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STUDY ON MYCOTIC DISSEMINATION AND PATHOLOGICAL FINDINGS ASSOCIATED WITH EXPERIMENTAL *CANDIDA ALBICANS* INFECTION IN BALB/C MICE

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ABSTRACT
Candidiasis is a one of zoonotic disease and a public health importance. To identify dissemination of *Candida albicans* and pathological findings associated with the experimental mycotic infection model. *C. albicans* strain were obtained from public health laboratory and reidentified, the dose were increased to 25% of LD50 ($5x10^5$ CFu/ml) to become 6.25 $x10^5$CFu/ml and 0.25 ml were injected intraperitoneally in group of mice (40), every 3 days 3 mice were sacrificed for a period of 30 days . *C. albicans* isolation were done from the different organs of mice and were found that *C. albicans* were persisted for 12-15 days in different organs of mice except that it persisted for 21 days in kidneys , liver and spleen. Different pathological lesions were recorded in the mice organs during the period of infection with *C. albicans* . Kidney showed interstitial nephritis with perivascular leukocytes Cuffing, microabscesses and purulent granuloma in liver hyperplasia of white pulp and red pulp with amyloidosis in spleen, interstitial pneumonic lesion with peribronchial lymphoid tissue hyperplasia, focal myocarditis and epicarditis. Microglia cell proliferation in brain, focal peritonitis, hyperplasia of lymphoid tissue of peyers patches and intestinal wall thickening and endometrial hyperplasia and endometritis and mucupurulent vaginitis.

KEYWORDS: *C. albicans*, zoonotic disease, balb/c mice, Candidiasis.

INTRODUCTION

Candida albicans is an opportunistic yeast pathogen that was frequently isolated from the mucosal surfaces, of normal individuals and it is capable to initiating variety of recurring diseases especially in the vagina, oral and gastrointestinal mucosa, it also can affect different systemic organs in the body[1,2]. Infections with *C. albicans* increased prodominently in the patients with immunodeficiency, following the using broad spectrum antibiotics and cancer therapy and after surgical operation and tissue transplantation[3,4]. Candidiasis is a common infection in man and animals. It affect poultry causing high mortality also , it affect cattle and associated with abortion and mastitis and affect most of different animals and even laboratory animals and it sure that candidiasis is one of zoonotic diseases [5,6] and so the importance of this diseases , this study aimed to identify the dissemination of *C. albicans* in the body organs of mice and to identify 1- pathological findings associated with experimental infection of this laboratory animal with this microbial infection .

MATERIALS & METHODS

Candida albicans obtained from the central public health laboratories and to ensure its purification, the following diagnostic methods had done including, cultural characteristics, microbiological examination, Germ tube formation chlamyolospores formation test. API candida Biomerieuxs, France). After determination LD50 for C. albicans [7] it is found that mice sensitive to lethal dose fifty $5x10^5$ CFU/ml) for this reason we increase the dose with 25% to become 6.25 x 10^5 CFU/ml , then 0.25 % of *C. albicans* were taken and injected intraperitoneally in 40 mice (Balb / c white mice) and 3 mice infected were killed at 3 days interval for 30 days , then isolation of *C. albicans* from different organs were done and pieces from different organs were taken in 10% formalin for fixation , then after processing routinely in histokinette , cut at 5 μm thickness and stained with hematoxyline and eosin and examined under light microscope [8] .

RESULTS & DISCUSSION

The dissemination of *C. albicans* in the different body organs of experimental intraperitoneally infected mice. During the experimental term (30 days), there is individual differences in appear and disappear of the infection in different body organs (Table – 1), It persist in liver, spleen and kidney for 21 days whereas in brain and other organ persist for 12-15 days post inoculation.

Table 1: Spread of C. albicans in different body organs of experimental intraperitoneally infected mice

Days	Liver	Spleen	Kidney	Intestine	Vagina	Uterus	Periton	Lung	Heart	Brain
3	+	+	+	+	+	+	+	+	+	+
6	+	+	+	+	+	+	+	+	+	+
9	+	+	+	+	+	+	+	+	+	+
12	+	+	+	+	+	+	+	+	+	+
15	+	±	+	+	±	+	±	±	±	±
18	+	-	+	±	-	-	-	-	-	-
21	±	-	±	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-			-	-	-
30	-	-	-	-	-		-	-	-	-

- Total No. of mice : 40 mouse
- Killed mice (4) each days including dead animals.
- Dose 0.25 ml of 6.25 x 10^5 cfu/ml to each mouse.
- (+) *C. albicans* isolated from organs of killed and dead mice .
- (-) No isolation of *C. albicans* from body organs.

These results agree with[9], they mentioned that *C. albicans* can affect liver, kidney, spleen, lung, brain, intestine in addition to uterus and vagina, when yeast inoculated intraperitoneally in mice and spread through blood stream and cause systemic candidiasis[10] which is evident in this study. *C. albicans* began to disappear from most of body organs such as liver, kidney, spleen & lung after 18-21 days post inoculation, these results agree with[11] whom mentioned that the clearance of these organ from *C. albicans* is related to developing the immune response against this microbial infection during this period of infection [12] .

Histopathological changes

Kidneys

The main lesions were consisted of infiltration of interstitial tissue with neutrophils and mononuclear cells (lymphocytes , macrophages and plasma cells) between renal tubules and adjacent glomeruli (Fig.1) and around blood vessels in addition to dilatation of Bowman capsule.

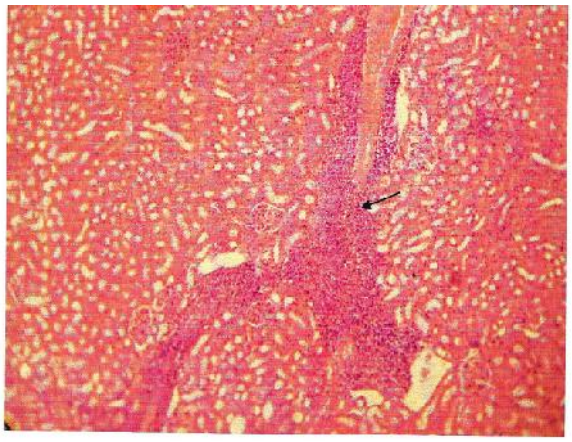

FIGURE 1: kidney interstitial nephritis characterized by extensive infiltration of lymphocytes and macrophages between renal tubules and glomeruli (arrow) (H& E) x 200

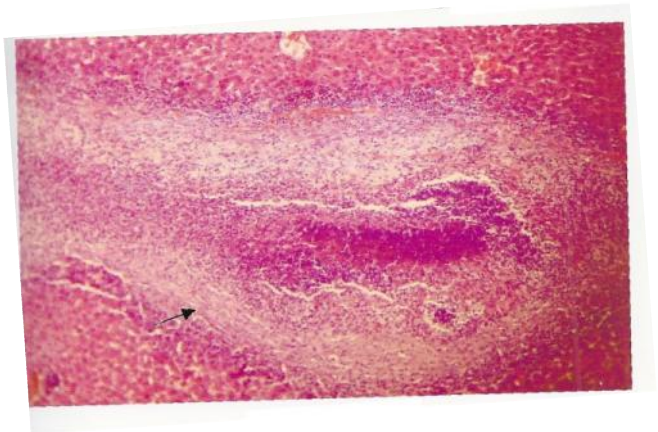

FIGURE 2 : liver : Cirrhosis , early suppurative granulomatous reaction with central caseasion surrounded by neutrophils , mononuclear cells (MNC) infiltration and fibroblast proliferation (arrow) , in addition to congestion of blood vessels (H&E)x200

Liver

There is congestion , hydropic degeneration with vaccuolation of hepatocytes and multifocal aggregation of neutrophils and edema in the adjacent area to central vein and in portal area , these cellular reactions cause a microabscess which gradually transform into suppurative granuloma especially in advance cases , with a central necrosis surrounded by neutrophils , mononuclear cells and giant cells with fibroblasts proliferation

Spleen

There is extensive hyperplasia of the white pulp region in per arteriolar sheath region (T cell region) and in the remainder area of the pulp (B cell region) (Fig- 3). Also there is reticuloendothelial cell hyperplasia in the red pulp and thickening of spleen trabecnlae. In certain section extensive amyloid deposition enclosing the white pulp.

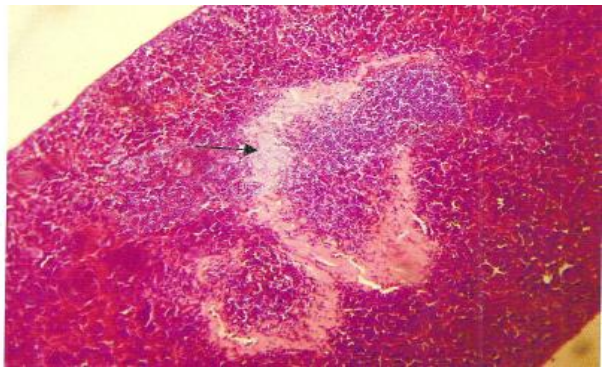

FIGURE 3: spleen Amyloid, sago spleen type amyloidosis inclosing the white pulp (arrow) (H&E) x 200

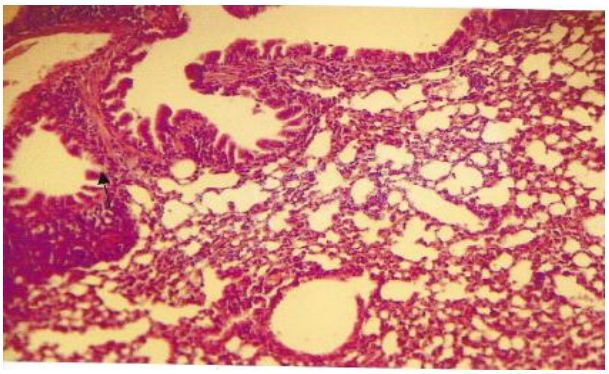

FIGURE 4 : lung peribronchial lymphoid tissue , hyperplasia (arrow) (H&E)x200)

Lungs

There is extensive interstitial pneumonic lesion characterize by thickening of alveolarwalls due to congestion of alveolar capillaries and infiltration of mononuclear cells (Fig 4) causing narrowing of alveolar Lumina, also there are a peribronchial lymphoid tissue hyperplasia and in advance cases a pulmonary fibrosis.

Heart

In the most sections there is infiltration of neutrophils and mononuclear cells between muscle fibers and on the epicardium

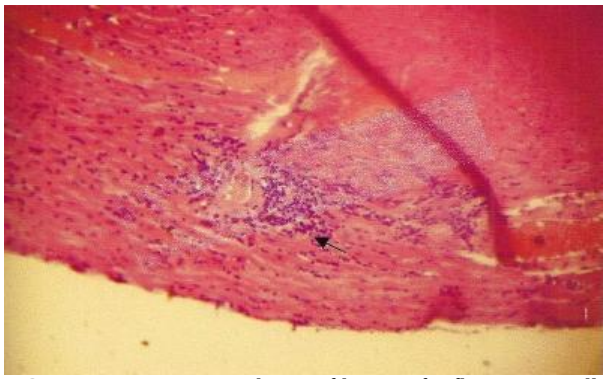

FIGURE 5: Heart Myocarditis , infiltraton of inflammatory cells between myocardial muscles fibers also congestion of blood vessels (arrow) (H&E) x 200)

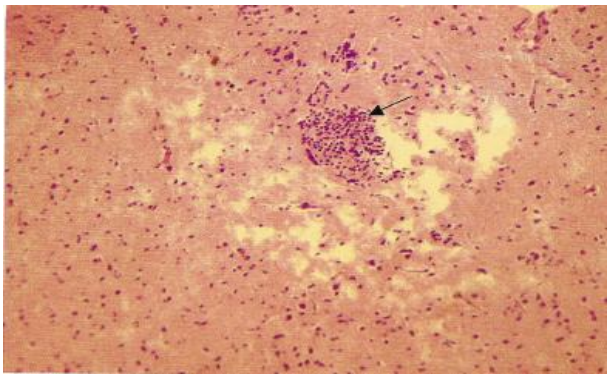

FIGURE 6: Brain focal gliosis characterized by focal proliferation of microglial cells with focal area of edematous liquification (arrow). (H&E) x 200

Brain

There is focal aggregate of neutrophils and mononuclear cells around blood vessels (perivasculor leukocyte cuffing) in addition to focal gliosis with focal proliferation of microglia cells (Fig 6). In certain sections focal meningitis characterized by infiltration of meanings with neutrophils and mononuclear cells and congestion of Blood vessels and edema.

Peritoneum

There is extensive infiltration of neutrophils and mononuclear cells in the adipose tissue and around the blood vessels of the peritoneal tissue (Fig -7)

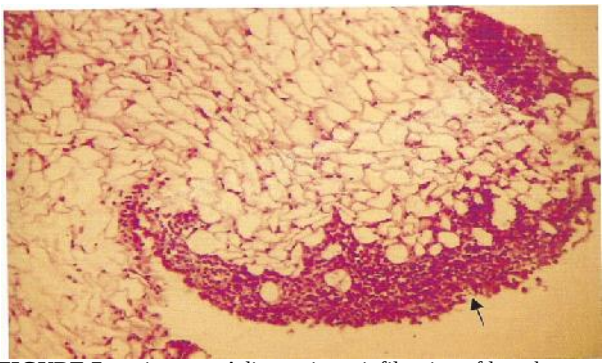

FIGURE 7: peritoneum Adipose tissue infiltration of lymphocytes and macrophage on the peritoneal surfaces (arrow) (H&E)x200

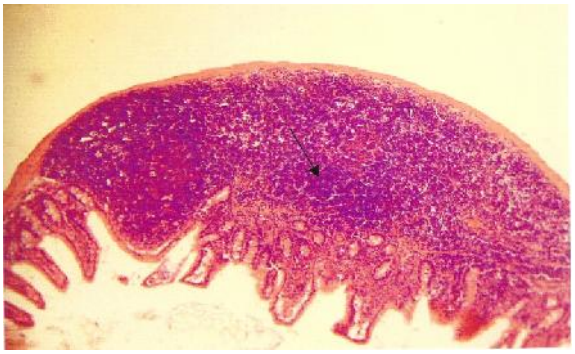

FIGURE 8: Intestine Reactive hyperplasia of peyer's patches with germinal center formation (arrow). (H&E) x 200

Intestine

There is extensive hyperplasia of the lymphoid tissue in the peyer's patch region causing thickening of intestinal wall (Fig – 8)

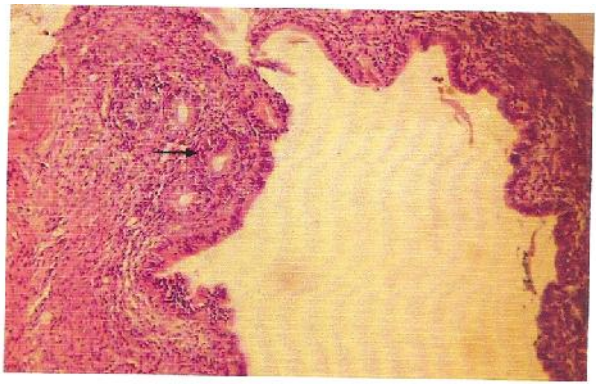

FIGURE 9 : Uterus endometrium sloughing of epithelial lining of endometrium and mucus exudates in addition to subendometrial inflammatory infiltration (arrow) . (H&E)x200

Vagina

There is extensive infiltration of neutrophils and mononuclear cells and congestion of blood vessels in vaginal wall and sloughing of mucosal epithelial lining with mucopurulent exudate in the vaginal lumen (Fig – 10).

This study revealed that the renal tissue is the one of the organs sensitive to *C. albicans* infection with production of different lesions due to proliferation of this microbial agent in renal tissue and as a result of less presence of phagocytic cells in renal tissue[13]. Liver is considered to be the 2nd target organ infected with *C. albicans* and associated with degenerative changes, abscessation and supportive granuloma formation, similar finding were observed by [9] due to proliferation of this microbe in liver tissue. Spleen showed extensive hyperplasia of white pulp and reticuloendothelal hyperplasia of Red pulp in addition to amyloid enclosing white pulp, similar finding in spleen were reported by [14] but with less degree and explained on the basis of the dose and virulence of the *C. albicans* , similar lesion in the lungs were reported by [15] , they considered that the lung is one of the target organs affected by *C. albicans* . similar findings were reported in the heart and brain of mice [14] with a focal inflammatory cellular reaction between myocardial fibers but with less degree and in brain of mice with microglia cell proliferation and perivascular leukocyte cuffing depending on dose and virulent of *C. albicans* [14] . Similar lesions were reported in periton (focal peritonitis) this agree with [16] and in intestine, hyperplasia of peyer's patches and intestinal wall thichenining due to inflammatory cell infiltration and goblet cell proliferation. This result agree with[17] who explained this lesion in intestine due irritation of mucosal surface by *C. albicons* . this study revealed that the endometrial hyperplasia , sloughing of their epithelial lining together with mucopurulent vaginitis and mucopurulent exudate filling the vaginal and uterine lumena occurred as a result of proliferation of yeast like

Uterus

There is extensive endometrial epithelial hyperplasia and infiltration of neutrophils and mononuclear cells in subendometrial region leading to thickening of uterus (Fig- 9). In other sections there is sloughing of epithelia lining of endometrium and presence of the inflammatory cellular exudates and mucus in the uterine lumen.

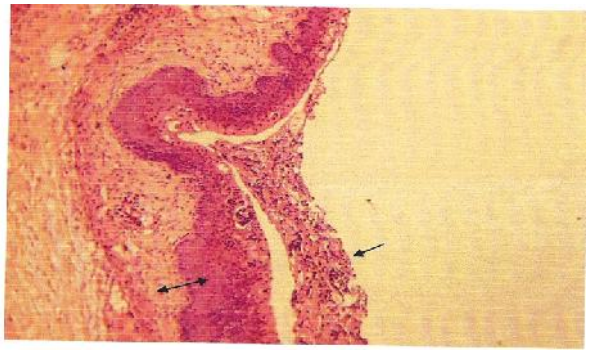

FIGURE 10: Vagina : Mucoperulent vaginitis : suppurative exudates (arrow) mixed with mucus secretion with sloughing of their epithelial lining , also some inflammatory cell infiltration in the vaginal wall and hyperplasia of their epithelial lining (double arrow) , (H&E)x200

cells of *C. albicans* which is more evident as a white patches in vaginal mucosa , this result agree with [18] .

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