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CASE SET #18

A Microbiology Case:

Pharyngitis Leading to Acute Poststreptococcal Glomerulonephritis

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Clinical Laboratory Investigations

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LEARNING OBJECTIVES

Upon completion of reading the case, the learner will be able to:

1. Describe the cause, epidemiology, typical presentation, laboratory findings, and progression of Acute Poststreptococcal Glomerulonephritis (APSGN).

2. Discuss the pathophysiology of APSGN and how it relates to symptoms.

3. Describe the treatment options and necessary management for APSGN.

Pharyngitis Leading to Acute Poststreptococcal Glomerulonephritis

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CASE PRESENTATION

A 6-year-old male presents to his primary care physician with complaints of fatigue, abdominal pain, and sore throat. His symptoms have persisted and worsened over the past five days. The patient's mother notes that her son has been very irritable and has been refusing to eat due to the pain he experiences upon swallowing. The patient has no significant medical history. During initial physical exam, the physician finds that the patient has a slight fever, petechiae on his hard palate, and very inflamed tonsils.

Based on the patient's age and symptoms, the physician's differential diagnoses include bacterial pharyngitis, viral pharyngitis, and infectious mononucleosis. A blood sample is collected from the patient and sent to the laboratory for a rapid mononucleosis test. This test comes back negative. The physician also swabs the back of the patient's throat to obtain a sample for a rapid strep test. The rapid strep test comes back positive for Group A *Streptococcus* species, the common causative agent of bacterial pharyngitis. The patient's symptoms along with his rapid strep result confirm the physician's suspicion of bacterial pharyngitis.

Strep throat is a bacterial infection typically caused by *Streptococcus pyogenes*, a Group A beta-hemolytic *Streptococcus* species. It is most common in school-aged children, and infections occur more often during the winter months.[1] Strep throat can be

easily treated with antibiotics, but the infection can lead to severe sequelae if left untreated. In this case the physician prescribes penicillin to treat the bacterial infection and advises his patient to get lots of rest.

Ten days later, the patient returns with complaints of persistent abdominal pain, headache, and dizziness. The patient's urine has also appeared brown for the past three days. During physical exam, the physician notes that the patient is hypertensive and is showing mild periorbital edema. The physician requests a urine sample from the patient and orders a urinalysis to investigate the discolored urine. He also collects a blood sample and orders a complete blood count (CBC) and basic metabolic panel (BMP). The CBC results are within normal range (Table I). The BMP shows elevated blood urea nitrogen (BUN), creatinine, and potassium levels. Urinalysis detects the presence of leukocytes, protein, and blood (Table III).

Table I: Patient's Hematology (CBC) Test Results

Test	Result	Reference Range	Units
White Blood Cell Count	9	4-11	10^9/L
Neutrophils	56	50-75	%
Bands	1	0-3	%
Lymphocytes	34	20-40	%
Monocytes	7	3-10	%
Eosinophils	1	0-3	%
Basophils	1	0-1	%
Red Blood Cell Count	4.5	4-6	10^{12}/L
Hemoglobin	13	12-17	g/dL
Hematocrit	39	36-52	%
Mean Corpuscular Volume	86.7	80-100	fl
Mean Corpuscular Hemoglobin	28.9	27-31	pg
Mean Corpuscular Hemoglobin Concentration	33.3	32-36	g/dL
Red Cell Distribution Width	14	11-15	%
Platelet Count	255	150-400	10^9/L
Reticulocytes	0.6	0.5-1.5	%

Table II: Patient's Chemistry (BMP) Test Results

Test	Result	Flag	Reference Range	Units
Blood Urea Nitrogen	31	*	7-20	mg/dL
Creatinine	1.7	*	0.8-1.4	mg/dL
CO_2	25		20-29	mmol/L
Glucose	99		64-128	mg/dL
Chloride	106		101-111	mmol/L
Potassium	5.6	*	3.7-5.2	mEq/L
Sodium	140		136-144	mEq/L

Table III: Patient's Urinalysis Test Results

Test	Patient Result	Flag	Reference Range
Color	Rust-Colored	*	Yellow
Clarity	Hazy	*	Clear
pH	5.5		4.5-8
Specific Gravity	1.020		1.005-1.025
Leukocytes	1+	*	Negative
Protein	2+	*	Negative
Glucose	Negative		Negative
Ketones	Negative		Negative
Blood	2+	*	Negative
Nitrites	Negative		Negative
Urobilinogen	Negative		Negative
Bilirubin	Negative		Negative

Due to the abnormal urinalysis results, the medical laboratory scientist performs a microscopic exam of the urine. She finds many red blood cells, moderate red cell casts, few granular casts, and few white blood cells (Table IV).

Table IV: Patient's Microscopic Urine Test Results

Test	Patient Result	Flag	Reference Range
Red Cells	Moderate	*	0-3/HPF
White Cells	Few	*	0-5/HPF
Casts	Moderate	*	0-1 Hyaline/LPF
Epithelial Cells	None Seen		Few/HPF

Bacteria	None Seen		None Seen
Crystals	None Seen		None Seen

HPF = high power field

LPF = low power field

The elevated BUN and creatinine levels along with the abnormal urine composition are associated with diminished renal function. Considering the patient's laboratory results and recent history of strep throat, the physician strongly suspects a case of Acute Poststreptococcal Glomerulonephritis (APSGN). He asks the patient's mother if her son took the full course of antibiotics prescribed to treat his bacterial pharyngitis. The patient's mother informs him that her son took the antibiotics for the first day, then stopped taking them once his symptoms subsided the following day.

The physician adds on an order for a complement C3 serum level to confirm his suspicion of APSGN. The patient's C3 level of 51.2 mg/dL is below the reference range of 88-252 mg/dL and is consistent with APSGN. Complement C3 values are decreased in 90% of cases of APSGN.[2]

Based upon a diagnosis of APSGN the physician prescribes penicillin to clear the remaining Group A *Streptococcus* organisms. He also prescribes a low-dose diuretic and instructs the patient to limit his salt and fluid intake for the next few weeks to help control the hypertension and edema. The physician schedules several follow-up appointments to monitor the patient's blood pressure, urine composition, and C3 level. The patient's blood pressure and edema normalize after two weeks. The C3 serum level returns to normal after six weeks. His hematuria and proteinuria gradually decrease and eventually resolve after six months. The patient makes a full recovery, but the physician continues to follow-up with the patient yearly to ensure that he remains in good health.

DISCUSSION:

Acute Poststreptococcal Glomerulonephritis is one possible sequelae of untreated *Streptococcus* Group A infections. Patients typically present with hematuria, hypertension, and edema. [3] APSGN can occur secondary to pharyngitis or skin infections caused by nephritogenic strains of Group A beta-hemolytic *Streptococcus* species.[2] Research has shown that there is a correlation between APSGN and the specific M protein serotype present on Group A *Streptococcus* species. Group A *Streptococcus* species that express M 1, 4, 12, 49, 55, 57, and 60 proteins are more commonly associated with APSGN.[2]

The disease has three phases (latent, acute, recovery) following the initial streptococcal infection. [3] The latent phase is the inactive, asymptomatic period between the initial infection and the onset of secondary symptoms. This latent period typically occurs approximately 1-3 weeks following pharyngitis, and 3-6 weeks following impetigo.[2] The acute phase is the nephritic phase where patients experience symptoms such as hematuria, oliguria, edema, hypertension, and back pain. [2] This phase generally lasts for one week. The final stage is the recovery phase where symptoms begin to subside. This can take several weeks or even months depending on the severity of the case.[3]

When streptococcal infections are left untreated the bacterial infection persists, and levels of anti-streptococcal antibodies, such as anti-streptolysin O, increase.[3] Antigen:antibody complexes form, and these complexes deposit in the basement membrane of the kidney glomeruli. The antigen:antibody complexes activate the

complement system, leading to inflammation. The integrity of the glomerulus is disrupted, making it possible for cells and proteins to pass through. This leads to hematuria and proteinuria in patients.[4]

During the body's inflammatory response neutrophils, eosinophils, and monocytes infiltrate. The renal endothelial and mesangial cells surrounding the blood vessels also respond to the damage and proliferate. This cell proliferation narrows the lumens of the glomerular blood vessels, causing a slower rate of blood flow and a decreased glomerular filtration rate (GFR).[2] Because of the decreased rate of filtering, patients may experience oliguria. Sodium and water are retained, which accounts for the hypertension and edema in patients.[3]

There is some debate as to the exact mechanism of immune complex deposition. Some researchers believe that preformed, circulating antigen:antibody complexes deposit in the glomeruli. Others believe that immune complexes form in situ; antigens have a strong affinity for the glomeruli, so they localize there, and then circulating antibodies bind to form immune complexes. Others believe that antibodies directly react with glomeruli due to molecular mimicry.[3]

Classic cases of APSGN are generally straightforward and relatively simple to diagnose based on a patient's symptoms (hematuria, oliguria, edema, and hypertension) and recent history of streptococcal infection. Antibody titers to streptococcal antigenic molecules such as antistreptolysin O, antihyaluronidase, and anti–DNAse will be elevated in patients with APSGN.[3] BUN and creatinine levels will be elevated due to decreased rate of glomerular filtration. Patients also show decreased

levels of complement C3 due to the activation of the complement pathway. Urinalysis results show hematuria, proteinuria, and red cell casts.[5]

In atypical cases, patients may lack a recent history of a streptococcal infection, have uncharacteristic symptoms, or could be completely asymptomatic. In these situations, additional laboratory testing may be needed to come to a definitive diagnosis. When APSGN is suspected, a renal biopsy may be performed. Light microscopy, immunoflourescent microscopy, and electron microscopy may be used to detect irregularities in the glomeruli. The glomeruli in patients with APSGN are hypercellular, and there may be some crescent formation in severe cases. Immunoglobulin G and C3 deposits appear along glomeruli capillary walls, and immune complex deposits are usually found along the glomerular basement membrane.[4]

Acute Poststreptococcal Glomerulonephritis is typically self-limiting. Treatment includes antibiotics to clear any residual streptococcal infection along with supportive care to treat symptoms.[6] Patients may need to take diuretics and restrict sodium and water intake to normalize hypertension and edema. If diuretics are not effective in lowering blood pressure, patients may need to take beta-adrenergic blockers or angiotensin-converting enzyme inhibitors. In very severe cases with significant kidney damage, patients may require hospitalization and dialysis.[5]

Physicians should closely monitor patients with APSGN until hypertension and edema begin to normalize. The acute phase of the illness usually resolves within one to two weeks.[4] However, monthly follow-ups are necessary to check blood pressure, BUN, creatinine, C3 levels, and urinalysis results to ensure that they are returning to normal range. Serum creatinine levels typically normalize within 4 weeks. C3 levels should

return to normal after 6-8 weeks. Abnormal urinalysis findings may persist for several months or even years.[4]

APSGN is more common in children than adults. It most often occurs in children ages 2-6, and it affects more males than females.[2] The incidence of APSGN has decreased in recent years. Today, the condition is most common in developing countries that do not have access to antibiotics.[7] Complications such as congestive heart failure, renal failure, uremia and azotemia may occur in severe cases, [6] but prognosis is usually very good, especially in children. [7] Recurrence of the condition is rare.[6]

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