STUDIES ON GASTRIC FUNCTIONS BEFORE AND AFTER SPLENECTOMY IN BILHARZIAL HEPATOSPLENOMEGALY

THESIS

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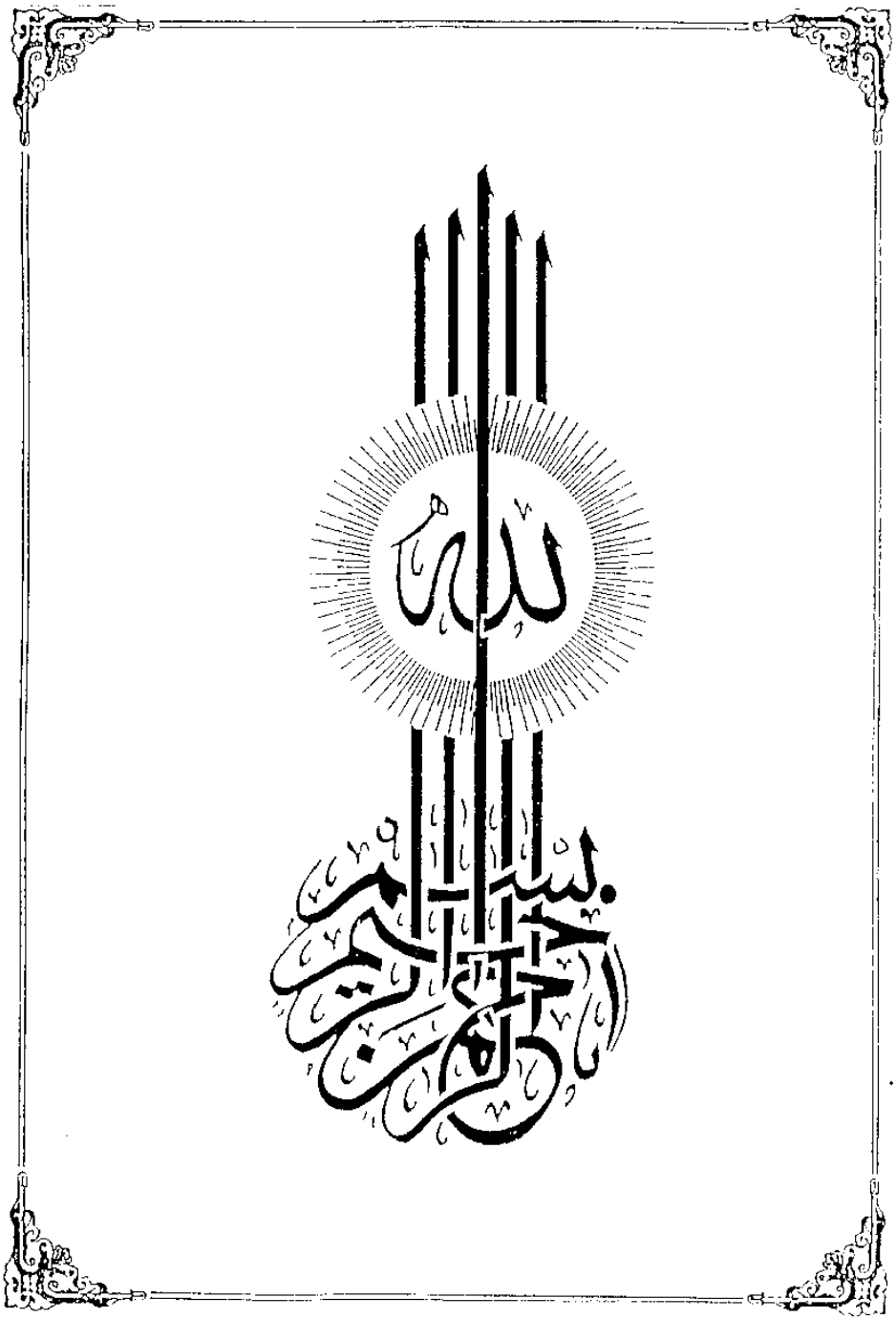
C O N T E N T S



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BILHARZIASIS OF THE LIVER

Bilharziasis is an endemic disease in Egypt the brunt of the disease usually fall on the liver.

The pathology and pathogenesis of the hepatic affection have been the subject of discussion for a long time but still needs further studies.

The disease is due to depostion of ova in the portal radicles.

The ova are laid in the terminal radicles of the mesenteric and haemorrhoidal veins, but fail to engage in the walls of the vessels, and thus are carried as emboli in the portal blood.

As the embolised ova reach the liver, they engage in the terminal radicles of the portal vein and escape into the large or fine portal tracts where they produce bilharzial granulomatous lesions which frequently extend beyond the portal tracts and encroach on the parenchyma.

In the early stages, the liver is enlarged and firm due to congestion and cellular infiltration around the deposited ova. As the disease progresses increasing fibrosis occurs with shrinkage of the liver, impairment of liver function and portal hypertension.

The early days studies on this subject were based on

autopsy findings, but more recently the needle biopsy of the liver enabled the research workers to investigate the earlier stages of the disease. More over, animal experimentation has helped much in the study of the evolution of the disease.

The autoimmune processes and their application in describing the bilharzial reaction, had given some clarification to the posible pathogenesis of the disease.

As early as 1904, Symmer's described the pathology of the disease in a paper entitled "Note on a new form of liver cirrhosis due to the presence of ova of bilharzia haematobium". He described the lesions in relation the deposited laterally Spined ova, and put it as "clay pipe-stem cirrhosis". This description applies to what we call now, the coarse bilharzial periportal fibrosis, a name applied by Hashem in 1947 who restricted the term cirrhosis to the lesions affecting the liver parenchyma and causing degeneration followed by regeneration, which is not the case in bilharziasis.

Day in 1924 described another type of lesion met with in Egyptians with hepatic affection. He noticed that some c cases showed diffuse infilteration of the liver different from that of Symmer's cirrhosis. He removed a piece of liver from the cases submitted to splenctomy and found diffuse ova with diffuse celluler periportal infilteration. This type

was called later by Hashem is 1947 as the fine bilharzial periportal fibrosis.

Incidence :

The records of the pathology Department in Kasr El Aini faculty showed that the incidence of bilharziasis in the years 1903 - 1908 was 14% of autopsied cases.

The bilharzial liver formed about 26% of the cirrhotic livers described among the autopsied cases (Elwi, 1962).

Hashem in 1947 revised the post mortem of more than 2006 autopsies done during the years 1933 - 1939, and he came to the following conclusions. Bilharziasis occurs at all ages between 10 and 70 years but it reaches its maximum in the fourth decade. The liver affection is more frequently associated with Schistosoma mansoni infection. Bilharzia ova were present in 100 % of livers of children examined, while they were present only in 75 % of livers in the adults.

Elwi in 1962 found that bilharzial fibrosis of the liver formed about 70 % of all types of cirrhosis met with in the autopsies of the last five years.

Elwi in 1962 found that the general incidence of bilharziasis in the autopsy material was 44 to 45 %, and that the

liver was affected in 37 % of cases of intestinal bilharziasis.

Erfan et al in 1957 found from their clinical studies that bilharzial liver formed 70 % of a series of 180 cases diagnosed clinically as hepatosplenomegaly and submitted to liver biopsy; 30 % of these cases were in the early infiltera-tion stages, while the 70 % were in various stages of fibrosis.

As regards the incidence of both types of fibrosis, it was noticed by Hashem in 1947 that the coarse rather than the fine type is on the rise, this was later emphasized by Elwi in 1962.

Pathogenesis:

The assdciation of liver affection with intestinal bilharziasis, has led many of the early workers on the subject to think of a causal relationship. However, after animal experimentation and after the advances in research work on autoimmune mechanisms more proofs were added for the consolidation of such a hypothesis. Ferguson and Day (1909)described the presence of splenomegaly with hepaticirrhosis in Egypt.

However, they considered the splenic enlargement as a result of infective agent, probably protozoal and perhaps leishmanial in origin. Day and Richard in (1912) considered splenomegally as a form of Banti's disease and advised splenectomy as a treatment for these cases.

It was El-Kadi who in 1923 noticed the association of intestinal bilharziasis, and both hepatic and splenic enlargement. He suggested the bilharzial infection as the cause of this triad, particularly when they responded to specific antibilharzial drugs.

Day in 1924 reported the association of hepatosplenomegaly with intestinal bilharziasis and found ova in the wedges removed from the livers during operations. He also reported the improvement of these conditions with specific antibilharzial therapy.

Hadson in 1924 in Nyassaland, described the histological picture of the liver in bilharzial cases, and Day in 1925 found that the Egyptian syndrome was very similar to that described by Hadson.

On the other hand, Ibrahim in 1928 did not accept the bilharzial nature of endemic hepatosplenomegaly, accusing Day's theory for hypnotising the various investigators. The occurrence of the disease in early childhood and its rarity above the age of 30 were considered as phenomena that can not be explained by the bilharzial etiology. He also reported that this endemic syndrome occured in localities free from bilharziasis, and said that he failed to cure the syndrome with tartar emetic.

The above two observations were considered as evidences against the bilharzial theory about the origin of the syndrome.

In another discussion he said that ova were demonstrated in the liver showing the ordinary multilobular cirrhosis, and he stated "the common combination of bilharziasis and the so called Egyptian splenomegally with multilobular cirrhosis of the liver made the etiologic relationship to bilharziasis difficult to settle". Again, Madden in 1928 concluded that Day's view regarding the bilharzial nature of the syndrome of endemic hepatosplenomegaly has not yet been entirely accepted.

Khalil in 1928 as a result of his clinical and epidemiological studies came to the conclusion the socalled Egyptian splenomegaly was caused by toxoemia due to chronic intestinal lesions. He again in 1935 stated that one cannot scientifically prove the entity of the endemic form of splenomegaly, but there was a feeling among the medical men of its existence.

Agaty in 1935 described the cirrhosis of the liver as being due to bilharzial ova deposition in the periportal tracts.

Yakoub in 1935 considered the splemonegaly to be secondary to liver affection and that both were caused by bilharziasis. He mentioned that if the condition was treated in the early stages and if no exposure to infection occurred, no residual lesion would be left. Abdel Shafi (1936) considered the liver affection as an acute form of Laennec's cirrhosis.

Most of the evidences favour the view that ova are the most important factor in the production of hepatic fibrosis in bilharzial infection.

Lee in 1927 after studying the effect of unisexual bilharzial infection of experimental animals, recognised that ova were the most important factor.

Hashem in 1947 demonstrated cirrhosis in liver of dogs after repeated injections of bilharzial ova in the portal vein of dogs. Melency in 1953, after experimenting with unisexual and bisexual infection concluded that the fertilized eggs and dead worms had produced most of the pathological changes in the liver. Hoyi-Husun in 1958 found that liver lesions occurred only around ova, and the severity of the lesions went hand in hand with the number of ova in animals infected with Schistosoma juponicum. He could reproduce the lesions by injecting ova directly in the liver of healthy mice. Dewitt in 1959 described a syndrome in experimental animals that closely resembled clinical hepatosplenic Schistosomiasis following infection with Schistosoma mansoni.

In this study he could rule out the importance of such factors like toxins, dead worms or malnutrition and concluded that Schistosoma ova could be the only responsible factor in the production of this syndrome.

Warren in 1961 after studying the effects of bilharziasis bi - and unisexual infection, on both well fed animals and animals kept on deficient diet, concluded that ova are the primary factor in the production of liver cirrhosis in bilharziasis.

The mode by which the ova produce cirrhosis, was believed to be due to the toxins which diffuses locally from the living miracidium. This was the idea of Hashem in (1947). However, Dewitt in (1959) did not accept the toxin theory, saying that this would attack the liver cells more diffusely and would be associated with severe derangement of liver function.

Also, Elwi in 1962 objected the use of the term toxins, so long it is not yet identified.

Recent researchers refer the pathological changes in the liver to the antigen antibody mechanism.

Hoyi-Husus in 1958 studying the histopathology of experimentally infected mice with schistosoma japonicum found successive presence of fine rays, and eosinophilic cells around maturing ova.

He thought that this may have some bearing to the immunologic process of the body.

Andrade in 1962 found that antigenic material with specific binding affinity to cirulating antibodies, were present in sera of patients with active schistosomiasis; this antigenic material was demonstrated immunocytochemically by him in the ova and hepatic granulomata.

Ghanem in 1962 using a modified latex fixation test, found positive cases in 22.9 % of non arthritic patients with bilharzial hepatosplenic affection, thus suggesting an immunologic rheumatoid like property.

Elwi in (1962) refusing the use of the term toxin, accepted the auto-immune process to explain the pathological reactions occurring in the liver.

Abdin in 1963 being struck by the diffuse lesions, as compared to the rarity of ova, put the auto-immune theory as the only satisfactory explanation for such a finding.

Mhhamed in 1963, prepared an antigen from both healthy non bilharzial liver material and from proved bilharzial liver, using these antigens, he tested the serum of bilharzial hepatosplenic cases by both complement fixation test and precipition reactions.

He found that the tests were positive in 7 out of 35 patients with proved bilharzial hepatosplenomegaly (20 %).

While all healthy subjects gave negative results. The tests were also positive in 29 % of Laennec's cases. He found no difference between the normal and bilharzial liver antigen. He was able to produce periportal fibrosis after 26 days by injecting liver antigen into normal rabbits.

The role of schistosoma ova in the production of the diffuse type of periportal fibrosis of the liver can be easily understood, but how such small sized ova can stop in the big portal veins to produce the coarse type; this was explained by Elwi in 1962. He revised the work of Elias and Popper in 1955 who found that big protal veins are only conduction veins. Such vascular pattern, Elwi said, allows the embolisation of a heavy number of ova in and around the large portal tracts and the development of the coarse type of periportal fibrosis.

The role of adult worm in the production of fibrosis of the liver has been questioned by many workers. Day in 1924, when he described the diffuse type of bilharzial fibrosis, put its etiology as oval, while that of Symmers, was put by him as due to death of worms in the big portal tracts. Again Hashim in 1947, noticing the rising incidence of the coarse type of fibrosis attributed it to the death of worms in the big portal tracts, leading to thrombophlebitis, and later to the coarse variety.

However Elwi in 1962 was emphasizing the rarity of observing thrombophlebitis in his material, though the coarse type is still increasing. Melency in 1953, found that living schistosoma worms in the mesenteric vessels do not stimulate