Pathology – 2nd lecture

Renal Block

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Urinary Tract Obstruction:

A. This obstruction may occur anywhere in the urinary system.

B. In children, the condition is most often due to congenital malformations (associated with reflux or other causes).

Urine retrograde may also happen in the case of flaccid bladder (bladder can't empty) Flaccid bladder can be a result of spinal cord injury.

C. In adults, the condition is most often acquired and usually occurring as a consequence of renal stones or benign prostatic hyperplasia.

D. Clinical manifestations include:

1. Renal colic, which is an excruciating pain caused by acute distention of the ureter, usually due to the transit (movement) of a stone.

Diagnosed by radiology

2. Hydronephrosis, which is progressive dilation of the renal pelvis and calyces. (Dilation before the point of obstruction & constriction after)

3. Infection, which is localized proximal to the site of obstruction and may lead to infection of the renal parenchyma.

Are caused by Obstruction

- Starts in the flank or loins regions and radiates to the testes. (It continues to the testicles because they have the same innervation)
- **Heamaturia**
- Dysuria
- Frequency

Pyelonephritis is almost always associated with lower UTI because of the ascending nature of the causative organisms.

INFECTIONS OF THE URINARY TRACT AND KIDNEY (PYELONEPHRITIS AND CYSTITIS):

Additional Reasons why women are more predisposed to UTI than men:
- The urethra is closer to the rectum than in males, and they are affected more to trauma during intercourse.
- In the case of Pregnancy: hormones like progesterone, cause relaxation of the muscles in the urinary tract, which predisposes stagnation and inflammation.

A. General considerations

1. The incidence of infection of the urinary tract and kidney is greatly increased in women, presumably because of the shorter length of the female urethra and the incidence is increased during pregnancy (because of pressure by the uterus).

→ During pregnancy, the uterus enlarges causing increasing pressure on the urethra and bladder.

2. This condition can be caused by hematogenous bacterial dissemination to the kidney or by external entry of organisms through the urethra into the bladder and in this case infection can spread upward from the bladder into the ureters (vesicounreteral reflux) and through the ureters to the kidney (ascending infection).

Or by infective endocarditis →

- Bacteria's growth increases in urine.
- With the reflux, urine here is a propeller of bacteria to the kidney.

3. Most frequently, the infection involves or is caused by the normal flora of the colon, most often Escherichia coli.

In male children, they may have a congenital malformation called posterior urethral valves and, it does not occur in females (PUV is the most common cause of lower urinary tract obstruction in male neonates

It causes obstruction → recurrent infection caused by stagnation in urine, high-grade fever (40 c^{o}) every now with leukocytosis.
Treated with antibiotics → case will resolve.
Obstruction to one or both kidneys is still not resolved. → Recurrent infection → chronic pyelonephritis.

B. Predisposing factors

1. Obstruction of urinary flow, such as that occurring with urethral obstruction in benign prostatic hyperplasia

2. Surgery on the kidney or urinary tract.

3. Catheters inserted the urethra into the bladder <<instrumination or cytoscopy (usage of a scope to examine the bladder)

4.Gynecologic abnormalities

In the pediatric age group: children may have disorders in the vesicoureteric junction that may cause reflux of urine up. Congenital muscles weakness at the junction is a prominent reason why this happens. The child will always present with fever + vomiting, regardless of the type of infection: otitis media, gastroentritis, UTI. The child will have dysuria but he can't express the pain his symptoms. You have to do a urine test, urine strips>> you will find + polymorphous cells in the urine.

C. Clinical manifestations

Focal inflammation in any part of the body: subacute endocarditis, pulmonary infection, soar throat, or even TB may erode an artery or vein and gets into the blood stream which gives hematogenous spread. This spread may either pick an organ (like the kidney, or single structures like the epididymis, or fallopian tubes. Hematogenous pread can also be seen in events of septicemia or miliary TB

1. Urinary frequency: a compelling necessity to void small amounts of urine at frequent intervals.

2. Dysuria: painful, burning sensation on urination

3. Pyuria: large numbers of neutrophils in the urine

Indicator of bacteria, WBCs casts → upper urinary tract infection.
*Casts are not found in lower UTI.

4. Haematuria: blood in the urine; urinary red cells are 'a nonspecific finding in urinary tract infection.

5. Bacteriuria: usually defined as more than 10^5 organisms per milliliter of urine: it must be distinguished from contamination of urine specimen by external flora.

6. Vomiting

7. Turbid, cloudy, and foul smelling urine

D. Additional diagnostically significant findings in acute pyelonephritis (acute infection of the renal parenchyma).

1. Fever, leukocytosis, flank tenderness, urinary white cells, and white cells casts in the urine (this latter finding is pathognomonic of acute pyelonephritis).
2. Greatly increased frequency in women, especially during pregnancy. (may come with diverticulum, outpouching of a hollow (or a fluid filled) structure in the body.)

E. Cystitis: Characteristics include pyuria and often hematuria, but urinary white cell casts are not found. **(UTI are caused by KEEPS)**

K: Kelibseila
E: E. coli
E: Enterobacteria
P: proteus
S: Staphylococcus

Pathology of Acute pyelonephritis:

- Normal sized or enlarged kidneys.
- Characteristic necrotizing abscess formation.
- Inflammation may first affect the interstitium but then may rupture into the tubules forming characteristic WBC casts (WBCs casts are found in pyelonephritis not in lower UTI)
  Casts are tiny tube-shaped particles made of certain cells (WBCs in pyelonephritis). These casts are formed in the tubules, and are formed by binding of these cells by certain proteins found in the tubules.
- In the acute stage of the disease of the glomeruli are intact, but maybe affected in later stages.
- Pyonephrosis may be seen after a certain amount of time.

Tubointerstitial nephritis is a term given when the inflammation is not of infectious origin

TUBULAR AND INTERSTITIAL DISORDERS OF THE KIDNEY.

Acute drug-included interstitial nephritis

Acute allergic interstitial nephritis, inflammation with no bacteria, they may present with renal failure.

1. Most often the trigger is penicillin derivatives (Synthetic forms) , such as methicillin, and other drugs/ such as nonsteroidal anti-inflammatory drugs and diuretics.

Chronic inflammation of the interstitium

2. The disease is most likely of immune etiology.

3. Acute interstitial renal inflammation including many eosinophils is characteristic.>> showing an allergic reaction
4. The nephritis resolves on cessation of exposure to the inciting drug. →

B. Renal papillary necrosis (necrotizing papillitis) is ischemic necrosis of the tips of the renal papillae.

Which leads to infarction

Prone to infection: pyelonephritis

1. This form of necrosis is most often associated with **diabetes mellitus**, in which it is related to renal infection and coexisting vascular disease. It is occasionally a catastrophic consequence of acute pyelonephritis.
2. **Because of the formation of septic embolism occlusion of the arteries that supply the papilla Ischemia with subsequent infarction, slough of papilla that end up going into the urine.**

Only if taken with aspirin

2. Renal papillary necrosis is also associated with long-term persistent abuse of **phenacetin**; most often when phenacetin in is used association with aspirin and other analgesics. This can lead to chronic analgesic nephritis, a chronic inflammatory change characterized by loss and atrophy of tubules and interstitial fibrosis and inflammation. Phenacetin is no longer approved for over-the-counter analgesia preparations (not allowed to be sold by pharmacies without prescriptions).

Because of it toxic metabolites

Suppress prostaglandins>> decreasing vasodilation >> predisposing ischemia

Clinical course (tubular & interstitial disorders of the kidney):

- Starts 15 days after exposure
- Fever
- Esoinophilia
- Rash may be seen
- Hematuria
- Leukocyturia
- Renal failure with resultant, ↑ serum creatinine level and oliguria

Pathology of Drug induced interstial nephritis:

- Edema
- Infiltration of Lymphocytes, macrophages, esoinophils and neutrophils.
- Interstitial granulomas with giant cells can be seen with some drugs, like: methicillin and thiazid.
- Glomeruli are many affected with NSAIDs with concorret nephrotic syndrome.

Chronic pyelonephritis. (Diffuse + globul glomerular sclerosis or fibrosis)

1. Coarse, asymmetric corticomedullary scarring and deformity of the renal pelvis and calyces occurs; these findings are essential for the diagnosis. At later stages the glomeruli may be affected not because of the disease, but because of the accompanying ischemia. It is a secondary phenomena because all this inflammation and edema will to local ischemia that will lead to fibrosis of the glomeruli. **(Contraction and damage of the kidney's may not be similar, one kidney maybe more damaged than the other).**

2. Characteristics include interstitial inflammatory infiltrate in the early stages and later by interstitial fibrosis and tubular atrophy; atrophic tubules often contain eosinophilic proteinaceous casts,resulting in an appearance reminiscent of thyroid follicles (thyroidization of the kidney).

3. Causes almost always include chronic urinary tract obstruction and repeated bouts (attacks) of acute inflammation.

The most important reason of stone formation is super saturation of elements in the urine

Urolithiasis:

This condition is characterized by the formation of calculi (stones) in the urinary tract Most often arise in the kidney (Pelvic, Calyces), and are usually unilateral. This incidence is increased in men

There is also familial tendency of stone formation.

A. Calcium stones account for 80% -85% of urinary stones.
   1. The stones consist of calcium oxalate or calcium phosphate, or both.
   2. They are radiopaque (can be seen by using x-rays), so there is no need for IVP.
   3. They are associated with hypercalciuria, which is caused by:
      a. Increased intestinal absorption of calcium.
      b. Increased primary renal excretion of calcium
      c. Hypercalcemia, which may be caused by:

(1) Hyperparathyroidism leads to nephrocalcinosis (calcification of the kidney), as well as urolithiasis.

(2) Malignancy leads to hypercalcemia because of osteolytic metastases or ectopic production of parathyroid hormone (often by a squamous cell carcinoma of the lung).

(3) Other causes include sarcoidosis, vitamin D intoxication (Prolonged exposure to normal sunlight does not produce an excess of vitamin D, but megadoses of orally administrated vitamin can lead to hypervitaminosis), and the milk-alkali syndrome (is characterized by hypercalcemia caused by repeated ingestion of calcium and absorbable alkali)

B. Ammonium magnesium phosphate (struvite) stones are the second most common form of urinary stones. These stones have to be in alkaline urine, because an alkaline medium helps decrease Phosphate's solubility.

The urine has to be alkaline.

How to treat it? Acidify the urine by giving the patient more vitamin C, but, if big stones they may Cause renal failure

Treated by surgery

Are usually Very big stones, so they are generally asymptomatic.

Very severe, because it's a silent stone → does not cause renal colic → after time it causes hydronephrosis, smaller kidney → it may then develop pyelonephrosis

1. These stones are formed in alkaline urine, which is caused most often by ammonia producing or "splitting" (urease-positive) organisms, such as proteus vulgaris or staphylococcus.

2. They are radiolucent.

3. They can form large staghorn (struvite) calculi (casts of renal pelvis and calyces).

Purine

The other half may form without high levels of uric acid in the body or urine but can form with acidic urine (<pH 5)

C. **Uric acid stones** are associated with hyperuricemia in approximately <u>half of the patients</u>; hyperuricemia can be secondary to gout or to increased cellular turnover, as in the leukaemias or myeloproliferative syndromes.

Favored when the urine is acidic

D. **Cystine stones** are almost always associated with cystinuria or genetically determined aminoaciduria.

Because purine is a component of DNA, which is mainly found in the nucleus, and because these patients are given cytotoxic therapy which fragments the nucleus, purine comes out and accumulation of purine on the blood stream, large development of uric