Histological Changes of Mice Liver Infected With Toxoplasmosis

Rana M. R. Kassabbashi,
Dept. of Anatomy, College of Medicine- University of Mosul.

Abstract
This study concerned with the effect of toxoplasmosis on the histology of mice liver. Two groups each of 10 mice were examined. Group (I) left as a control while group (II) were those mice inoculated intraperitoneally with placental fluid containing Toxoplasma Gondii parasite to induce the infection. After 10-15 days of inoculation, the livers of the two groups were examined histologically. Results showed many histological changes in the livers of infected mice, while there were no changes in the livers of the control group. Histologically the livers of the second group showed the presence of Toxoplasma Gondii tachyzoites and tissue cysts invading the hepatocytes resting between the endothelial cells of the sinusoidal liver capillaries, together with intense inflammatory cellular infiltrate concentrated mainly around the central veins of the liver lobules, with congestion and hemorrhage within the central veins, dilated sinusoidal capillaries were also very obvious with distortion in the shape of the hepatocytes and foamy appearance of those cells. All these changes indicated that the infection with Toxoplasma Gondii parasite could affect all organs in the body especially the liver.

Key words: histological changes, mice, liver, toxoplasmosis

Introduction
Almost 13% of the world population is affected by Toxoplasma Gondii parasite (1). Toxoplasma Gondii is an obligate intracellular parasite, it moves with gliding activity and penetrate the host cell. Actively it invade many tissues including muscles, brain, intestine, placenta and liver (2). After initial growth at the site of injury, the parasite will be disseminated via blood stream and finally localized within the host cells causing rapid cell death with rupture and liberation of the organisms and soluble antigens (3).

Toxoplasma Gondii causes many changes when they invade the cell, those changes are particularly due to the DNA damage that is provoked by the infection (4). Nearly all the internal organs and tissues will be affected after infection with Toxoplasma Gondii parasite, this will lead to many pathological changes ranging from mild congestion to severe degeneration involving mainly liver, spleen and pancreas (5,6).

The basic structural unit of the liver is the hepatocyte (liver cell), those cells are grouped in interconnected plates. Each classical liver lobule is formed of a polygonal mass of tissue in which the hepatocytes are radially disposed. Between those cells a sinusoidal liver capillaries and bile canaliculi are present. At the center of each hepatic lobule there is a central vein. Portal areas are present at the corners of the lobule and are occupied by the portal triad which consist of a branch of portal vein, a branch of hepatic artery and a part of the bile duct system (7,8).

The liver is the organ in which nutrients absorbed from the digestive tract are processed and stored. The natural infection with Toxoplasma Gondii parasite is acquired by ingestion of encysted organisms which are released in the digestive tract then they invade the intestinal tissues and then disseminate via blood stream (9). So we expect the liver will be affected greatly through this pathway. In this study an attempt was made to evaluate the effect of infection with Toxoplasma gondii parasite on the histology of mice liver.

Materials and Methods
Experimental animals: 6-10 week old male mice were used for the experiment. 20 mice were isolated and maintained on normal diet, they were grouped into two groups: the first group (10 mice) were left as a control, while the second group (10 mice) were inoculated intraperitonealy with...
placental fluid containing Toxoplasma Gondii parasite.

Isolation of Toxoplasma Gondii parasite: Pregnant women infected by acute toxoplasmosis and their infection was proved by ELISA test showing the presence of IgM antibody against the parasite in their blood were chosen as a source of Toxoplasma Gondii parasite. After labour the placentae were taken from those women and a piece of placental tissue about 30-50 gm. in weight were taken, cut into small pieces and grinded using pistil and mortal followed by placing them in a homogenizer added with 0.9% normal saline followed by adding the enzyme trypsin (0.25% in NaCl solution). This mixture was then placed in an incubator for one hour. Filtration of this mixture was made using filter paper to remove large pieces of tissue, followed by placing the mixture in a centrifuge for 10 minutes then phosphate buffer saline (PBS) was added to the precipitate with normal saline solution. To prevent bacterial contamination, a solution of normal saline containing 1000 IU of penicillin and 100 mg of streptomycin was also added to the above solution (10).

Route of infection: Intraperitoneal inoculation of 0.5-1 ml. of the placental tissue suspension were made for group two mice, after about 10-15 days those mice were scarified and the liver tissues were taken for further study (10).

Preparation of tissues for histological analysis: Liver tissues were kept for few days in 10% neutral buffered formalin solution. Then each liver was cut into 1 cm. thick slices, dehydrated by alcohol, cleared with xylol and finally embedded in paraffin and paraffin blocks were made.

Using Reichert Rotary microtome serial paraffin sections of 5µm. thickness were made and the sections were then stained with Harries Hematoxylin and Eosin

Results

Histological examination of group I mice livers reveals normal lobular pattern of liver cells with radial arrangement of hepatocytes around the central veins. Between the hepatocytes, sinusoidal capillaries were clearly seen (fig. 1).

In the second group examination of mice livers infected with toxoplasmosis revealed many marked histological changes including:

The presences of Toxoplasma Gondii parasite (tachyzoites and bradyzoites) distributed through out the liver tissues, invading the hepatocytes and kupffer cells and even were seen lying on the endothelial surface of the sinusoidal liver capillaries. Tissue cysts were clearly identified between the hepatocytes (fig. 2 and fig. 3).

Chronic inflammatory cellular infiltration was very obvious especially around the central veins and in the portal area. Those cells were mainly lymphocytes (fig. 4).

Loss of the normal lobular pattern of the liver with abnormal liver cells having a foamy appearance were observed in four cases out of ten of the second group (fig. 5), this is also associated with dilated central vein and sinusoidal capillaries between the hepatocytes hemorrhage and congestion of the central veins within the liver lobules (fig.6).

Discussion

Toxoplasmosis remains a serious disease and in many studies were carried out on Toxoplasma Gondii parasite and its effect on tissue histology the liver remains one of the most important organs affected by this infection and remains a preferable site for growth and multiplication of Toxoplasma Gondii parasite (5,6).

In experimental models of infection with Toxoplasma Gondii parasite, acute mortality can result either from a failure to control the parasite number or due to the excessive immunological response against the infection (9). In the present study many histological changes were observed in mice livers infected with Toxoplasma Gondii parasite compared with the control group.

The presence of tachyzoites and tissue cysts inside the hepatocytes and within the sinusoidal liver capillaries indicated that, the liver is one of the important organs involved and affected during the parasitaemia stage of infection (12), it is very well known that the hepatocytes are active metabolic cells and when such parasite invade the cell it can lead to disturbances in...
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its metabolic activity which intern leads to shape distortion, which could be due to edema and accumulation of fluid within the cells. Similar changes were also found by other workers and some relate the disturbances in the hepatocyte function and shape to the DNA damage in the liver cells provoked by infection with *Toxoplasma Gondii* (4,5,6).

Microscopic examination also revealed intense infiltration of the liver with mixed inflammatory cells, these cells leave the blood and enter the tissues as a part of the immunological response of the mice to the infection with *Toxoplasma Gondii* parasite, this change was also mentioned by other workers (9,13).

So mechanisms of liver damage and the histological changes induced by *Toxoplasma Gondii* infection is either due to a direct effect of the parasite on the tissues leading to cell death and tissue damage or it could be related to indirect effect of infection due to the excessive immunological response to the parasite (13).

References

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Fig (1): Normal hepatic lobules and hepatocytes arrangement around the central vein in normal mice liver (H&E 100x).

Figure (2): Mice liver infected with *Toxoplasma Gondii* parasite, Tachyzoites (arrow heads) inside the hepatocytes and sinusoids (H&E 400x).
Figure (3): Mice liver infected with *Toxoplasma Gondii* parasite, the presence of tissue cysts (arrow) between the hepatocytes (H&E 400 xs).

Figure (4): Chronic inflammatory cell infiltration around the central veins in mice liver infected with *Toxoplasma Gondii* parasit (H&E 100x).
Figure (5): Abnormal liver cells with foamy appearance in mice liver infected with Toxoplasma Gondii parasite (H&E 400x).

Figure (6): Dilated sinusoidal liver capillaries (arrow heads) with congested central vein (arrow) in mice liver infected with Toxoplasma Gondii parasite (H&E 100x).