Blood flukes (Schistosomes)

Lect.2

Chronic schistosomiasis:

In chronic schistosomiasis, tissue injury is mediated by egg-induced granulomas and subsequent appearance of fibrosis. About 2/3 of eggs are trapped in tissue.

Early lesion: The major pathogenic lesion is the granulomatous response observed around eggs trapped in the tissue which contain miracidium secret enzymatically active and immunologically stimulatory antigen (egg soluble antigens) which lead to cellular and humoral immune responses → focal areas of necrosis (pseudoabscess) which disappear and replaced by epitheliod cells with giant cells surrounding the dead egg (forming pseudotubercles). Dead egg may calcified or disappear.

Late lesion: The granulomatous process may complete heal or may progress to fibrosis and scar formation. Accumulation of extracellular matrix (collagen) causes the major pathologic lesion in late stage.

Urinary schistosomiasis (-S. haematobium)

The disease caused by S. haematobium is called bilharziasis, urinary schistosomiasis, or endemic haematuria.

After the worms mature in the sinuosoids of the liver, they migrate from that organ, and reach the vesical, prostatic and uterine plexuses by way of the hemorrhoidal veins.

The eggs are deposited in the wall of bladder and lower ureters (LUT) or to a lesser extent in the uterus, vaginal wall, prostate, rectum or other organs.

1-In acute stage, eggs invade the bladder wall and escape into lumen of the bladder causing symptoms as terminal haematuria (is the classical presenting feature), (s.t. complete haematuria), dysuria, frequency (nocturnal and diurnal), urgency and dull pain in the loin and supra-pubic region. Urinary symptoms
usually are not seen for 3 to 6 months after infection and may not develop for a year or more.

Patients with *S. haematobium* infection are more symptomatic than those with intestinal schistosomiasis.

Also, the bladder wall becomes increasingly infiltered with eggs that have become entrapped, and around which **granulomas** form (pseudoabscess → pseudotubercle), **papillomas** appear. So the early stage is cellular, and may cause **acute obstructive uropathy** and **mucosal ulcers** due to sloughing of mucosa.

Granulomas in the bladder wall cause bleeding, mucosal dysplasia and organ dysfunction, particularly in the trigone region.

2-In **late stage**, fibrosis and thickening of the bladder wall occur. So lesions of this stage (late) is acellular and fibrotic which called **sandy patches** (patchy fibrotic thickening of bladder mucosa and submucosa). Bladder wall may calcified and defrmed.

Obstruction of the ureteral openings or of the neck of the bladder (in early or late stage) may lead to back pressure with subsequent hydroureter and hydronephrosis → chronic stasis of urine which predispose to calculus and UTI (ascending bacterial infection) esp. with *Salmonella*. So, *S. haematobium* infection may be complicated by bacteriuria, lower urinary tract infection, chronic pylonephritis and renal failure as a late sequel.

The uterine cervix is the most common site of *S. haematobium* infection in women, and granulomatous inflammation of the cervix is a common manifestation.

In males, heavy infections may involve the urethra, prostate, seminal vesicles, and even the spermatic cord and penis.

Genital schistosomiasis may increase the risk of acquiring HIV infection and could predispose to cervical cancer.
Both *S. haematobium* and *S. mansoni* may invade the placenta to give rise to a granulomatous placentitis.

**Intestinal schistosomiasis (−*S. mansoni and S. japonicum*)**

1-Eggs of *S. mansoni* and *S. japonicum* may be deposited at any point in the corresponding venules leading to the inferior and superior mesenteric veins respectively.

2-In **early stage**, (cellular granulomatous reaction) local damage to intestinal wall caused by egg deposition and escape into the lumen of intestine and form the **dysenteric type of manifestation**, in which (pseudoabscess →pseudotubercle) formation may give rise to schistosomal dysentery, accompanied by abdominal pain, cramping, and frequent bloody or blood-flecked stools, with finding of eggs in stool, weight loss and anemia. Also eggs that are unable to escape provoke the formation of **granulomas** with patchy mucosal ulcerations.

3-In **late stage**: Acellular fibrotic lesion→

   a- fibrosis, thickening of bowel wall and pseudotumers.

   b- **Adhesions** to other loops of bowel and to mesentery and **constrictions** secondary to the fibrosis compound the functional problems.

   c- Intestinal **Polyps** may form from mass of eggs deposited in the submucosa, with their surrounding granulomas, and if in the rectum may **prolapse** through the anal sphincter.

   d- Fibrosis of the submucosa in the areas of egg deposition explains the decrease in egg passage in chronic infection.

**Ectopic lesions**

1- **Hepatic schistosomiasis**: Although the intestines are involved primarily in *S. mansoni* and *S. japonicum* infections, but egg embolism (escaped mesenteric eggs to portal veins) results in **secondary involvement of the liver** and form the **hepatosplenic type of manifestation**, in which eggs swept back to the liver with portal blood flow lodge in the finer branches of the portal system. Around them **granulomas** and **intense inflammatory reaction developed**, which may lead to
periportal fibrosis if the infection is heavy enough, that may cause liver cirrhosis (pipe stem cirrhosis).
The main sequele of hepatic fibrosis is obstruction to portal blood flow which lead to portal hypertension which can cause collateral blood flow, ascites, varicies and hematemesis due to bleeding varicies, hypersplenism (splenic reticular tissue hyperplasia) → splenomegaly.

Hepatosplenic involvement is the most important cause of morbidity in *S. mansoni* and *S. japonicum* infections which may present in addition to above with anaemia, jaundice, thrombocytopenia, hypergammaglobulinemia and hyboalbminemia. Patients may remain asymptomatic until the manifestation of hepatic fibrosis and portal hypertension.

In hepatosplenic schistosomiasis, anemia results from:

1-bleeding. 2-hypersplenism. 3-anemia of chronic disease. 4-the ingestion of RBCs by adult worms.

**2-Pulmonary schistosomiasis:** after portal hypertension caused by *S. mansoni* and *S. japonicum*, collateral pathways shunt parasite eggs to the lungs. So, eggs may pass through rectal, esophageal and gastric portocaval shunt into caval system, bypassing the hepatic filter to reach the pulmonary capillary bed through the right side of the heart → granulomatous process in the arteries and vascular obliteration → pulmonary arterial hypertension → cor pulmonale and right heart failure.

In *S. haematobium*, egg can migrate directly to lungs and induce pulmonary inflammation.

**3-Neuroschistosomiasis:** result from migration of adult parasites and the resultant entry of eggs into cerebral (*S. japonicum*) or vertebral venous plexus (*S. mansoni* and *S. haematobium*)
Association of schistosomes with other diseases:

1- **Salmonellosis:** An association between chronic salmonellosis (persistent salmonella bacteremia) and schistosomiasis caused by *S. mansoni* and *S. japonicum*, has been reported from many areas,

The organism not always *S. typhi*. This is called Salmonella-Schistosome syndrome. Patients with long duration of low grade fever, Widal test positive, and relapsed after response to treatment against Salmonella infection, but when there is treatment for schistosomes, the fever will be relieved (without relapse).

**Mechanisms of this type of association:**

1- Macrophage system is impaired in some patients and Salmonella can survive inside the macrophage.

2- The B-cell function may be depressed and the level of Abs is insufficient to sterilize the organisms.

3- Salmonella can proliferate inside the schistosomes’ integument and intestinal tract (service as intravascular reservoir for bacteriological relapse).

Salmonella urinary tract infection are also described with *S. haematobium*.

2- **Hepatitis:** co-infections with hepatitis B and C have been reported, which could be due to a immunologic response to chronic schistosomiasis may interfere with the development of a curative immune response to hepatitis b- administration of injectable drugs or blood transfusions used to treat schistosomiasis prior to 1980s.

3- **Nephritic syndrome** is occasionally seen in both *S. mansoni* and *S. haematobium* infections.

4- **Cancer:** *S. haematobium* infection results in sequamous metaplasia of the urinary bladder and ureter mucosa.

A clear association between chronic *S. haematobium* infection and sequamous cell carcinoma of LUT has been established.
**Diagnosis**

1-Finding of eggs:

A-Eggs of *S. haematobium* in urine (rarely in stool) by:

a- G.U.E. especially in heavy infection (direct wet preparation)

b- Concentration method either by 1-centrifugation of urine or by 2-filtration of urine by filter with specific pores (as Whatman No. 1 filter). {early stage}.

-Midday urine specimen is used for recovery of *S. haematobium* eggs (the time of peak egg excretion).

- More than one sample may be need.

- In chronic stage, no egg passed in urine.

B-Eggs of *S. mansoni* and *S. japonicum* in stool by:

a- Simple saline smear (wet preparation) in heavy infection.

b- Concentration methods (as modified formol-ether concentration method or by filtration).

c- Kato-Katz thicksmear. It is a quantitative technique, which is recommended because intensity of infection is associated with morbidity.

2-Egg-hatching technique: viable ova can be hatched from specimens (urine or stool) and the diagnosis made by examining for miracidia by mixing specimen in water and exposing them to light results in miracidia in the supernatant in few hours.

3-Cystoscopy, proctoscopy and colonoscopy to:

a- See the morphological changes on the inner surface of the bladder or intestine (rectum and colon) such as granulamatosus and fibrotic changes (sandy patches).

b- Recovery of eggs and examine the histopathological changes in the organ wall by biopsy as rectal biopsy.
4-Biopsy: from the bladder wall, uterine cervix, or the vagina, in *S. haematobium*, and from intestinal wall (rectal biopsy) in *S. mansoni* and *S. japonicum*, s.t. *S. haematobium* for recovery of eggs, esp. in light and chronic infection (with negative repeated urine or stool examination for egg).

5-Serological tests: CFT, FAT, IHT, LAT.

The serological tests are important in:

1- Acute schistosomiasis because the symptoms are not specific.
2- Stool and urine negative cases especially in light infection.
3- Uncommon manifestations (as cerebral schistosomiasis).

6-Detection and quantification of schistosomal antigens in serum and urine.
- can identify patients with active infection (important in endemic areas)

- The sensitivity of this test decreased in light infection.

- This test is used in monitoring the efficacy of schistosome chemotherapy.

7-PCR (polymerase chain reaction).

8-Aldehyde test: positive due to high serum globulins (hypergammalobulinemia).

9-Intradermal skin test (schistosomian skin test): become positive after few months of infection.