

## Second Attack of Acute Poststreptococcal Glomerulonephritis; Report of Two Cases

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Recurrent or a second attack of acute poststreptococcal glomerulonephritis have been known to be extremely rare. Acute exacerbation in chronic glomerulonephritis and recurrence of acute poststreptococcal glomerulonephritis would be distinguishable clearly by histopathological, immuno-fluorescent and electron microscopic studies from renal biopsy material.

Recently we dealt with two cases of a second attack of APSGN in a 9 year old girl and a 12 year old boy and reviewed the literature and the possible mechanism is discussed.

Key words; APSGN, acute poststreptococcal glomerulonephritis

Acute exacerbations following reinfection of streptococci in chronic glomerulonephritis have been reported (Seegal *et al.*, 1940; Vernier *et al.*, 1959) but recurrence or second attack of previously "cured" (clinically and laboratorily) acute poststreptococcal glomerulonephritis (APSGN) has been known to be extremely rare (Jennings & Earle, 1961; Kushner *et al.*, 1961; Rammelkamp, 1952).

Recurrence of APSGN was reported first in 1947 by Ramberg with his eleven cases. Thereafter, a few reports about second attacks of APSGN have followed (Bernstein & Stillerman, 1960; Roy *et al.*, 1969).

In Korea, a number of reports concerning clinical studies of APSGN in children were reportend (Kim, 1958; Kim, *et al.*, 1963; Koo *et al.*, 1969; Ryu *et al.*, 1969; Song *et al.*, 1968), but in none of the cases was a second attack of APSGN found.

Recently we have had experience with two cases of a second attack of APSGN which occurred eleven months and four years from the initial episodes respectively and these were confirmed by renal biopsies with light, immunofluorescent and electron microscopic studies.

### CASE 1

A 12 years old boy was admitted to hospital with gross hematuria and facial edema of three days duration. Six days prior to admission, he developed sore throat and mild fever, and 3 days later, the urine was dark and puffiness appeared on the face.

He had an admission eleven months ago when he developed exactly the same symptoms as the present illness and was diagnosed as APSGN with high ASOT (480) and was treated with oral penicillin for ten days but a renal biopsy was not done and he was discharged 7 days later with some improvement.

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After discharge, he was followed by PMD with serial urinalyses, and only a few occasions of proteinuria were noticed without any clinical symptoms. When he was in the hospital at that time, one of his brothers (7 years old) also developed APSGN and now his brother is doing well clinically and biochemically.

Physical examination on recent admission revealed no hypertension and normal vital signs. Edema was seen of both eye-lids, and the throat was slightly injected and marked pitting edema was found of both pretibial and ankle joints. Hemoglobin was 11.6 gm%, hematocrit 33.7%, leukocytes (11,500/mm<sup>3</sup>), platelets (330,000/mm<sup>3</sup>) were normal and the sedimentation rate was slightly increased to 15 mm/HR. ASOT was elevated to 1:340, BUN 30 mg% and serum creatinine 0.8mg%. Total serum protein was 7.0 gm%, albumin of 3.5 gm%, cholesterol 130 mg%, C<sub>3</sub> complement was decreased to 21 mg% (normal 43-200 mg%), protein excretion of 24 hours urine collection was 147 mg and creatinine clearance was 68.2 ml/min/1.73 mm<sup>2</sup>. Throat culture grew out group A  $\beta$ -streptococci but the urine culture was sterile. Proteinuria along with microscopic hematuria continued till the end of the first week but proteinuria had completely disappeared by the second week. Urinalyses were performed on the whole family because of the previous family history of glomerulonephritis but none of the other family members showed abnormal findings. Audiogram and ophthalmologic examination were done to rule out the possibility of Alport's syndrome but no abnormality was found. Excretory urogram revealed a normal nephrogram and ureteropelvic system. Percutaneous renal biopsy was performed on the 7th hospital day. During hospitalization, he was managed

with bed rest, low salt diet and oral penicillin and discharged the next day after renal biopsy. Follow-up serial urinalyses after discharge disclosed continuous microscopic hematuria up to six weeks and C<sub>3</sub> complement slowly elevated to 32mg% by four week, 68 mg% at six week and clinically did very well.

#### Pathological Findings; RB-78-100 (S-78-6294)

The remaining sections after frozen cuts contain only four glomeruli which show markedly increased cellularity with polymorphonuclear leukocytes, swollen endocapillary cells and some widening of mesangial matrix (Fig. 1). There is no sclerosis or crescent. The tubules, interstitium and the blood vessels are also not remarkable.

The immunofluorescent study with monospecific antisera shows very slight fluorescent granular deposits of IgG along the peripheral loop with  $\pm$  intensity, and abundant granular deposits of C<sub>3</sub> with ++ to +++ intensity along the loop and also within the mesangium with  $\pm$  intensity. IgA, IgM, IgE, Fibrinogen and Albumin were negative (Fig. 2).

Electron micrographs show characteristic subepithelial electron dense "humps" in the paramesangial portion (Fig 3), partial foot process fusion and replacing the endothelium partly by a portion of a polymorphonuclear leukocyte (Fig 4), and PML is intimately applied to a large portion of the luminal surface of the basement membrane (Fig 5).

## CASE 2

A 9 years old girl was admitted to the hospital due to microscopic hematuria. Nine days prior to admission, she developed a sore

throat and was treated with penicillin on an ambulatory basis under the impression of acute follicular tonsillitis and microscopic hematuria was found incidentally by routine urinalysis and she was advised admission for further work up. She was hospitalized four years ago because of acute poststreptococcal glomerulonephritis. Although the  $C_3$  level was not checked at that time, her physical findings and increased ASOT with macroscopic and microscopic hematuria was compatible with the diagnosis of APSGN. She has been followed since discharge and her microscopic hematuria completely disappeared one year later.

Physical examination on recent admission revealed blood pressure 110/90, and no edema was found. Hemoglobin was 11.8 gm%, hematocrit 34.0%, leukocytes 5,500/mm<sup>3</sup>, ESR 2 mm/HR, ASOT 1:340, BUN 12 mg%, serum creatinine 0.8 mg%, and total serum protein 7.8 gm% with albumin of 4.8 gm%. Hepatitis B surface antigen and antinuclear antibody were all negative. Throat culture disclosed  $\alpha$ -streptococci and  $C_3$  complement was 120 mg%. Urinalysis showed many RBCs with a trace of protein. All of the laboratory results were not sufficient to reach any diagnosis. Intravenous pyelogram for renal biopsy preparation was normal. Percutaneous renal biopsy was performed on the 5th hospital day and she was discharged the next day. Urinalysis one month later showed no microscopic hematuria and also the ASOT was down to 1:85 and ESR 10 mm/HR, and repeat  $C_3$  complement still remained at a normal range (135 mg%).

**Pathological Findings; RB-79-36 (S-79-1259)**

Only the electron microscopic study was available. Electron micrographs show slight

mesangial matrix widening, swollen endothelial cells, some red blood cells and polymorphonuclear cells, with narrowed capillary lumen to variable degrees. The foot processes are partly fused, and subepithelial electron dense humps were rarely found (Fig 6).

Because of processing failure, immunofluorescent study could not be done and histopathological section showed extreme artifact, but no fibrosis or cellular infiltrations in the interstitium were present.

## Discussion

Following the first report about recurrence of APSGN in 1947 by Ramberg in his eleven cases, a few reports about second attacks of APSGN have been presented. Bernstein and Stillman (1960) reported three cases of recurrence which occurred between two years and 30 years after full recovery from the initial attack, and another two cases which recurred 13 months and 26 months later respectively from the initial disease of pyoderma infection were reported by Dodge (1968). But these two cases were found to be acute exacerbations in chronic glomerulonephritis by renal biopsy. Vernier *et al.* (1959) reported six cases but the findings of chronic glomerulonephritis was seen also with that of acute glomerulonephritis, i.e., infiltration of many polymorphonuclear leukocytes in glomeruli characteristic of APSGN and extensive tubular atrophy with severe fibrosis of glomeruli characteristic of chronic glomerulonephritis. Roy *et al.* (1969) reported twelve cases of a second attack of APSGN which occurred between 9 months and 82 months after the initial disease in their follow up of 590 patients with APSGN for 15 years.

Recovery from acute poststreptococcal glo-

merulonephritis was thought to be permanent (Loeb *et al.*, 1938). Acute exacerbation in chronic glomerulonephritis was confirmable by renal biopsy (Vernier, *et al.*, 1959). Acute exacerbation in chronic glomerulonephritis and a second attack of acute poststreptococcal glomerulonephritis would not be differentiated clinically because hematuria and proteinuria can also continued for months or years in the latter but be distinguishable clearly by histopathological, immunofluorescent and electron microscopic methods.

In our cases, histopathological findings show no interstitial fibrosis or cellular infiltrations. Glomerular sclerosis or hyalinization are not present. Highly cellular glomeruli with infiltration of polymorphonuclear leukocytes are only seen. Immunofluorescent findings show small amounts of granular deposit of IgG, and abundant granular deposits of C<sub>3</sub> mainly along the peripheral loop and some in the mesangium. Along with the findings, electron dense subepithelial deposits "hump", and polymorphonuclear leukocytes are seen. These findings are all characteristics of APSGN.

These characteristics are similar to an initial attack of acute poststreptococcal glomerulonephritis. Generally, APSGN occurs 10 days to two weeks after a streptococcal infection but transient hematuria can appear on the 3rd to 4th day of infection. This is due to direct damage to the glomeruli by streptococcal toxin (Steson *et al.*, 1955; Siegal *et al.* 1955). Strains of nephritogenic streptococci have been known to be 12, 4, 6, 19 and 25 serotypes but recently more types with increasing numbers have been reported to be nephritogenic. These reports are suggestive of more instances of newly known nephritogenic streptococcal infection and these are

related to secondary attacks of APSGN (Roy *et al.*, 1969).

Another report by Potter (1965) disclosed that proper penicillin therapy within ten days of streptococcal infection might suppress type-specific immune response and then type-specific antibody to nephritogenic streptococci is not formed by about half of their cases. These give another suggestion that proper penicillin therapy at an early stage of streptococcal infection may lead to a second attack of APSGN due to lack of immune response.

In our two cases of a second attack of APSGN, full doses of penicillin at the first attack might suppress formation of type-specific antibody and give another chance to reinfection by streptococci but also new different types of nephritogenic streptococci might be related to these second attacks.

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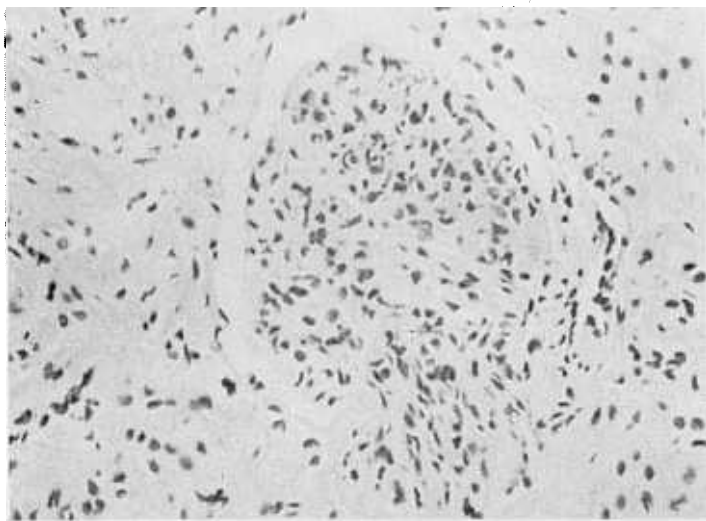


Fig. 1. Case 1. HE stain 430×

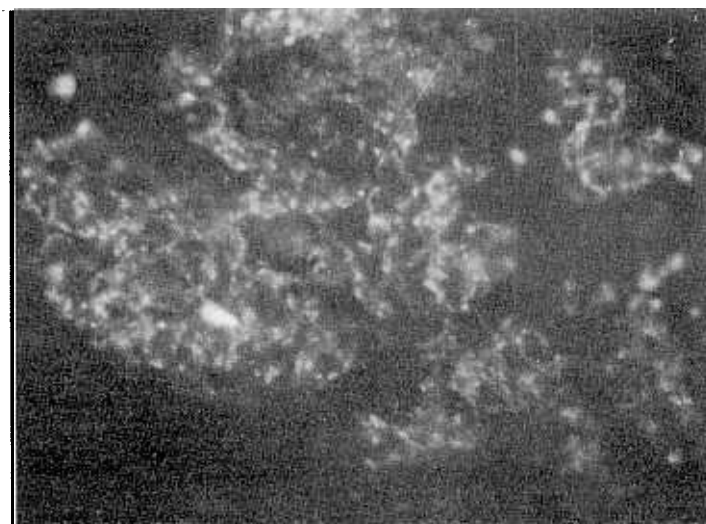


Fig. 2. Case 2. C3 IF stain 430×

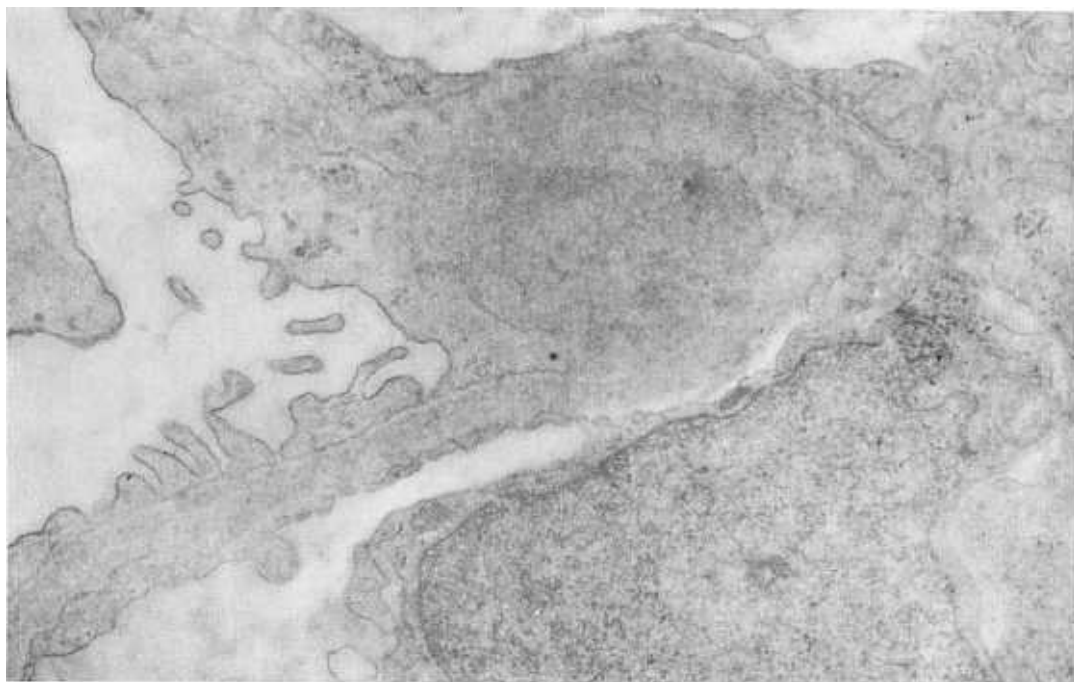


Fig. 3. Case EM 30,000×

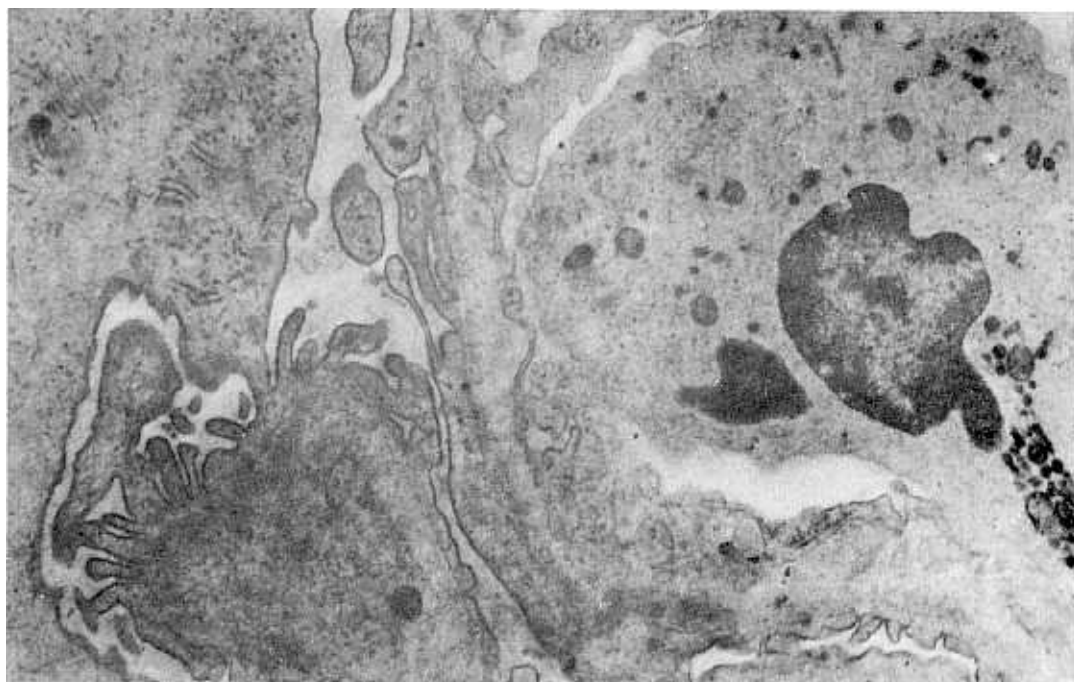


Fig. 4. Case 1. EM 16,000×

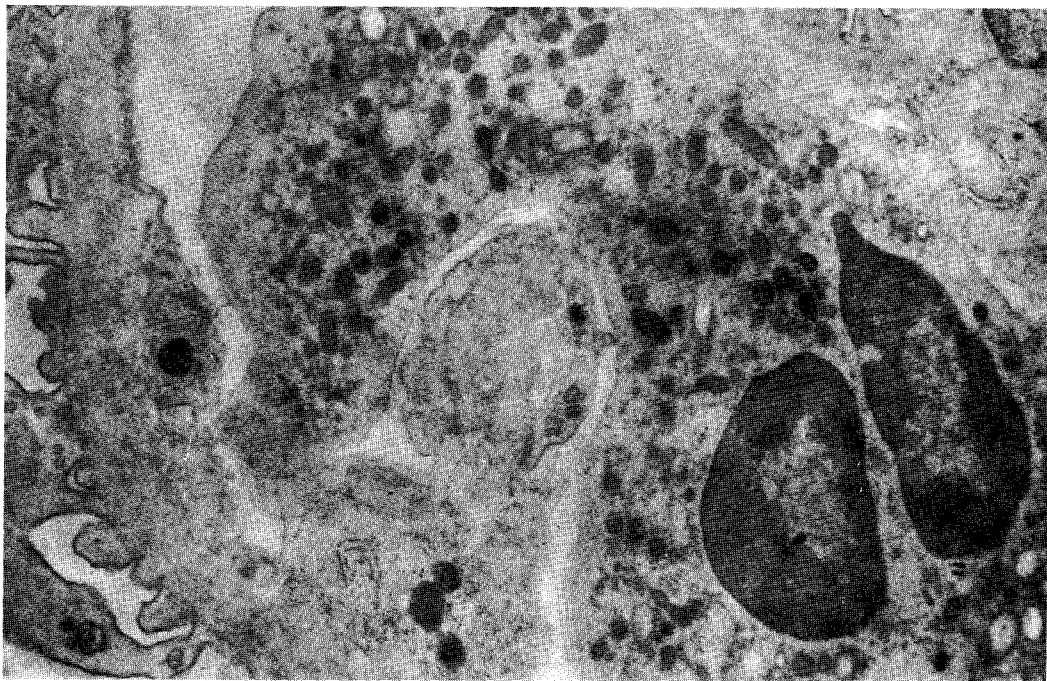


Fig. 5. Case 1. EM 22,500×



Fig. 6. Case 2. EM 40,000×