

Complement-mediated warm autoimmune hemolytic anemia associated with acute poststreptococcal glomerulonephritis: a pediatric case report

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ABSTRACT

Acute poststreptococcal glomerulonephritis (APSGN) is one of the most common causes of acute nephritic syndrome in childhood; however, hematological complications are rarely associated with this disease. This article presents a case of a 6.5-year-old male who presented with complaints of pallor and fatigue after a recent upper respiratory tract infection and was diagnosed with autoimmune hemolytic anemia. During hospitalization, the patient developed hypertension, oliguria, and gross hematuria; further evaluation revealed elevated antistreptolysin O levels and markedly low serum complement component 3 levels, leading to a diagnosis of APSGN. The direct antiglobulin test revealed immunoglobulin G negativity along with complement positivity, findings consistent with complement-mediated warm-type autoimmune hemolytic anemia. The patient received corticosteroid therapy, supportive treatment, and antihypertensive agents; following treatment, rapid improvement in hemoglobin levels and complete resolution of renal and hematological findings were achieved. This case highlights the rare association of APSGN with complement-mediated autoimmune hemolytic anemia, emphasizing the need to consider immune-mediated hematological complications in children with unexplained anemia associated with nephritic syndrome.

Keywords: Acute poststreptococcal glomerulonephritis, autoimmune hemolytic anemia, complement-mediated hemolysis, direct antiglobulin test

INTRODUCTION

Acute poststreptococcal glomerulonephritis (APSGN) is one of the leading causes of acute nephritic syndrome in childhood, typically occurring 1–3 weeks after infections caused by nephritogenic group A beta-hemolytic streptococci.^{1,2} APSGN is characterized by hematuria, edema, hypertension, oliguria, and, in particular, a transient decrease in serum complement component 3 (C3) levels.^{1,2} Although APSGN is primarily a renal immune complex-mediated disease, it is known that streptococcal infections can lead to various immune-mediated sequelae outside the kidney.³

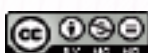
Hematological complications are not typical features of APSGN. Immune-mediated cytopenias, particularly immune thrombocytopenic purpura, have been reported rarely; however, the association of APSGN with autoimmune hemolytic anemia (AHA) is extremely rare.^{4,5} The number of pediatric cases reporting this association in the literature is quite limited, leading to limited evidence regarding the evaluation and management of the disease.^{4,5}

Warm-type AHA usually develops through immunoglobulin G (IgG) autoantibodies and is often associated with IgG positivity in the direct antiglobulin test, sometimes also with complement positivity.^{6,7} In rare cases, only complement (C3d) positivity may be detected along with IgG negativity, and this serological pattern may be associated with clinically significant hemolysis.^{8,9} Therefore, the occurrence of complement-mediated warm-type AHA in conjunction with APSGN presents a diagnostically challenging and clinically instructive picture.

This article presents a case of a 5-year-old male patient with APSGN and C3d-positive, IgG-negative warm-type AHA who responded well to corticosteroid treatment.

CASE

A previously healthy 6.5-year-old male patient was admitted to the hospital with complaints of pallor and fatigue that had



persisted for a week. His history included an upper respiratory tract infection approximately 10 days prior to admission. The patient and his family had no known history of kidney or blood diseases.

On physical examination, the patient appeared pale and had mild scleral icterus. His blood pressure was 140/80 mmHg, which was above the 95th percentile for his age and height. No peripheral edema was detected. Abdominal examination revealed no hepatomegaly; however, abdominal ultrasonography showed borderline splenomegaly.

Laboratory tests revealed hemoglobin 7 g/dl, hematocrit 20%, mean corpuscular volume 76.9 fL, white blood cell count 15,800/ μ L, and platelet count 443,000/ μ L. The reticulocyte count was increased at 8%. Lactate dehydrogenase level was 284 U/L, total bilirubin was 2.1 mg/dl, and indirect bilirubin was 2.01 mg/dl, consistent with hemolysis.

The direct antiglobulin test was positive for complement component 3d and negative for IgG. Cold agglutinins and Donath–Landsteiner antibodies were negative. The peripheral smear showed polychromasia, anisocytosis, poikilocytosis, normoblasts, and spherocytes; no schistocytes were detected. Based on these findings, a diagnosis of AHA was made, and oral prednisolone therapy was initiated at a dose of 2 mg/kg/day.

On the third day of corticosteroid treatment, the patient developed gross hematuria, oliguria, and persistent hypertension. Urinalysis revealed 3+ proteinuria, 3+ hematuria, and 1+ urobilinogen. Urine microscopy showed numerous erythrocytes and erythrocyte casts. Serum urea level was 83 mg/dl, and creatinine level was 0.41 mg/dl.

Further evaluation revealed an antistreptolysin O level of 1500 IU/ml (normal <240 IU/ml). Serum C3 level was markedly low at 3 mg/dl, while complement component 4 level was normal. These findings supported the diagnosis of APSGN developing concurrently with AHA.

The patient was monitored with fluid restriction, antihypertensive treatment including amlodipine and enalapril, and continued corticosteroid therapy. The hemoglobin level increased by approximately 2 g/dl within two weeks. Corticosteroid therapy was gradually discontinued within six weeks. At follow-up, the patient was normotensive, her anemia had resolved, and her renal function had completely returned to normal.

DISCUSSION

APSGN is one of the most common causes of acute nephritic syndrome in childhood and develops following group A beta-hemolytic streptococcal infections.^{1,2} The pathogenesis of the disease is related to immune complex deposition and complement activation and is characterized by transient hypocomplementemia.^{1,2} In contrast, hematologic abnormalities are not typical features of APSGN.

Extrarenal immune complications of APSGN have been reported rarely. Among these, immune thrombocytopenic purpura is more frequently described, while the association of APSGN with AHA is extremely rare.^{4,5} Most of the

few pediatric cases reported in the literature involve male patients and have a history of recent streptococcal infection. This suggests a common immune mechanism triggered by streptococcal antigens.^{3,5}

In the presented case, a rare serological pattern of warm-type AHA was observed in conjunction with APSGN. Only complement component 3d positivity was detected, along with IgG negativity in the direct antiglobulin test. Although warm-type AHA usually develops through IgG autoantibodies, in rare cases it may occur with only complement positivity.^{8,9} In this case, since erythrocytes are coated only with complement, their recognition by macrophages may be delayed, and clinically significant hemolysis may develop despite atypical laboratory findings.⁸

The pathogenesis of complement-mediated, IgG-negative hemolysis has not been fully elucidated. It is thought that low-affinity or transient IgG antibodies initiate complement activation and then dissociate from the erythrocyte surface, leaving only complement particles behind.^{9,10} Previous studies have reported that although more severe anemia may be observed in patients with complement-positive warm-type AHA, the response to corticosteroid treatment is generally good, especially in cases secondary to infection.^{8,11}

Streptococcal infections can present with a wide variety of clinical manifestations.¹²⁻¹⁶ In this case, the history of streptococcal infection, the development of APSGN, and the simultaneous onset of hemolytic anemia strongly support an immune-mediated mechanism. The rapid improvement of both clinical and laboratory findings after corticosteroid treatment strengthens the diagnosis of secondary AHA.^{4,8}

CONCLUSION

This case contributes to the rare association of APSGN and AHA and demonstrates that immune-mediated hematologic complications must be considered in children with unexplained anemia and nephritic syndrome.

ETHICAL DECLARATIONS

Informed Consent

Informed consent was obtained from the legal guardians of the pediatric patient described in this report. Where developmentally appropriate, assent was also sought from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

Concept: S.T., Ş.T., Ü.A.T., M.A.; Design: S.T., Ü.A.T.; Control: S.T., Ş.T.; Resources: S.T., M.A.; Materials: Ş.T., M.A.; Data Collection and/ or Processing: S.T., M.A.; Analysis and/or Interpretation: S.T., Ş.T., M.A.; Literature Review: S.T., Ş.T., M.A.; Writing the Article: S.T., Ş.T., M.A.; Critical Review: S.T., Ş.A.

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