IMMUNOGLOBULINS PATTERN IN DIFFERENT TYPES OF ASCITIC FLUID

THISIS
SUBMITTED IN PaRTIAL FULFILMENT
OF THE DEGREE OF M.S. IN GENERAL
MEDICINE

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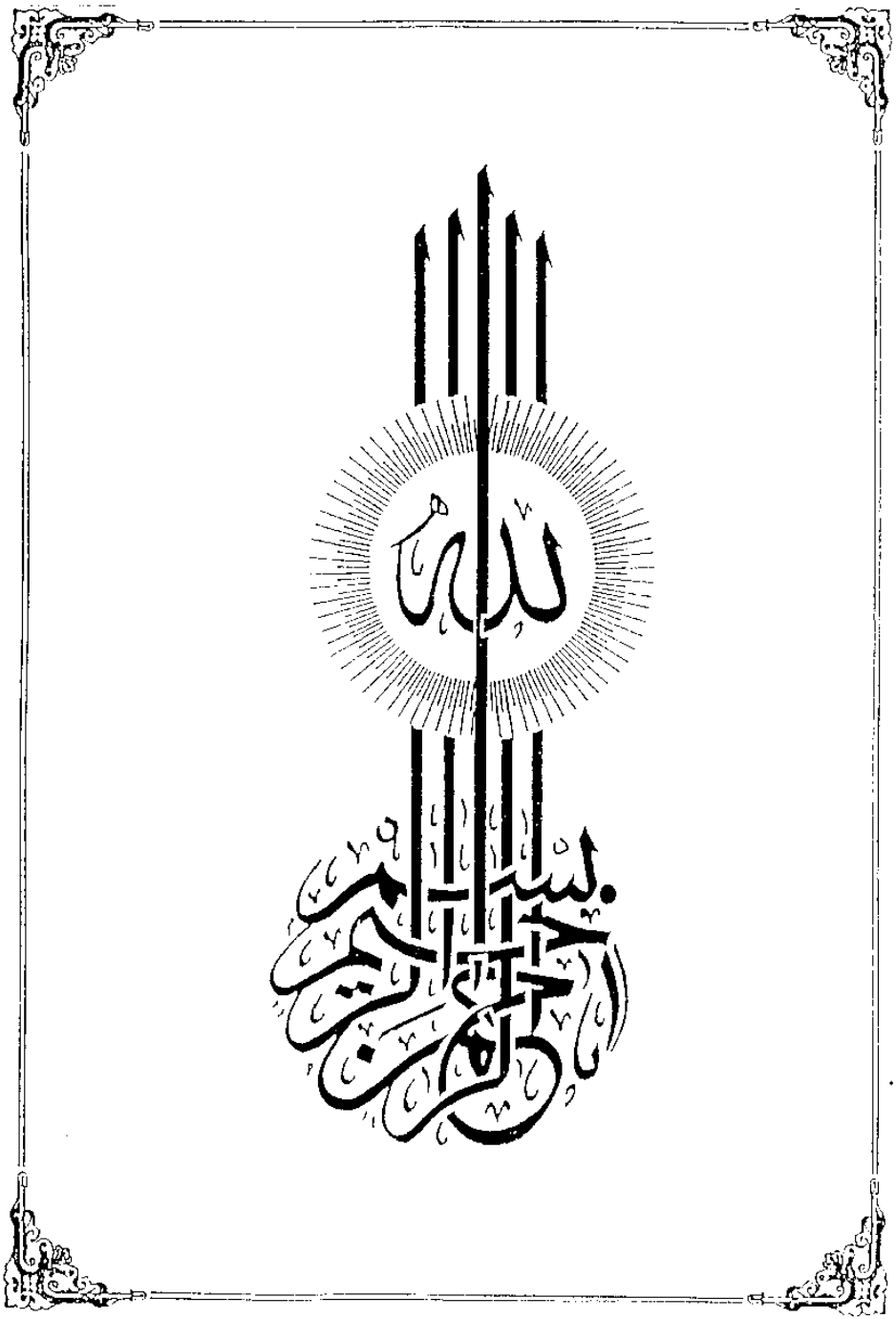
1982

ACKNOWLEDGEMENT

It is a great pleasure to express my sincere thanks and gratitude to Prof. Dr. Aly Moanis Professor of General Medicine, Ain Shams University and Prof. Dr. Mohammad Khairy Makled Professor of Parasitology and Senior Immunologist, Ain Shams University. They have chosen the subject and were after every step by their guidance, they revised initial manascipts and contributed to its final forms.



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Introduction and Aim of Work

Ascites means a collection of fluid in peritoneal cavity due to either general or local causes. The general causes include : liver cirrhosis, cardiac, renal and nutritional diseases. The local causes are tuberculous peritonitis, malignancy either primary or secondary, acute peritonitis, pseudomyxoma peritonii, obstruction of thoracic duct and Meig's syndrome. Generally the commonest cause of ascites is liver cirrhosis (Berner 1964). In Egypt the commonest cause of ascites is bilharziasis. Ascites means parenchymal decompensation of liver in case of schistosomiasis. Smither and Terry (1969), noticed that immunity in bilharziasis develops gradually over several years. The major stimulus to the development of homologous immunity against S. mansoni in rhesus monkey is the presence of antigens associated with living adult worms and not the eggs. So if we are able to induce immunity among farmer exposed to bilharzial infection, this will help us in preventing the disease and its complications. Many workers have been worked in this field. Direct transfer of about 80 pairs of adult S. mansoni worms into the hepatic portal system of normal monkey resulted in complete resistance to challenge with 2000 cercariae. Makled (1972), and Bassily, et al (1972), studied the serum immunoglobulins in schistosomiasis, a

statistically significant rise of Ig G level was found in all stages of the disease while Ig M level was significantly raised only in active S. mansoni. infection Ghanem, et al (1973), found significant increase of serum glycoproteins in schistosomal hepatic fibrosis cases and they attributed this increase mainly to active fibrinogenesis and tissue destruction, and partly to secondary parathyroid over-activity and impaired glucose tolerance as well as to an associated autoimmune mechanism.

Immunoelectrophoretic pattern of sera and ascitic fluid proteins in post hepatic cirrhosis and bilharzial hepatic fibrosis were studied by Shoukry, et al (1972). They found normal or slightly lowered serum total protein, decreased albumen, increased glycoproteins, decreased transferrin and haemopexin. The latter was not detected in sera and ascitic fluid of post infective hepatic cirrhotic patients, and increased Ig M with normal Ig A and Ig G but the latter was increased among a number of cases of both types.

Immunoglobulins pattern of sera and ascitic fluid in bilharzial hepatic fibrosis were studied by Ata, et al (1977). They found that IgG, IgA, IgM, and IgE were all detected in the ascitic fluid but no correletation could be

found between their level in ascitic fluid and that in serum. In ascitic fluid Ig G represented more than 90% of the total globulins compared to about 55% in serum. It is known that Ig G diffuses more readily than the other immunoglobulins into the extravascular body spaces while Ig A appears selectively in sero-mucous secretions. Ig M, on the other hand, is largely confined to the blood stream due to its high molecular weight.

The mean serum values for Ig G, IgM, and IgA in the presented ascitic bilharzial cases were higher than those reported for normal Egyptian control (El-Rasiky, et al 1974).

Immunological studies are not widly applied on sera and ascitic fluid of non-bilharzial type (malignancy, renal, cardiac and tuberculous). The clinical diagnosis of free fluid in the peritoneal cavity is an easy bed side procedure, but an elaborated aetiological diagnosis is a real difficult diagnostic task.

The aim of the present work is to estimate the different immunoglobulins in the ascitic fluid of different aetiologies using Mancini technique (1965) and this may be of diagnostic value.

Bilharzial Ascites

Ascites complicating bilharzial liver fibrosis, needs two factors for its production. The first one is hepatic affection with schistosomiasis and the second is portal hypertension. These factors have been studied by many authors.

Koppisch (1937), stressed that in man most of the dammage is accompanied by ova if sufficiently deposited over several years, ultimatly leading to progressive fibrosis of the portal tract.

Hashem (1947), studied experimentally the effect of schistosomal worm extracts injected intraperitoneally and through the portal veins of animals with no significant liver changes. Injection of living eggs resulted in pathological lesion similar to those seen in the evolution of the human disease. He concluded that the terminal picture was essentially the result of fibrosis encroaching on the vascular supply of the liver parenchyma causing some distortion of their normal architecture.

Maleny, et al. (1953), concluded that most of the pathology was produced by fertilized ova and dead worms forming localized lesions which if numerous en-

ough lead to extensive scarring.

Dewitt and Warren (1959), did not accept the toxin theory claiming that this would attack the liver cells, more diffusely and would be associated with severe derangement of liver function.

Hamilton, et al. (1959), stated that intrahepatic thrombophlebitis and periphlebitis owing to the death of adult worms and ova are the common dominators in the pathogenesis of the disease, they added that anti-bilharzial therapy probably has an important influence on the production of liver fibrosis.

Andrade, et al. (1961), were also able by immunocyto chemical methods to demonstrate antigen-antibody complexes in the liver of mice infected with S. mansoni, thus, providing support for the immunological nature of such a self perpetuating hepatic involvement.

Warren (1961), concluded that ova are the primary factor in the production of liver fibrosis in this disease.

Hashem, et al. (1962), also studied the effects of various deficient diets on the evolution of the disease in animals and concluded that dietary deficiency may make

the liver more vulnerable to schistosomal infection in its earliest stage. In later stages, deficiency of diet creates an unfavourable medium for the proper development and reproduction of worms during the infection.

Abdin (1963), put the autoimmune theory as the only satisfactory explanation for the marked and diffuse portal thickening where ova are few or absent.

Ghanem (1964), 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.

Anti-liver antibodies have been also demonstrated by Mohamed (1963), in the serum of some cases of hepatic bilharziasis using normal and bilharzial liver homogenates as antigen.

Humberto (1963), used dead adults schistosomes as emboli in the portal system of mice and obtained lesion similar to those already described with the usual cercarial infection. Thus providing evidence that dead worms can produce hepatic lesions.

Warren, et al. (1967), found that sensitization

could be transferred between histo-compatible mice with lymph nodes or splenic cells, but not with sera. These results strongly suggested that the schistosome egg granuloma is essentially cell - mediated type of immunological response as a manifestation of delayed hypersensitivity.

Stenger et al., (1967), studied the liver of mice infected with S mansoni cercaria by electron microscope early and late in the course of the disease. They noticed that in the early phases paragranulomata and liver cells displayed subcellular alteration indicative of hepatocellular damage, while late in the course of infection, liver cells showed normal structure.

Boros and Warren (1970), demonstrated the immunological aetiology of the granulomas. They could isolate from the eggs antigens responsible for the host reaction. After the egg being laid by the worm, the eggs embryonate within a few days to begin to secrete soluble substances which pass through the pores of egg shell as they contain enzymes which facilitate the passage of the eggs through the tissue. These secretions sensitize the host resulting in the development of thymo-lymphocytic memory cells, following sensitization, the further antigenic secretion

stimulate the memory cells to release their lymphokines, which can affect the migration of both macrophages and eosinophile, resulting in the formation of a granuloma. A large area of tissue is destroyed by inflammatory reaction, probably due to release of lymphotoxins, lysosomal enzymes and perhaps to some toxic substances in the egg secretions.

Warren, et al. (1972), found that offspring of hyper-infected female mice with acute mansoniasis form relatively small granuloma and ascribed this to an acquired tolerance immunity.

Lichtenberg (1955), investigated the intrahepatic portal radicles in human mansoniasis. He described gradual substitution of some of the intrahepatic portal veins by granulomas, sclerosis and narrowing with intrahepatic thrombophlebitis and sometimes capillary talengiectasis with angiomatoid appearance.

Bogliolo (1957), studied the vascular pattern of this disease. In early cases, the distribution and architecture of the portal venous tree, all confrom to the normal pattern. In late cases, there was diminution of many of the portal venules of the fourth order branches, but the trunk and principle branches maintained the normal

mode of diversion and distribution. In both early and late cases, there was a newly formed vascular sheath made up of innumerable small vessels closely interlacing into a dense network which systemically surrounded the branches of the whole portal tree. This was never described in Laennec cirrhosis. In the latter, the portal tree is greatly reduced with amputated tortious irregular branches and the arterial tree also show the same tortousity and irregularities. These newly formed vessels were derived from the portal tree and not from the hepatic veins or the hepatic artery.

Aidaros, et al. (1961), described occlusive intimal thickening with angiomatoids as a pathogenetic feature of the disease and was attributed to abnormal communication between the portal and hepatic artery circulations as a result of portal hypertension.

Warren, et al. (1972), found that large mumber of eggs released into the mesenteric circulation by the illuminating microcope are trapped in the presinusoidal venules partially blocking the blood flow. No significant degree of obstruction occured until the formation of the large avascular granuloma which completely shut off portal flow, neovascular formation occurred in the succeeding scar tissue, but these vessels appeared to be

supplied largely by the hepatic artery, perfusion of sinusoids was maintained and liver parenchymal functions remained unimpaired. The marked obstruction to portal flow resulted in portal hypertension, congestive splenomegaly and the development of porto-systemic collaterals.

Mechanism of ascites formation

Ascites implies liver failure and portal venous hypertension. It complicates all forms of cirrhosis. Both local factors and changes in renal function have to be considered.

Local factors :

A raised pressure at the venous end of the splanchnic capillaries, consequent to portal hypertension, and a reduced plasma albumin concentration will favour transudation of fluid into the peritoneal cavity by altering the starling equilibirum. In one study, the measured changes in portal pressure and plasma ablumin concentration alone were sufficient to account for ascites formation (Wilkinson, et al 1963).

Further more, if these were the only factors, the ascitic fluid should have the characteristic of a transudate with a very low protein concentration. The protein present in ascites may be derived largely from hepatic lymph. Characteristic of cirrhosis is a partial block to hepatic venous outflow (post- sinusoidal portal hypertension) and in some cases this may be so marked that blood flows retrogradely from the liver into the portal vein (Warren et al. 1968). Secondary to the venous out-