ELECTIVE (SSC5a) REPORT (1200 words)

A report that addresses the above four objectives should be written below. Your Elective supervisor will assess this.

Intestinal schistosomiasis: pathophysiology, transmission, diagnosis, and control.

Introduction

Schistosomes are type of platyhelminth that causes severe chronic disease in millions of people across the world being the second most transmitted parasite after malaria (2). Intestinal and hepatic disease is cause mostly by *s. mansoni* with 83 million cases whereas urogenital disease is caused by *S. haematobium* (114million cases) .

Schistosomiasis causes 20 million cases of severe morbidity per year and 300,000 deaths most of which (90%) are concentrated in Sub Saharan Africa (3) (4). The distribution of this disease corresponds to the rives and oasis in the maps where freshwater snails can be found, although distribution of water from this sources can contribute to the spread of schistosomiasis into areas that lack natural water supplies (5).

Schistosoma mansoni life cycle

The free swimming cercariae forms found in fresh water can penetrate the skin of humans, once they penetrate the skin, they lose their tail and become schistosomula larvae which migrate through the lungs into the circulation. Schistosomes are blood flukes, therefore the adults are found in the veins. Intestinal species, travel through the portal system until they reach the mesenteric veins where they form worm pairs. Once they mate, they produce eggs that migrate trough the tissues causing pathology in the host. The eggs are passed into the environment through faeces (6).

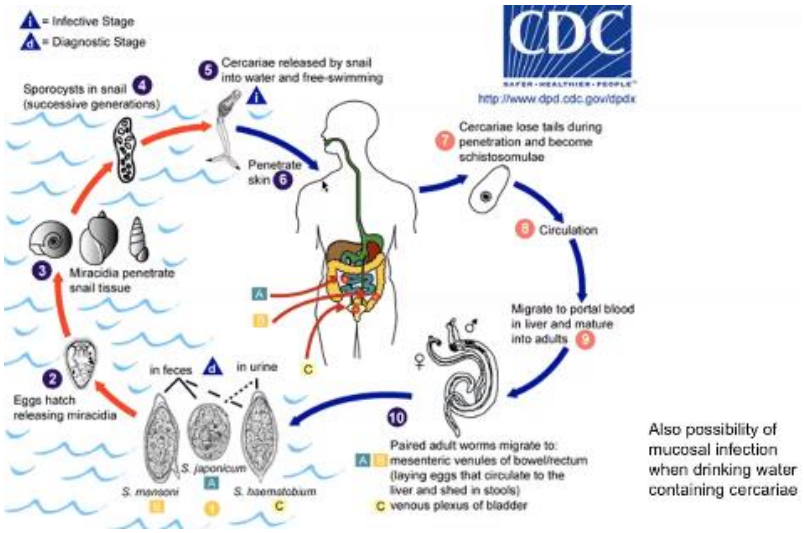

Figure 1 Life cycle of Schistosomiasis mansoni (1).

Once the egg meets fresh water they hatch and a miracidia emerges from the egg, the eggs are resistant to desiccation and can last up to 2 weeks in the environment. The ciliated surface of the miracidium allows movement through the water. Miracidia also have penetration glands that contain the enzymes needed to penetrate the snails. Once in the snails, they colonise the mantel and develop into mother sporocysts. As they develop into daughter sporocyst they migrate to the snail hepatopancreas and develop into millions of cercariae (7). The snail then sheds the infective larvae by light stimulus to increase the chances of meeting a host .

Pathophysiology of chronic schistosomiasis

Intestinal schistosomiasis, pathology occurs as the passage of eggs leaves behind ulceration and haemorrhages as well as induction of an immune rection that leas to a thickening of the mucosal layer and polyp formation (8).

In hepatosplenic schistosomiasis, the eggs become entrapped on the presinusoidal vessels of the liver, this triggers a granulomatous response to wall off and calcify the eggs which leads to periportal fibrosis. The periportal fibrosis increases the pressure of the portal system which opens the portosystemic shunts leading to caput medusa and oesophageal varices which are at great risk of rupturing resulting in a fatal haematemesis if not promptly treated. Portal hypertension also increases the hydrostatic pressure therefore pushing more water out of the capillaries which results in oedema and ascites. In chronic hepatic schistosomiasis there is also damage to the liver which leads to liver fibrosis and decreased function resulting in decreased albumin production which contributes to the ascites by lowering the oncotic pressure (9).

The formation of granulomas is leads to disease symptoms and morbidity, but their formation is vital for the hosts survival, without the formation of granulomas, the host will die of a liquefactive necrosis in within a few days. When the antigen from the eggs is picked up by the immune system, the ribonucleases omega 1 extracted by the eggs modulates the immune system to favour a Th2 response with high levels of IL4, IL5, IL13 and IL10. (10) It has been stablished by using knockout mice that IL4 and IL13 are essential in the development of the granuloma. Although they both contribute to granuloma formation, only one is needed to produce a sufficient response and fibrosis has only been associated with IL13 in both mice (known outs do not develop fibrosis) and humans where a dose dependent

relationship between IL13 and fibrosis has been stablished (11). Although Th1 are not dominant they are still needed, Th1 responses limit the size of the granuloma and produce INF-gamma that protects against fibrosis. After 15 weeks of infection, IL10 production increases which leads to a downregulation of the immune system further limiting the expansion of the granuloma and the formation of fibrosis (12).

Current diagnostics

Diagnosis of the acute stage o schistosomiasis is challenging; serology diagnosis is the gold standard, but it takes up to 3 weeks after the onset of symptoms for a patient to test positive (13). ELISA test of the egg antigens only offers 50% sensitivity and are often combined with indirect hemagglutination test that have a sensitivity of 90%. This results on a test with 90% sensitivity and 92% specificity (14). If the patient test positive on ELISA, and Enzyme linked immuno-transfer blot can be done as confirmation (15). Marked eosinophilia is also found in most of the patients and can be elevated 32 weeks after treatment, other inflammatory markers such as sedimentation rate, C-reactive protein and serum amyloid A are moderately elevated (16). During the acute phase there is a generalised state of hypercoagulability that can be detected with an elevated D-dimer and thrombin. Although there are little studies radiology can be used district patchy infiltrates can be seen in lung x-rays corresponding to trematode pulmonary migration (17).

Parasitological diagnosis of chronic schistosomiasis is made by Kato-KatZ thick stool smear as per WHO recommendation. This technique requires at least 50mg of faeces and has a specificity of 100% although the sensitivity varies with the infection rates. Formalin may also be used to concentrate the stool and increased the sensitivity (18) . Molecular techniques such as PCR in blood or faecal samples can be used thought all phases of clinical infection, and as a treatment evaluation marker (19). Furthermore, clinical tests looking for the effects of the infection can also be useful in guiding the diagnosis. Those include full blood counts detecting eosinophilia, anaemia and thrombocytopenia, INR to assess lover function, abdominal ultrasound and markers of liver fibrosis (pro-collagen peptides type III and IV, the P1 fragment of laminin, hyaluronic acid, fibrosin, tumour necrosis factor αR-II, and sICAM-1) (20).

Control of schistosomiasis

WHO has set the goal of eliminating schistosomiasis as public health burden by 2025. This has been primarily tried to be archived by prophylactic mass drug administration campaign (MDA). Most MDA will target school aged children leaving a large proportion of at-risk population untreated rendering them ineffective. Mathematical models have repeatedly shown the importance covering the entire at risk population in endemic areas to prevent re-infection, however this has not been archived (21). To address this, the WHO has created a new guideline for elimination which includes focusing on fresh water snail control, ensures quemotherapy is available for at group risk currently missed stresses the importance of repeated treatment in hot spot areas and included a focus on WASH strategies as a method of control (22) .

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