Hereditary Spherocytosis Presenting with Immunoglobulin A Nephropathy in Post-Splenectomy

Yoshinosuke Shimamura, MD, Takako Akimoto, MD, Norihito Moniwa, MD, Koichi Hasegawa, MD, Yayoi Ogawa, MD, and Hideki Takizawa, MD

1 Department of Nephrology, Teine Keijinkai Medical Center, Sapporo, Hokkaido, Japan
2 Hokkaido Renal Pathology Center, Sapporo, Hokkaido, Japan

Hereditary spherocytosis is a familial hemolytic anemia. In this report, we describe a rare case of hereditary spherocytosis complicated by IgA nephropathy which was successfully treated with an angiotensin converting enzyme inhibitor. This is the first time that such a case in an adult has been documented. We describe a 72-year-old Japanese male who presented with hereditary spherocytosis, accompanied by Immunoglobulin A nephropathy, in which an angiotensin converting enzyme inhibitor (ACEi) led to a decline in proteinuria. Clinicians should recognize that hereditary spherocytosis with IgA nephropathy can occur in the post-splenectomy patients.

Keywords: hereditary spherocytosis, IgA nephropathy, angiotensin converting enzyme inhibitor

Introduction
Hereditary spherocytosis (HS) is a common inherited chronic hemolysis, and is treated with splenectomy in almost all patients. The association of HS with IgA nephropathy (IgAN) in a child has been reported in the literature. However, HS associated with IgAN in an adult case has not been reported before. In this report, we provide an adult case of HS who presented with microscopic hematuria and proteinuria, diagnosed with IgAN, in which an angiotensin converting enzyme inhibitor (ACEi) led to a decline in proteinuria.

Case Presentation
A 72-year-old male was referred to our medical center with hematuria, proteinuria and progressive kidney dysfunction for further investigation. He had a past medical history of HS confirmed by a mutation in the Protein 4.2 gene, and had undergone splenectomy at the age of 69 years. Other past medical history included congestive heart failure, hypertension, and multiple admissions of pneumonia. His medications were carvedilol, aspirin, and amiodarone. His family history also includes HS in his two children. The results of

Corresponding author: Yoshinosuke Shimamura, MD
Department of Nephrology, Teine Keijinkai Medical Center, 1-12 Maeda, Teine-ku, Sapporo, Hokkaido 006-8555, Japan
E-Mail: yoshinosukeshimamura@gmail.com
Received for publication 27 November 2014 and accepted in revised form 24 September 2015
© 2016 Japan Primary Care Association
testing four years before admission reported mild microscopic hematuria (5–9 erythrocytes per high-power field) and serum creatinine level of 1.14 mg/dL. On admission, physical examination revealed a normal blood pressure and no significant findings. Laboratory data showed: red blood cell count 251 × 10^6/µL, hemoglobin 8.2 g/dL, white blood cell count, 9380/µL, platelet count 140 × 10^9/µL, serum creatinine 4.25 mg/dL, urea nitrogen 48.2 mg/dL and estimated glomerular filtration rate (eGFR) 12 mL/min per 1.73 m² according to the Modification of Diet in Renal Disease equation. The Coombs’ test showed negative results, and hemoglobin electrophoresis was normal. Urinary protein was 0.85 g/day. Urinary sediment revealed >100 erythrocytes and 1–4 leukocytes per high-power field, and dysmorphic erythrocytes were also noted. On ultrasonography, both kidneys were normal sized. The spleen was not visualized. Immunological studies showed Immunoglobulin G, 1210 mg/dL (normal range 770–1,550 mg/dL); IgA, 1,049 mg/dL (normal range 76–376 mg/dL); Immunoglobulin M, 77 mg/dL (normal range 47–217 mg/dL); complement 3, 80 mg/dL (normal range 70–210 mg/dL); complement 4, 16.3 mg/dL (normal range 10–40 mg/dL). MPO-ANCA, proteinase 3-specific ANCA, anti-GBM antibody, cryoglobulins, and viral serology (hepatitis A, hepatitis B, hepatitis C, cytomegalovirus, and human immune deficiency virus) were negative. A percutaneous renal biopsy was performed. Light microscopy (Figure 1) revealed mild a proliferation in the mesangial matrix of the glomeruli. Global sclerosis was observed in two out of twenty three glomeruli. There was no crescent. Immunofluorescence studies demonstrated mesangial deposits of IgA and C3 (Figure 2). Electron microscopy found a proliferation of mesangial cells and a dense deposit in the paramesangial area (Figure 3). These findings were consistent with IgAN. ACEi, enarapril 2.5 mg daily, was commenced in an attempt to provide the optimal approach to achieve a reduction in proteinuria. On the follow-up visit, serum creatinine level remained 4.40 mg/dL and the microscopic hematuria continued. By contrast, his blood pressure and serum potassium level remained in normal range, and proteinuria improved 4 months after the initiation of therapy.

Discussion
In this case, we made two important clinical observations. First, we found that this is the first reported adult case of HS with IgAN. Second, ACEi helped reduce the proteinuria in this case.

Figure 1. Light microscopy of the kidney biopsy revealed mild proliferation in the mesangial matrix (arrow) of the glomeruli (Hematoxylin-eosin, x40).

Figure 2. Immunofluorescence microscopy demonstrated mesangial deposits of IgA (immunofluorescence x40).

Figure 3. Electron microscopy showed the proliferation of mesangial cells and dense deposit (arrow head) in the paramesangial area (x100).
First of all, this is the first reported case of HS with IgAN. IgAN can be associated with many other diseases, particularly with a number of autoimmune diseases and liver diseases. There are some case reports of IgAN with splenectomy. Biyiki NK et al. reported on a 17-year-old boy with IgAN and HS. Morino et al. reported on a 14-year-old boy who had had a splenectomy at the age of two years for idiopathic thrombocytopenic purpura, which resulted in IgAN. However, to the best of our knowledge, this is the first literature reporting the association of HS with IgAN in an adult. We speculate the splenectomy may play an important role in the pathogenesis of this case. Some researchers showed that IgA synthesis was increased in peripheral blood mononuclear cells from post-splenectomy patients. Another study showed that the amount of IgA deposits in the glomeruli was raised when the uptake of immune complexes by organs of reticuloendothelial system was reduced. Therefore, both over production of IgA and decreased clearance of IgA due to the splenectomy may lead to susceptibility of IgAN.

Our second observation is that ACEi helped reduce the proteinuria in the concomitant case of HS and IgAN. It has been reported that angiotensin converting enzyme inhibitors decrease proteinuria in IgAN. Another researcher reported that ACEi prevented the progression to end-stage kidney diseases by modulating the effects of angiotensin II via angiotensin II type 1 receptor on the production of tissue growth factor-beta and collagen types I and III, as well as on intrarenal hemodynamics. In this case, we successfully treated our patient’s proteinuria. However, the therapy for concurrent cases of HS and IgAN is still unknown because there have been no comparative therapeutic trials, and clinical experience is lacking. We did not use corticosteroids in our patient because Kidney Disease Improving Global Outcomes guidelines recommend six months of glucorticosteroids only when there is persistent proteinuria over 1 g/day, and eGFR greater than 50 ml/min per 1.73 m.2

This case report has limitations that must be noted. First, we are not able to exclude the possibility of the existence of these two diseases accidentally. In this regard, we assert that the splenectomy contributed to an acceleration of IgAN because hematuria, proteinuria and renal function obviously deteriorated after the splenectomy in this case. Second, there was a discrepancy between the clinical courses and the renal pathological findings. We assume that the history of congestive heart failure, hypertension might contribute to the deterioration of kidney function in this case, which is supported by the presence of global sclerosis in the renal pathology.

Conclusion
In conclusion, we report an adult case of IgAN in HS after splenectomy. Health care professionals should recognize IgAN can occur in the post-splenectomy patients. In addition, this report may provide important clues in terms of the pathophysiology of concomitant cases of these diseases. Further reports should be accumulated to determine whether the splenectomy contributes to the nephritogenic role of IgAN and which treatments could be effective in such cases.

Competing interests
The authors declare that they have no competing interests.

Acknowledgements
We acknowledge the support of all members of the nephrology staff in Teine Keijinkai Medical Center.

References


