Acute myocardial infarction in patients of nephrotic syndrome: a case series

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Thromboembolic complications have been frequently reported in patients with long-lasting nephrotic syndrome (NS). Although thrombotic complications in the venous system are common in patients with NS, arterial thromboses associated with NS are much less common. However, coronary thromboses are extremely rarely observed. So, NS is a rare cause of acute coronary syndrome (ACS). As such, the incidence, pathogenesis, and treatment of these patients have yet to be clearly defined. In the current literature, publications contain less than 15 patients, most of whom are young children.

Serious clotting factor disturbances can be observed, such as changes in platelet hyperfunction, increased plasma fibrinogen, abnormalities of the fibrinolytic system, and acquired deficiencies of coagulation inhibitors. However, increased platelet aggregation and antithrombin III (AT III) deficiency are the most important factors in this hypercoagulable state in the NS. A hypothesis for hypercoagulable state in NS suggests a clinical correlation between thromboembolism and the underlying renal disease (especially minimal change glomerulopathy). Patients with chronic excess proteinuria and long-term exposure to abnormalities of hemostasis and lipid profiles appear to have a high risk of developing cardiovascular disease.

In our study, we evaluated the characteristics of eight patients admitted to our hospital with a diagnosis of acute myocardial infarction (AMI) by ECG, clinical presentation and myocardial enzyme. They were all diagnosed NS before AMI. To our knowledge, this is the first study of multiple cases of NS associated with AMI.

In this case study, the cases presented here were retrospectively collected from a database of Jinling Hospital in which who had AMI. From 1800 patients who had been admitted to our Department for AMI, we found eight cases of combined NS. These patients were enrolled in the study from 2008 through 2016. All patients were diagnosed with NS and meanwhile AMI based on symptoms, electrocardiogram and myocardial enzyme. Follow-up at one year was achieved in 62.5% patients.

Two of the patients were female (25%) and six of the patients were male. The age range was between 29 and 72 years with a mean age of 55 years (54.5 years for men, 56.5 years for women). Seven patients (87.5%) are taking oral hormone therapy for a long time. Patients with specific pathologic diagnosis were membranous nephropathy (MN) while three of them have no data. The most infarcted area is inferior wall (62.5%). Three patients died during hospitalization. Severe hypoalbuminemia and proteinuria can be observed in most of the patients (Table 1).

Three people had coronary angiography and stent implantation. Two patients were treated with percutaneous transluminal coronary angioplasty (PTCA) only and two with thrombus aspiration or thrombolysis. The incidence of cardiogenic shock was 3/8 (37.5%). The rate of no reflow or slow blood flow 3/8 (37.5%). In most patients, thrombosis is seen in coronary angiography, rather than in coronary atherosclerosis. Some people only do PTCA or thrombus and take the medicine in the coronary artery. The lesion of the blood vessel is dominated by the left anterior descending (LAD) and the right coronary artery (RCA). Most patients are found with either no reflow or slow blood flow (Table 2).

The first report on coronary heart disease complicating NS was published 1969 by Berlyne and Mallick, who described the occurrence of AMI in four patients with NS due to glomerulonephritis. Now the combination of these
Table 1. Baseline clinical characteristics of patients.

| Patients | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|
| Age, yrs | 29  | 54  | 65  | 59  | 58  | 72  | 62  | 41  |
| Gender   | Male| Male| Male| Male| Male| Female| Male| Female|
| Hypertension | No  | No  | Yes | Yes | No  | Yes | Yes | No  |
| Diabetes | No  | No  | No  | No  | Yes | No  | No  | No  |
| Dyslipidemia | Yes | No  | No  | No  | No  | No  | No  | No  |
| Smoking | No  | Yes | No  | Yes | No  | Yes | No  | No  |
| Previous heart disease | No  | No  | No  | No  | No  | No  | No  | No  |
| Troponin I, ng/L | ND  | 42.03 | 1.71 | 117.9 | NA  | NA  | NA  | 50  |
| Oral glucocorticoids treatment | Yes | Yes | Yes | Yes | Yes | No  | Yes | Yes |
| Pathological diagnosis | ND  | MN  | MN  | ND  | MN  | MN  | MN  | ND  |
| Albumin, g/L | ND  | 25.8 | 30.8 | 18.1 | 19.8 | 33.3 | 25.9 | 16.1 |
| Proteinuria | No  | Yes | Yes | Yes | Yes | NA  | Yes | Yes |
| The interval between the diagnosis and the onset of the disease | 21 years | 5 months | 3 years | 1 year | ND  | 6 years | 2 years | 1 months |

Table 2. Angiography characteristics.

| Patients | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|
| Culprit vessel | LAD | LAD | RCA | LAD | ND  | RCA | ND  | RCA |
| Multi-vessel lesions | Yes | No  | Yes | Yes | No  | Yes | ND  | No  |
| Severe calcification | No  | No  | Yes | No  | ND  | No  | ND  | No  |
| Diffuse lesion | Yes | No  | Yes | Yes | No  | Yes | ND  | No  |
| Treatment | PTCA | Thrombus spiration | PTCA | Stent | Thrombolysis | stent | ND  | Stent+thrombus |
| Number of stents | 0   | 0   | 0   | 2   | 0   | 3   | ND  | 1   |
| Length of stents | ND  | ND  | ND  | 52 mm | ND  | 63 mm | ND  | 23 mm |
| Thrombus spiration | No  | Yes | No  | No  | No  | No  | No  | Yes |
| Cardiac shock | No  | No  | Yes | Yes | Yes | No  | ND  | No  |
| No reflux or slow blood flow | No  | Yes | Yes | No  | ND  | No  | ND  | Yes |
| Intravascular medicine | No  | Yes | No  | No  | ND  | No  | ND  | Yes |

MN: membranous nephropathy; NA: not available; ND: no data.

We presented a case series of AMI secondary to NS mostly due to MN. In our cases, the age distribution is between 29 and 72 years old. It’s interesting that the AMI occurs in patients of NS at all ages, not only young people. We also summarized the treatment of these patients. Most of the patients were treated with percutaneous coronary intervention and recovered well.

Most patients with coronary angiography can see a thrombosis, rather than an atheromatous plaque. In the treatment, some patients had a PTCA and did not implant stent, and the blood clots were taken from the blood clot. Coronary thrombosis can be seen in hypercoagulable states such as in the antiphospholipid syndrome, NS, and factor XII and protein S deficiencies, etc.[7–10] The possible pathogenesis of AMI in NS has been discussed in the former study.[11] The underlying mechanisms of the “thrombophilia” of the NS are multiple but seem related with an imbalance of prothrombotic factors. Firstly, factors associated with coagulation are enhanced. The proteinuria associated...
with NS leads to the loss of low molecular weight protein, such as factors IX, XI, and XII, as the liver tries to compensate for the hypoalbuminemic state, there is an increased synthesis of factors II, VII, VIII, X, XIII, and fibrinogen.12–14 Thrombocytosis and increased platelet aggregation and adhesiveness also contribute to the hypercoagulable state. Platelet hyperaggregability correlates with serum cholesterol concentrations. Secondly, factors associating with anticoagulation are weakened. Antithrombin III, a coagulation inhibitor significant reductions can be observed especially when the serum albumin concentration is below 20 g/L.

However, protein C and protein S are coagulation inhibitors whose decline has not been clearly implicated in arterial thrombosis in the NS. Thirdly, the imbalance of fibrinolytic system, with decreased concentrations of plasminogen and raised levels of plasminogen activator, contributes to the “thrombophilia”.15 There is evidence of decreased fibrinolytic activity with hypertriglyceridemia, which often occurs in the NS.16 And the extent of alterations in imbalance of prothrombotic factors correlate with the degree of hypoalbuminaemia. A serum albumin of less than 25 g/L is a significant risk factor for combined arterial and venous thrombosis in the NS.17 Other factors that contribute to the hypercoagulable state are a thrombocytosis and increased platelet aggregation and adhesiveness. Platelet hyperaggregability correlates with serum cholesterol concentrations.18,19 Many of these abnormalities were evident in our patient and may have caused coronary thrombosis without atherosclerotic plaque rupture.

Most of our patients are MN, which is a glomerular disease characterized by NS and typical changes on renal biopsy. Most patients present with a NS (80%). In the past, MN was considered as a presentation of chronic serum sickness. With research evolvement, MN like other glomerular diseases is now thought to be an autoimmune disease.20 Oral hormone therapy is considered beneficial in the medium risk group (normal plasma creatinine, proteinuria between 4 and 8 g on a maximal conservative treatment).

In conclusion, the cases report indicates that AMI is a rare complication of the thrombotic tendency in nephrotic syndrome. Br J Clin Pract 1994; 48: 218–220.

Fujimura O, Gulamhusein S. Acute myocardial infarction: thrombotic complications of nephrotic syndrome. Can J Cardiol 1987; 3: 267–269.

Hamsten A, Norberg R, Bjorkholm M, et al. Antibodies to cardiolipin in young survivors of myocardial infarction: an association with recurrent cardiovascular events. Lancet 1986; 1: 113–116.

Manzar KJ, Padder FA, Conrad AR, et al. Acute myocardial infarction with normal coronary arteries and factor XII deficiency. Br Heart J 1985; 53: 230–234.

Krishna K, Hiremath S, Lakade S, Davakhar S. Acute myocardial infarction in nephrotic syndrome. J Assoc Physicians India 2015; 63: 67–68.

Fahal IH, McClelland P, Hay CR, Bell GM. Arterial thrombosis in the nephrotic syndrome. Postgrad Med J 1994; 70: 905–909.

Kendall AG, Lohmann RC, Dossetor JB. Nephrotic syn-

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drome. A hypercoagulable state. Arch Intern Med 1971; 127: 1021–1027.
14 Takeda Y, Chen AY. Fibrinogen metabolism and distribution in patients with the nephrotic syndrome. J Lab Clin Med 1967; 70: 678–685.
15 Cameron JS. Coagulation and thromboembolic complications in the nephrotic syndrome. Adv Nephrol Necker Hosp 1984; 13: 75–114.
16 Simpson HC, Mann JI, Meade TW, et al. Hypertriglyceridaemia and hypercoagulability. Lancet 1983; 1: 786–790.
17 Bellomo R, Atkins RC. Membranous nephropathy and thromboembolism: is prophylactic anticoagulation warranted? Nephron 1993; 63: 249–254.
18 Remuzzi G, Mecca G, Marchesi D, et al. Platelet hyperaggregability and the nephrotic syndrome. Thromb Res 1979; 16: 345–354.
19 Carvalho AC, Colman RW, Lees RS. Platelet function in hyperlipoproteinemia. N Engl J Med 1974; 290: 434–438.
20 Couser WG. Membranous nephropathy: a long road but well traveled. J Am Soc Nephrol 2005; 16: 1184–1187.