic function depression, interatrial and interventricular septum thickening were detected. Her transthoracic echocardiography was significant in terms of cardiac amyloidosis. Due to this condition, a renal biopsy was performed on the patient for renal involvement of amyloidosis and found histopathologically significant for monoclonal immunoglobulin storage deficiency findings. Biopsy material reported to be compatible with monotypic mild chain deposition disease. Bone marrow aspiration biopsy was performed in terms of hematological involvement and resulted as hypercellular bone marrow consistent with interstitial lambda monotypic plasma cells which are dominated by the granulocytic series. Rectal biopsy and adipose tissue biopsy were performed and resulted negatively. In her abdominal ultrasonography, there was no pathological finding other than mild effusion in the right pleural area. The colonoscopy report was compatible with internal hemorrhoids and nonspecific colitis. In blood tests, CD38, CD56, CD 138 were positive. Vasculitis panel (as systemic lupus erythematosus and Sjogren's antibodies, etc.) were negative. Antithrombin III, protein C, and protein S levels were in a normal range. Immunoglobulins as IgA, IgG, IgM were within a normal range. Serum free-light chain results were as follows: Free Kappa Light Chain (24 Hours urine) 75.95 mg / 24 Hours, Free Lambda Light Chain (24 Hours urine) 33.81 mg / 24 Hours, Beta-2 Microglobulin 1.8500 mg / L (N). Immunoelectrophoresis (24 Hours urine) were as follows: Albumin 47.3 [L], Alpha-1 Globulin 7.6 [H], Alpha-2 Globulin 17.8 [H], Beta-1 Globulin 6.1 (N), Beta-2 Globulin 4.6 ( N), Gamma Globulin 16.6 (N). Monoclonal protein was not detected in Protein Electrophoresis (urine 24 Hours). Lambda monoclonal gammopathy was detected in Serum Immunofluorescent Electrophoresis (Figure 3).

One month later after the procedure, conventional cranial MRI (Magnetic Resonance Imaging) was performed to the patient. In the MRI, limited diffusion findings were observed at the caudate, lentiform nucleus, external capsules and insular cortex level on the right hemisphere. The lesion was in hyperintense signalling feature and consistent with late subacute stage intraparenchymal hematoma and subarachnoid hemorrhage at Sylvian fissure and right temporal lobe level, and diffusion restriction in white matter at the right centrum semiovale and basal ganglia were observed (Figure 4). On carotid vertebral ultrasonography (CVUSG), both vertebral arteries were in normal patterns and velocities, and flow was within normal limits, and the total flow was over 200 ml /min. On her transthoracic echocardiography, left ventricular ejection fraction was 50%, spab (systolic pulmonary arterial pressure) was 45. The patient underwent a 24-hours Holter test and found that there were intermittent irregular ventricular tachycardia attacks. She was externalized with enoxaparin treatment. After discharge, the patient’s neurological, cardiological and hematological follow-ups were continued.

Figure 1. Brain CTA examination: Extracranial and intracranial sections of the left external and internal carotid arteries, bilateral ACA and left MCA are patents. The right MCA M1 segment occlusion and refractions of opaque material by collaterals are observed in the M2 and M3 segments.

Figure 2. 9 x 16 mm hematoma views measured at the corona radiata level at the head of the right caudate nucleus and right lentiform nucleus, and a secondary hemorrhagic transformation was observed. Subarachnoid hemorrhage was observed in the right temporal and parietal sulcus. Hyperdense hemorrhage was observed in the right MCA neighborhood. Secondary compression of the right lateral ventricle was also observed.

Figure 3. In serum immunofixation electrophoresis, IgG Lambda monoclonal gammopathy was detected.
Hypertension and diabetes mellitus; echocardiographic population, mainly atrial fibrillation, hyperlipidemia, risk factors for stroke are similar to those in the general Ischemic stroke may be the first sign of amyloidosis. The accumulation due to her normal kidney function. Region was considered as asymptomatic renal light chain involvement in terms of amyloidosis in the cardiac vascular structures as in our case (5-7). The patient with amyloid deposition is limited to tubulointerstitium and/or nephropathy can be seen without proteinuria if the amyloidosis. In amyloid nephropathy, nephrotic syndrome due to multiple myeloma or a monoclonal gammopathy of unknown origin. Mild immunoglobulin chains in circulation can be shown in serum and urine (3). Systemic amyloidosis associated with cardiac and renal amyloidosis; Multiple myeloma, Waldenström macroglobulinemia or other plasma cell dyscrasias. In AL amyloidosis, these light chain immunoglobulin chains are most commonly stored in the kidneys, heart, lungs, skin, tongue, vocal cords, striated muscles, bone marrow, liver, spleen, autonomic and peripheral nervous system that lead to progressive organ failure (4). Kidneys are the most commonly involved organ in AL, AA, apoA1, and apoA2 and fibrinogen Aa amyloidosis. In amyloid nephropathy, nephrotic syndrome and end-stage renal failure (ESRD is classic, but amyloidosis. Increased bleeding can be caused by one or more of several causes, including the reduced activity of factor X, vascular infiltration with amyloid, and abnormal liver function due to amyloid deposition. Many studies support a decrease in factor X level and related hemorrhagic complications (15). Our patient underwent thrombectomy and thrombectomy showed a complete resolution in the occluded area and there was no hemorrhagic sign during the digital subtracted angiography (DSA) process. In her control cranial CT, subarachnoidal and intraparenchymal hemorrhage was observed (Figure 2) and she had still a hematoma appearance in the parenchymal area in the control MRI one month later (Figure 4).

**DISCUSSION**

The most common type of systemic amyloidosis, AL amyloidosis, has a prevalence of 8.9/1,000,000. AL type amyloid proteins are composed of mild chains of immunoglobulin in different proportions. It often develops due to multiple myeloma or a monoclonal gammopathy of unknown origin. Mild immunoglobulin chains in circulation can be shown in serum and urine (3). Systemic amyloidosis associated with cardiac and renal amyloidosis; Multiple myeloma, Waldenström macroglobulinemia or other plasma cell dyscrasias. In AL amyloidosis, these light chain immunoglobulin chains are most commonly stored in the kidneys, heart, lungs, skin, tongue, vocal cords, striated muscles, bone marrow, liver, spleen, autonomic and peripheral nervous system that lead to progressive organ failure (4). Kidneys are the most commonly involved organ in AL, AA, apoA1, and apoA2 and fibrinogen Aa amyloidosis. In amyloid nephropathy, nephrotic syndrome and end-stage renal failure (ESRD is classic, but amyloidosis. Increased bleeding can be caused by one or more of several causes, including the reduced activity of factor X, vascular infiltration with amyloid, and abnormal liver function due to amyloid deposition. Many studies support a decrease in factor X level and related hemorrhagic complications (15). Our patient underwent thrombectomy and thrombectomy showed a complete resolution in the occluded area and there was no hemorrhagic sign during the digital subtracted angiography (DSA) process. In her control cranial CT, subarachnoidal and intraparenchymal hemorrhage was observed (Figure 2) and she had still a hematoma appearance in the parenchymal area in the control MRI one month later (Figure 4).

Conclusions

Although systemic amyloidosis is not common in cerebrovascular disease etiology compared to other metabolic disorders, prevalence is very high, especially with cardiac involvement. In our case report, we emphasized a case recently diagnosed with cardiac amyloidosis and presenting with an acute stroke. We believe that early diagnosis and close follow-up and effective treatment are important for the patient's survey to prevent possible embolic events in systemic amyloidosis.
Conflict of interest: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports.
Patient informed consent: Before commencing the study, the aims and content of the study were explained to all participants, and their written consent was obtained.

REFERENCES