MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

DISTANCE LEARNING CENTRE

DEPARTMENT OF „NEPHROLOGY, HEMATOLOGY AND GASTROENTEROLOGY“

LECTURE № 1

FOR E-LEARNING IN „NEPHROLOGY“

FOR MEDICAL STUDENTS

TITLE: **ACUTE GLOMERULONEPHRITIS**

PREPARED BY:

PROF. DR. VASIL TODOROV DSC

PLEVEN, 2020

ACUTE GLOMERULONEPHRITIS

Epidemiology. AGN is decreasing in USA, Europe and UK, but continues to be a significant cause of morbidity worldwide as indicated by reports from Africa, Australia, Middle East, South America. In Pakistan, Malaysia and India the acute endocapillary glomerulonephritis is the most common histologic presentation of primary renal disease with streptococcal etiology.

Children in age 5-15 years are most commonly affected, but AGN can occur in any age. In endemic countries about 5% of the patients are younger than 2 year and about 10% - older than 40 years of age. *Both sexes are affected equally* .

Etiology. Group A streptococci of M types 1, 2, 4, 6, 12, 18, 25, 31, 49, 60 have been isolated from patients with glomerulonephritis. Specific M types as 47, 49, 55, 57, 60 are associated with impetigo resulting in nephritis.

The throat infection with streptococcus 49 M type carries a 5% risk of nephritis, while the same infection of the skin carries a risk 5 times larger. Overall the risk of AGN after streptococcal infection has been estimated to be about 15 %.

Pathogenesis. Repeated infection of *M-protein* alone or in association with fibrinogen results in nephritis with localization of M-protein-fibrinogen complexes in glomeruli. Furthermore there is cross-reactivity between glomerular basement membrane and M-protein. Nevertheless it appears unlikely that M-protein is the relevant antigen in nephritis. The New York Medical College group isolated in 1976 year an antigen – *endostreptosin* . Villareal et al., 1979, isolated from cultured supernatants of nephritogenic strains s.c. *nephritis strain associated protein*. Another antigen – a *cationic proteinase,* isolated from nephritis-associated streptococcus was demonstrated in renal biopsies. In addition, the sera of patients with PSGN have *antibodies against glomerular basement membrane* components such as heparan sulphate proteoglicans, collagen type IV and laminin.

Traditional explanation of the pathogenesis of AGN gave a cen-tral role to **immune complexes** formed in circulation and eventually deposited in the glomeruli, where they recruited the complement cascade and inflammatory cells, thereby triggering a pathogenic reaction.

Traditionally AGN has been considered a disease caused by deposition of circulating immune complexes.

Pathology. The kidneys are slightly enlarged and pale, with smooth surface. The typical microscopic changes are these of *diffuse endocapillary nephritis*: increased number of endothelial and

mesangial cells is found in glomerular tuft, which seems to feel Bowman's space. In the first month there are neutrophil and monocyte infiltration, a finding referred to an exudative GN.

Immunoglobulin G, M and components of the complement are localized in glomeruli. The last one can damage membrane by cell-independent mechanisms, related to chemical mediators of inflammation produced by, macrophages and mesangial cells.

Ultrastructural studies have shown electron-dense deposits in subepithelial, endothelial and intramembranous position. Deposits in subepithelial space have a dome-liked appearance and are called "humps"; they are characteristic, but not exclusive and tend to disappear after 6 weeks. The humps contain IgG. The basement membrane under the humps can show local abnormalities.

Exocapillary proliferation with extensive crescent formation has been found in some cases, which usually are characterized clinically by progressive nitrogen retention. It has been stated, that crescentic poststreptococcal GN has better prognosis than others.

Clinical manifestations

The usual locations of streptococcal infection are throat and skin, but other sites are possible. The latent period of postimpetigo nephritis is 3 to 6 weeks.

Streptococcal pharyngitis can cause few symptoms associated with cervical/ lymphadenopathy, fever and tonsillar purulent exudate. The latent period after upper respiratory tract infection is 1 to 3 weeks.

AGN is subclinical in the majority of cases and is manifested by microscopic hematuria. The prospective studies give a subclinical-clinical ratio of 4,0.

Clinicaly nephritis is manifested with typical nephritic syndrome.

Hematuria is present in practically all patients. Exceptionally the urinary sediment could be normal. Glomerular hematuria is mani-fested by red cell casts and by dysmorphism in 80% of hematuric cases.

Edema is the chief compliant in almost two-third of the patients. Generalized edema is found in one-third of the patients.

Blood pressure is elevated in more than 80% of patients. Pa-tients or relatives in about half of cases notice diminished urinary output.

Congestive *heart failure* is a complication related to excessive fluid retention.

Somnolence, convulsions and coma in association with severe hypertension are characteristic of hypertensive *encephalopathy*; papiloedema and increased cerebrospinal fluid pressure are not always present and local vasoconstriction has been implicated in the pathogenesis of this complication.

Malaise, weakness and anorexia were present in a half of patients, and nausea, vomiting and dull lumbar pain are less common.

Proteinuria is found in 80% of the patients, but only in 10% of them it exceed 2 g/d. The nephrotic syndrome is present in less than 4 %.

The improvement of acute nephritic syndrome begins 4-7 days after the start of the treatment. The child becomes free of edema and normotensive 1-2 weeks later. Microscopic hematuria may persist for a year.

Serologic findings in AGN include detection of antistreptococcal antibodies, increasing level of serum Immunoglobulins, anti-immu-noglobulins, immune complexes, decreasing of serum complement. Antistreptolysine O titers /ASO/, antiDNase, antihyaluroni-dase are well known markers of streptococcal infection. The se-verity of nephritis and the titers level are not related. ASO titer increases 1-3 weeks after infection, reaches the maximum after 3-5 weeks and normalizes in the following months.

Prognosis. Mortality is low – 5-1%, due to complications such as pulmonary edema, hypertensive encephalopathy, sepsis. Poo-rer prognosis in adults may correspond with coexistence of other diseases – diabetes, liver and cardiac ones. The prognosis is excellent in those patients, who recover from the initial acute epi-sode, although progression to chronicity was known to occur in some cases.

The prognosis is different in adult and children. 30-55% of adult have abnormal urine sediment or proteinuria 10-15 year after acu-te episode. In children the similar cases are 10 times less frequent.

Diagnosis. It is not too difficult in the classical forms of the disease. The typical constellation of signs and symptoms includes: anamnestic data for previous streptococcal infection, seasonality and age of the patient, triad of Volhard, oliguria, normal specific gravity of the urine, slightly increased levels of urea and creatinine. It may be helpful to estimate the serum complement, antibodies against streptococcal antigens /AST/ or to isolate Streptococcus from the infection site. Serum levels of hemolytic complement /C_{50}/ and C_3 are depressed. Serum levels of IgG and IgM are increased in most of patients.

Treatment. It has to be carried out in a hospital and in a specialized clinic for kidney disease. The regimen is “in bed”. Its strictness depends of the severity of the main disease and the presence of complications. Patients should be kept under close observation, because a seemingly mild case

may develop severe hypertension and oliguria. During the first days the diet is “thirst and hunger”. All patients benefit from restriction of sodium and fluid intake.

The volume of the taken water has to be strictly suitable to the urine output.

Etiologic treatment includes 10-14 days course with Ampicillin, 4x1,0 g. It is possible to be used Penicillin, 4 mln. UI/d. In persons allergic to penicillin, erythromycin /250 mg every 6 hours in adults, or 40 mg/kg BW in children, for 10 days/.

Prolonged rophylactic therapy should be done with benzyl penicillin 1 200 000 UI, every 7-15 days in the following two months after the first antibiotic course.

Pathogenic therapy is simple and non-specific. Calcium gluconas, amp., 10%, 10 ml and Vit. C, amp. 500 mg, twice daily intrave-nously are usual combination for 10 days.

Symptomatic therapy includes medication for subcutaneous ede-ma, hypertension, cardiac failure and brain edema. Loop diuretic furosemid can be administered parenterally or orally in daily dose 20-80 mg. Angiotensin converting enzyme /enzaim/ inhibitor captopril is used in dose 50-150 mg/d. Nifedipine, 10 mg sublingually after breaking capsule could in 1 hour to decrease blood pressure. Parenteral diazoxide, hydralazine or sodium nitroprusside are appropriate choice if hypertensive en-cephalopathy is present. Hyperosmotic solution of mannitol and diazepam intravenously are indi-cated to treat brain edema. Pulmonary edema should be trea-ted with diuretic, tourniquets, oxygen. Digitalis is contraindicated because is ineffective.

Oliguria, uremia and hyperkalemia in very rare cases could be treated with dialysis.