TEACHING ARTICLE

ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS (APSGN)

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Acute Post streptococcal Glomerulonephritis (APSGN) is a delayed nonsuppurative complication of pharyngeal infection or impetigo with certain nephritogenic strains of group A β hemolytic streptococci. APSGN following pharyngitis is most commonly associated with serotype M-12, but following impetigo M-49 is most commonly identified. The disease is closely associated with low socioeconomic status and overcrowding. Improving the living conditions significantly reduces the incidence (1, 2).

Pathogenesis

The pathogenetic mechanisms leading to renal damage are not fully understood, however, circulating immune complexes are associated with glomerular damage. Theories on the pathogenesis of post streptococcal glomerulonephritis could be summarized as follows: a direct toxic effect of streptococcal products on the glomeruli, antibody elicited by the nephritogenic streptococci may cross- react with one or more renal antigens leading to antibody-mediated glomerular injury or circulating immune complexes composed of streptococcal antigen and antibodies deposited in the glomeruli.

The evidences for immunologic injury are: a There is a latent period between infection and the development of nephritis b) hypocomplementemia is almost always present during the acute phase of the disease c) immunoglobulins, complement, and antigens that react with streptococcal antisera can be detected in involved glomeruli d) several investigators have demonstrated the presence of streptococcal antigens in the glomeruli of these patients (3, 4).

Pathophysiology

Symptomatology in acute post streptococcal glomerulonephritis is due to the result of reduction in glomerular filtration rate. The surface of glomerular filtration is markedly reduced because of the inflammatory process and renal blood flow is reduced. This results in elevation of creatinine and blood urea nitrogen. The child becomes acidotic and because of enhanced absorption of fluid and solute in the distal tubule and collecting tubule; oliguria or anuria results clinically.

Because of fluid retention and expansion of intravascular volume, the child develops hypertension and edema.

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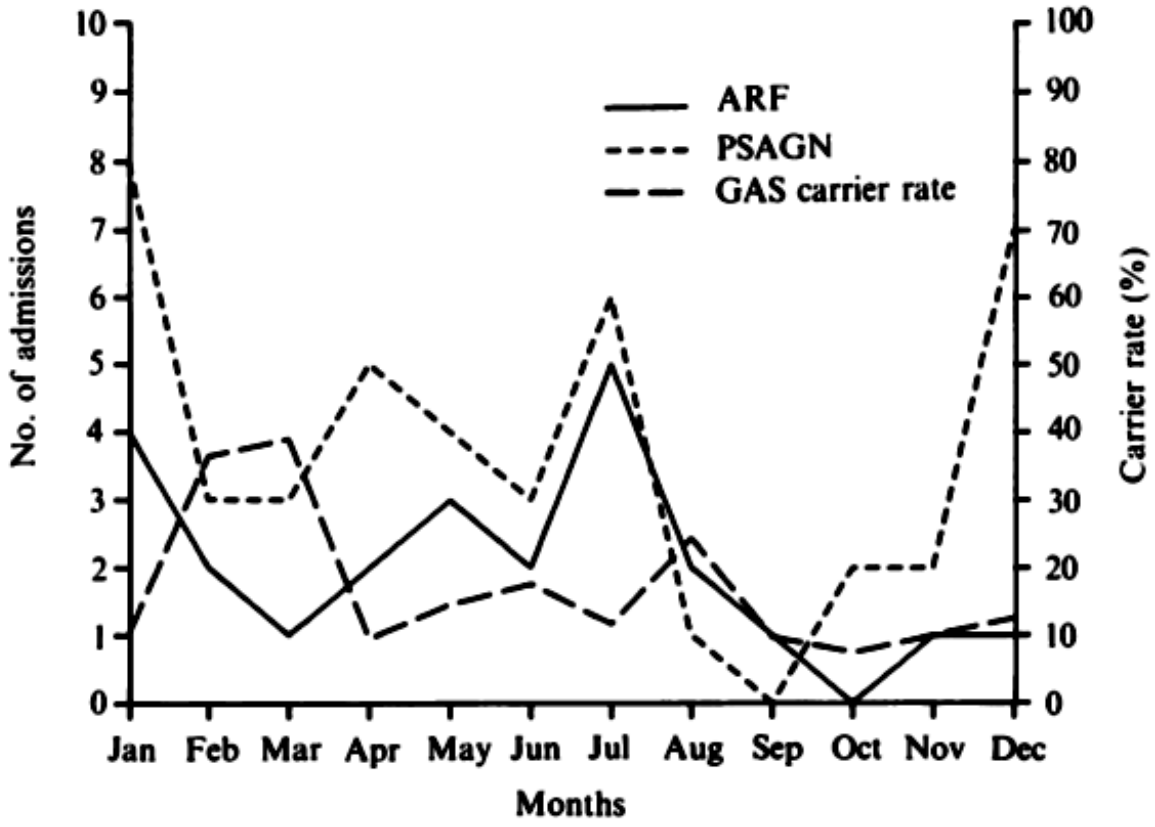
The child could be isonatremic or could develop dilutional hyponatremia. Serum potassium and phosphate levels are elevated, serum calcium level could be normal or reduced (4, 5).

Epidemiology

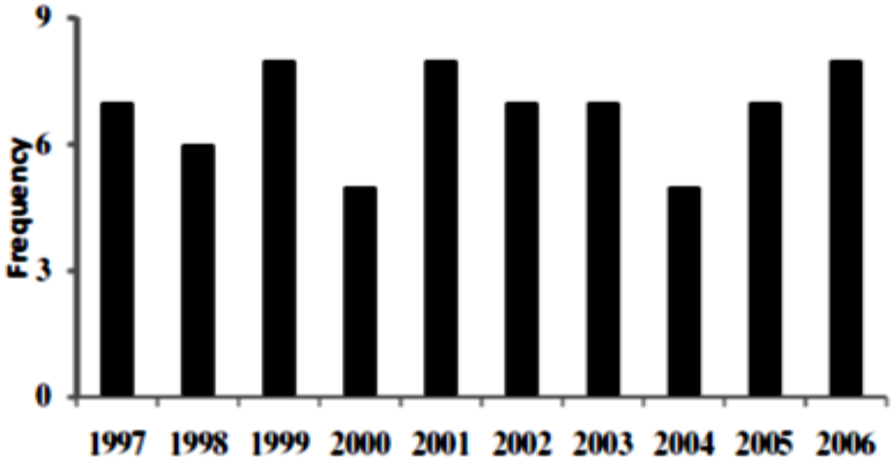
It is the commonest glomerular disease in children. It occurs sporadically but might also occur in epidemics in some rural communities and over crowded urban living conditions. It usually follows pharyngitis in winter and early spring, and impetigo in summer and fall. A study in a tertiary referral hospital in Addis Ababa has shown that admissions due to APSGN in children were highest in the months of December and January (6, 7). A Nigerian study showed two peaks in the occurrence of APSGN May- July and October to January (8).

Graph 1. Streptococcal infections among Ethiopian children



Number of monthly admissions of ARF patients and APSGN patients in the Ethio- Swedish Children's Hospital, Addis Ababa during 1990 and GAS carrier rate among apparently healthy school children.

Graph 2. Yearly distribution of APSGN in Nigerian Children



Incidence might be difficult to determine because of a high rate of asymptomatic or mild cases but overall attack rate is 10-15 %. Only < 5 % of cases are less than 2 years of age probably because group A streptococcal pharyngitis is uncommon in this age and children in this age are not able to mount immunologic response against group A streptococcal infection. The youngest child affected in literatures is 8 months old. It is most common in children between 5 to 15 years of age (9, 10).

Clinical features

The triggering event is an initial infection with streptococcal pharyngitis or skin infection. The usual skin infections in underprivileged populations of Africa are infected scabies and jiggers. Latent period is 7-14 days following pharyngeal infection and up to 6 weeks following impetigo. Subclinical cases are common. Previously healthy child classically presents with gross hematuria, oliguria, edema, acute renal dysfunction and symptoms of hypertension. Occasionally, the child presents with ascites, pleural effusions or congestive heart failure. Severe cases may develop encephalopathy and seizure (9, 10).

Laboratory diagnosis

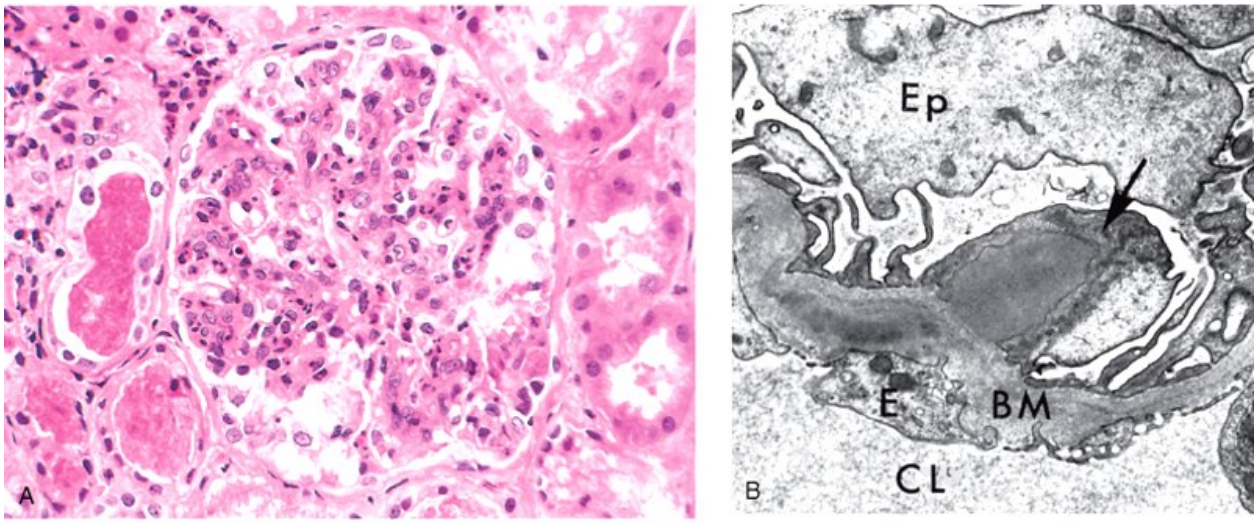
Urinalysis usually shows hematuria and leukocyturia. Sometimes associated red blood cell casts are seen. Urine dipstick usually shows low grade proteinuria (+1 or +2 sometimes nephrotic range proteinuria).

Blood urea nitrogen and creatinine are elevated but could also be normal in mild cases. ASO titer elevated in APSGN following throat infection but it rarely rises after streptococcal skin infection.

The best single antibody titer to measure is anti DNase B antigen the other alternative is Streptozyme test. If there is an active lesion, culture throat swab or from pyoderma. C3 complement is low (9-11).

Histology

Renal biopsy should be reserved for those cases with atypical presentation, have a protracted course and when the child fails to improve in three to four weeks. Biopsy shows focal or diffuse proliferation of mesangial and endothelial cells, infiltration of glomeruli by polymorphonuclear leukocytes and sub epithelial immune complexes (humps) (4, 9-11).



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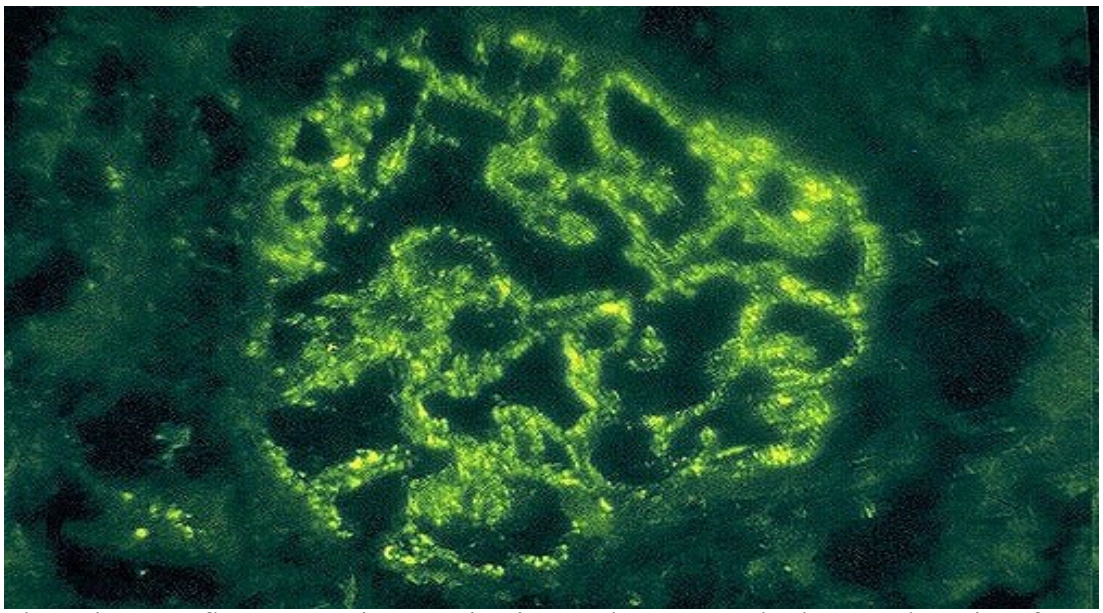
Above (left) light microscopic picture shows diffuse hypercellularity of the mesangial and endothelial cells, inflammatory cell infiltration and narrowing of the capillary lumen. Electron micrograph picture (right) shows the typical electron dense deposits “humps” on the epithelial side (Ep) of the basement membrane (BM) due to sub epithelial immune complexes. E- endothelial cell, CL- capillary lumen.



The above immunoflorescent microscopic picture shows granular bumpy deposits of complement 3 and IgG.

Treatment Strategy

No specific treatment, but the management is that of acute renal failure or treatment of complications. Though a 10-day course of systemic penicillin is recommended to prevent the spread of the nephritogenic organisms, there is no evidence that antibiotics change the course of the illness. In our experience most children with AGN present after the clearance of either the throat infection or pyoderma or they might have trivial symptoms at the onset of infection and throat swabs are not yielding. In such cases antibiotics will not help. Some patients present with pulmonary congestion, fever and cough and chest x-ray might be interpreted as pneumonia, in such situations we treat them for pneumonia. Resistance to penicillin is unusual and a seven to ten days course is given but for penicillin allergic patients erythromycin could be used (1,4).

Activity does not need to be restricted, except in the acute phase of the illness.

Fluid and salt restriction is indicated in situations where there is an evidence of fluid retention manifested by edema, hepatomegaly, ascitis, congestive heart failure and pulmonary edema. In our experience, severe clinical manifestation are the reasons for seeking medical attention and children with AGN present with full blown picture of nephritic syndrome but ascitis and low serum albumin are not usual findings. The 24 hours urine out put has to be measured for planning future fluid management.

The twenty four hour fluid requirement shall be limited to insensible loss plus any output. The estimated insensible loss is 400ml/m^2. This fluid shall be replaced as electrolyte free fluid since insensible losses do not contain significant electrolytes. Unless the child is unable to take orally, oral intakes shall be encouraged other than giving IV fluids.

Hypertension and other signs of volume overload shall be treated with frusemide to promote diuresis. In our experience loop diuretics alone are enough for the control of hypertension but sometimes add nifedipine if diuresis has not taken place within 24 hours and if the patient is still oliguric. Most of the patients' signs of congestion and hypertension improve or resolve within one week but there are few cases whose hypertension remains for up to 2-3 weeks. By the time of discharge from hospital, all anti-congestive or anti-hypertensive medications shall be discontinued. Hypertensive encephalopathy shall be treated with sodium nitroprusside.

Hyperkalemia, hyperphosphatemia and acidemia might occur in severe cases. Monitor urea and potassium level. Restrict potassium and phosphate intake and alkalinize with sodium bicarbonate. Hyperkalemia may temporarily be treated with rectal or oral exchange resins, administration of insulin with glucose and counteracting the effect of hyperkalemia with the administration of calcium gluconate. These temporary measures might fail and dialysis might be required. We have few patients who required peritoneal

dialysis due to failure of the other supportive measures. The outcome to peritoneal dialysis is excellent (3, 12-14).

Watch for recovery within 7 days, keep high index of suspicion for diseases other than acute post-streptococcal glomerulonephritis.

Prevention

Post streptococcal sore throat or skin infection has to be treated but it is not yet clear whether antibiotic treatment prevents APSGN. Immunity against streptococcal infection is type specific and long lasting. Recurrence is rare and it ranges between 0.7 to 7%.

A ten days course of oral or intramuscular penicillin or erythromycin in penicillin allergic patients is the choice of treatment to prevent the spread of streptococcal infection especially in resource limited situations. Cephalosporins are also alternatives (4).

Prognosis

About 95% of children recover without sequel but prognosis depends on the severity of glomerular injury. Studies have shown that if more than 50% of the glomeruli are involved with crescent formation the prognosis is poor. Persistence of hypertension and nephrotic range proteinuria are also indicators of poor renal outcome.

By 8 weeks; C3 must return to normal, proteinuria might resolve but it may remain positive for about six months, (microhematuria may continue up to 1-2 years). Less than 5% of patients suffer chronic renal impairment (11, 15).

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