

Thrombocytopenia during the course of acute poststreptococcal glomerulonephritis

Velibor Tasic, Momir Polenakovic

Department of Nephrology, Clinic for Children's Diseases, University Clinical Center, Skopje, Republic of Macedonia

SUMMARY: Tasic V, Polenakovic M. Thrombocytopenia during the course of acute poststreptococcal glomerulonephritis. Turk J Pediatr 2003; 45: 148-151.

A four-year old boy was admitted to the hospital due to acute thrombocytopenic purpura. Three days later he developed edema, hematuria and hypertension. The diagnosis of acute poststreptococcal glomerulonephritis was based upon the evidence of previous sore throat, hypocomplementemia and increased antistreptolysin O titer. Renal biopsy was contraindicated due to thrombocytopenia. An extensive work-up was done to exclude membranoproliferative glomerulonephritis and systemic diseases such as hemolytic uremic syndrome or systemic lupus erythematosus. The clinical outcome of the nephritis and thrombocytopenia was excellent in respect to both conditions. To the best of our knowledge concurrent occurrence of acute thrombocytopenic purpura and poststreptococcal glomerulonephritis is very rare; there are only four similar cases reported in the literature. A careful work-up and follow-up are mandatory to exclude systemic disease.

Key words: poststreptococcal glomerulonephritis, thrombocytopenia, child.

Acute poststreptococcal glomerulonephritis (APSGN) is the most common glomerulopathy among children in our community. Typical features of the disease are acute onset with appearance of hematuria, edema and hypertension. In typical cases the diagnosis is easily established upon the history of antecedent streptococcal infection, acute onset of nephritic signs, transitory depression of C3 complement level, isolation of group A beta hemolytic streptococci from throat swab or pyoderma, and significant titer of streptococcal antibodies¹. Early recognition of the disease and appropriate treatment (diuretics, antihypertensive drugs, salt restriction) improve the prognosis of the acute episode. Otherwise the long-term prognosis of the disease is excellent². The unfavorable prognosis of the disease is due to early mortality and a rapidly progressive clinical course.

Hematological changes are not typical for APSGN. Anemia, frequently seen in children with APSGN, is not real and is due to circulatory congestion and consequent hemodilution. Hematological parameters improve spontaneously after induction

of diuresis.

In this work a four-year-old boy with acute thrombocytopenic purpura and APSGN is reported. There was a favourable outcome in respect to both conditions.

Case Report

A four-year-old boy was admitted at the Hematology Department of the Clinic for Children's Diseases Skopje because of appearance of epistaxis and mild petechial purpura located on the lower extremities and abdomen. There was history of sore throat seven days previously. The initial infection was characterized with fever, hyperemia of the throat and purulent exudates covering the tonsillar lacunae. Throat swab was not taken at that time. The child had been prescribed intramuscular penicillin 400,000 U for three days and after that oral penicillin V for seven days. The parents adhered strictly to the general practitioner's prescription. On admission, there was no organomegaly or lymphadenopathy. Other physical findings were unremarkable. The urinalysis was normal but hematological tests revealed thrombocytopenia

$0.1 \times 10^{11}/L$. Immediately, a bone marrow aspiration was performed, which displayed normal morphology of the cell lines, but large numbers of megakaryocytes were seen including some juvenile forms, consistent with the diagnosis of idiopathic thrombocytopenic purpura. Treatment with prednisone 1.0 mg/kg was commenced.

On the third hospital day there was clear evidence for localized edema (facial and pretibial),

steroid treatment was reduced and after four weeks withdrawn. The complement level normalized in the convalescent phase (C3 1.14 g/L, C4 0.42 g/L) and three months later there was resolution of the urinary abnormalities. During the five-year follow-up the child did not display any systemic manifestation and was normotensive, with normal values for C3 and C4 complements, preserved renal function and

Table I. Patient's Clinical and Biochemical Data

	Time from the disease onset				
	3 days	2 weeks	6 weeks	1 year	5 years
Blood pressure (mmHg)	130/100	110/70	95/65	100/70	
115/60					
Proteinuria (dipstick)	2+	1+	1+	∅	∅
Hematuria (dipstick)	3+	1+	1+	∅	∅
Creatinine ($\mu\text{mol}/L$)	148	84	59	51	55
C3 (g/L)	0.42	0.57	1.14	1.23	1.16
C4 (g/L)	0.17	0.42	0.42	0.33	0.38
ANA	∅	ND	∅	∅	∅
Thrombocytes ($\times 10^{11}/L$)	0.1	0.8	2.12	3.1	2.54

ND : not done.

oliguria, gross hematuria and hypertension (135/100 mmHg). The examination of the urinary sediment showed presence of numerous red blood cells (all with dysmorphic morphology), and hyaline and granular casts. There was mild increase of the degradation products and (urea 16 mmol/L, creatinine 148 $\mu\text{mol}/L$) but there was no change in the levels of serum electrolytes and proteins. The levels of the complements were decreased (C3 0.42 g/L, C4 0.17 g/L). The antistreptolysin O (ASO) titer was determined three times: on the 4th hospital day (640 U/ml; normal <250 U/ml), on the 14th hospital day (500 U/ml) and one month later (166 U/ml). Anti-nuclear antibody (ANA) and anti-DNA were negative. Platelet-associated IgG antibodies were not detected. There was no growth from the throat swab. Since the differential diagnosis included the possibility for hemolytic uremic syndrome (HUS), peripheral blood smear was analysed, and a normal morphology of red blood cells was found.

Thrombocytopenia contraindicated renal biopsy. Further clinical course of the disease was favourable with resolution of the nephritic signs and normalization of the thrombocyte count. The

normal hematological parameters (Table I).

Discussion

Idiopathic thrombocytopenic purpura (ITP) is a disorder in which platelets, sensitised by autoantibodies, are destroyed by the reticuloendothelial system. Two-thirds of the children with acute ITP have a history of an infectious illness a few days to a few weeks before the onset of thrombocytopenia. In the majority of them there is evidence of previous infection such as varicella zoster virus, rubella, Epstein-Barr virus, influenza, or human immunodeficiency type 1 virus infection³. The diagnosis of ITP has been a clinical one because assays measuring platelet-associated IgG have low sensitivity. Recently introduced assays that measure antibodies against specific platelet glycoproteins (GP) offer the possibility of improved sensitivity and specificity⁴.

We report a case of a boy with concurrent appearance of acute thrombocytopenic purpura and APSGN. The presence of thrombocytopenia and acute nephritic signs strongly suggest the possibility for HUS or systemic lupus

erythematosus (SLE). Anemia is the principal feature of HUS and it is microangiopathic, but it was not seen in the patient's blood film. Clues suggesting SLE may be nephritis, thrombocytopenia and hypocomplementemia. The age of the child, male gender and negative serology (ANA and anti-DNA) are findings not compatible with SLE⁵. The clinical course of SLE is characterized by favourable effect of steroid treatment, but the disease requires prolonged immuno suppression, and relapses appear when tapering or withdrawal of steroids is too fast^{5,6}. The steroid treatment in this case was short (4 weeks) and during the five-year follow-up there was neither evidence for systemic manifestation or hypocomplementemia. The normalization of the complement in the convalescent phase and the favourable clinical course are also strong nonindicators for membranoproliferative glomerulonephritis (MPGN). Although streptococcal infection may trigger the disease activity in children with MPGN and cause confusion due to the increase of the ASO titer, the latent period is usually 1-3 days, whereas in this case it was 10 days. The renal biopsy was contraindicated due to thrombocytopenia.

The clinical course suggested two separate entities: acute thrombocytopenic purpura and APSGN. The following criteria were suggestive of APSGN: acute onset of the disease with hematuria, hypertension and edema, transitory hypocomplementemia and elevated ASO titer. Hematuria may also be a feature ITP. This possibility is unlikely due to the dysmorphic type of hematuria and the presence of pathological cylinders. The hypertension might be an iatrogenic complication due to steroid therapy. In our case hypertension resolved after disappearance of edema, although we continued to treat the child with the same steroid dose.

The fact that group A beta hemolytic streptococcus was not isolated was expected since the initial infection (sore throat) had been treated with penicillin.

There are reports in the literature for the association of HUS and APSGN^{7,8}. In these reports the clinical picture of the HUS was classical, and thrombocytopenia was only one symptom during the course of HUS.

Kaplan and Esseltine⁹ were the first to report the association of acute thrombocytopenia and

APSGN. Their two patients also had biopsy confirmation for APSGN. Rizkallah MF et al.¹⁰ described a case of a 5.5-year-old boy who presented clinically with acute idiopathic thrombocytopenia and APSGN. The diagnosis of APSGN was confirmed by renal biopsy after normalization of the platelet count.

Concerning the etiology of this rare association, one might point to the previous streptococcal infection, although our search through Medline failed to reveal a causal relationship between streptococcal pharyngitis and ITP. We can only assume that the precipitating factor for both diseases was the previous streptococcal infection. Although not firm, evidence for the association of these two is based on previously reported cases, including a recently published case report by Muguruma et al.¹¹, but that association may have been by chance. The authors speculate about the pathogenesis of associated diseases through production of autoantibodies cross-reactive against group A beta hemolytic streptococci and against platelets. The very mild course of APSGN in their patient was explained by increased splenic destruction of platelets loaded with these immunoglobulins and subsequent amelioration of the renal injury. This hypothesis cannot explain the more severe course of the nephritis in our case. The common feature of the previously reported four cases and this one is that all children fully recovered from nephritis and none developed steroid-dependent thrombocytopenia.

Renal biopsy was performed only in one case¹⁰. On admission one might consider renal biopsy as an excellent tool to resolve the differential diagnostic difficulties but at that time the biopsy would have been dangerous in the presence of such severe thrombocytopenia. Six weeks after admission the child still had minimal proteinuria and hematuria, but he was clinically well and his complement normalized, highly suggesting the favourable (posts-streptococcal) etiology of his glomerulonephritis. At that point the biopsy was of no practical importance for the patient's further management. The academic value of the biopsy in the later course of the disease was also very questionable, since typical acute exudative proliferative changes and humps could resolve and transform in to more non-

specific mesangioproliferative lesions. Thus, a careful work-up and follow-up were mandatory to exclude systemic disease.

REFERENCES

1. Rodriguez-Iturbe B. Acute poststreptococcal glomerulonephritis. In: Schrier RW, Gotschalk CW (eds). *Diseases of the Kidney*. Boston: Little Brown; 1988: 1929-1947.
2. Tasic V, Polenakovic M, Kuzmanovska D, Sahpazova E, Ristoska N. Prognosis of poststreptococcal glomerulonephritis five to fifteen years after an acute episode. *Pediatr Nephrol* 1988; 12: C167.
3. Rand ML, Wright JF. Virus-associated idiopathic thrombocytopenic purpura. *Transfus Sci* 1998; 19: 253-259.
4. Warner MN, Moore JC, Warkentin TE, Santos AV, Kelton JG. A prospective study of protein-specific assays used to investigate idiopathic thrombocytopenic purpura. *Br J Haematol* 1999; 104: 442-447.
5. Cameron JS. Lupus nephritis in childhood and adolescence. *Pediatr Nephrol* 1994; 8: 230-249.
6. Ponticelli C. Treatment of lupus nephritis-the advantages of a flexible approach. *Nephrol Dial Transplant* 1997; 12: 2057-2059.
7. Medani CR, Pearl PL, Hall-Craggs M. Acute renal failure, haemolytic anemia, and thrombocytopenia in poststreptococcal glomerulonephritis. *South Med J* 1987; 80: 370-373.
8. De Chadaverian JP, Goodyer PR, Kaplan BS. Acute glomerulonephritis and hemolytic uremic syndrome. *CMA Journal* 1980; 123: 391-394.
9. Kaplan BS, Esseltine D. Thrombocytopenia in patients with acute poststreptococcal glomerulonephritis. *J Pediatr* 1978; 98: 974-976.
10. Rizkallah MF, Ghandour MH, Sabbah R, Akhtar M. Acute thrombocytopenic purpura and poststreptococcal acute glomerulonephritis in a child. *Clin Pediatr (Phila)*