Pathogenesis of Huge Splenomegaly in El-Minia Province

THESIS

Submitted in Partial Fulfillment for the Requirement of M. D. Degree (Tropical Medicine)

By

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1994

ACKNOWLEDGEMENT

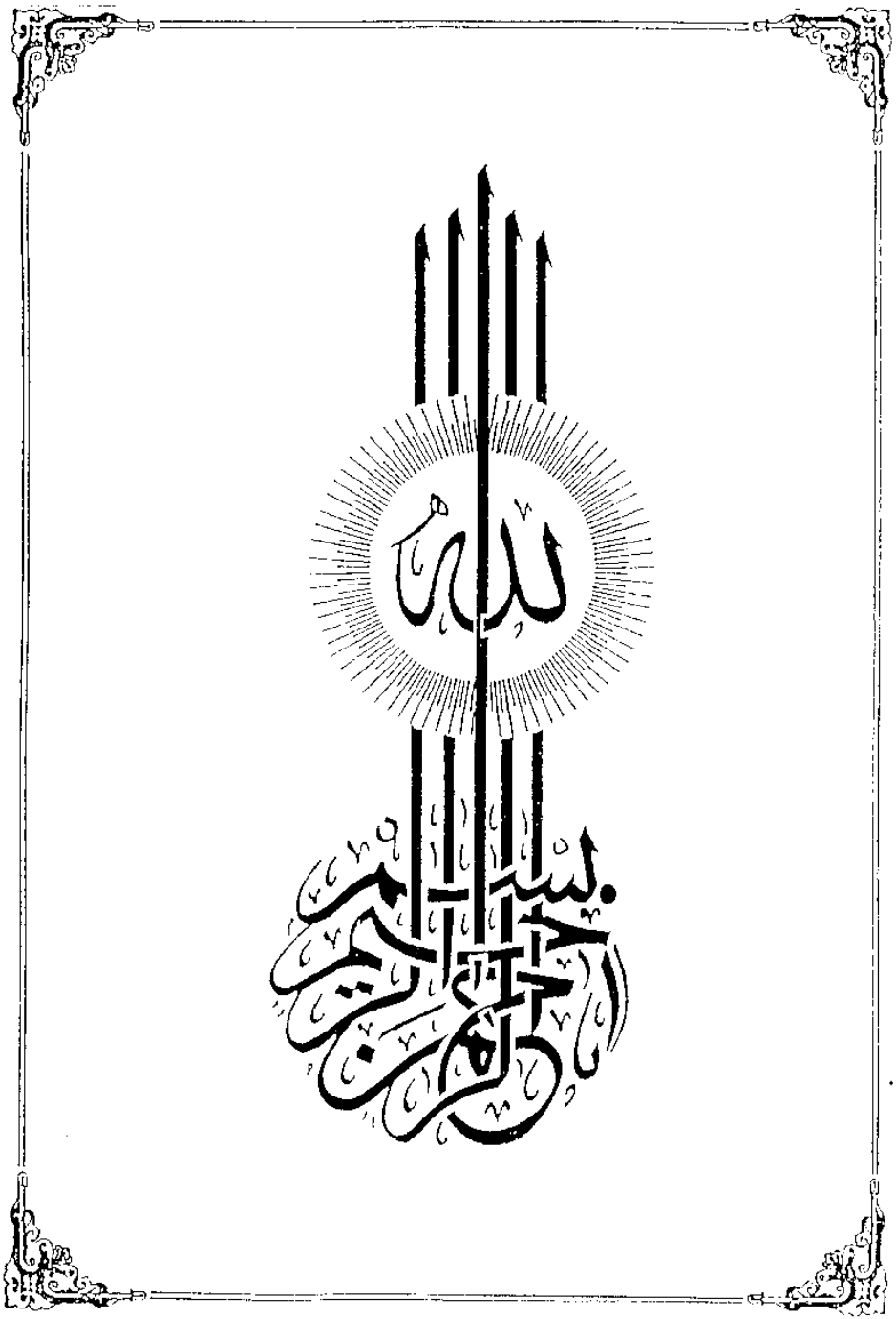
I would like very much to express my deepest gratitude to *Prof. Dr. Mohamed Fathy Abdel- Wahab,* Professor of Tropical Medicine, Faculty of Medicine, Ain- Shams University, to whom I am greatly indebted for his continuous supervision, active participation, cooperation and revision of all parts of the work.

I am also greatful to *Prof. Dr. Talaat M. El-Deeb,* Professor of Pathology, Faculty of Medicine, Ain- Shams University who helped me so much in completing this work.

A lot of thanks to *Dr. Ahmed A. El- Kateeb,* Assistant Professor of Tropical Medicine, Ain- Shams University for his kind help and encouragement.

Sincere acknowledgement to *Prof. Dr. Tareef H. Sallam,* Professor of Clinical Pathology, Faculty of Medicine, Ain- Shams University for his encouragement and helping especially in the interpretation of the splenic aspirate smears.

I would like to express my deepest gratitude to *Dr. Madeha M. A. Makloul,* Lecturer of Tropical Medicine, Faculty of Medicine, Minia University for her encouragement and helping especially in the endoscopical part of the work.



Many thanks to *Dr. Tarek M. S. El-Sharkawy* Lecturer of Pathology, Faculty of Medicine, Ain- Shams University for his very kind help, cooperation and valuable suggestions.

Thanks to all the Staff and Colleagues in the Department of Medicine, Minia University for their helping and encouragement.

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INTRODUCTION:

The spleen being a major reticuloendothelial organ, is the largest lymphoid organ in the body and plays a pivotal role in host defense by clearing microorganisms and antibody - coated cells. The spleen also is important for antibody synthesis especially against soluble antigens **(Trimble 1991).**

Huge splenomegaly was considered when it reached to or below the level of umbilicus down to the iliac fossa, right or left **(Atta 1969, Hart 1985).**

In massive splenomegaly as may be encountered in patients with idiopathic myelofibrosis, chronic myeloid leukemia, Tropical splenomegaly syndrome, Gaucher's disease and Kala - azar, spleen weight may reach 20 - 30 times normal. In such patients splenic regional blood flow may exceed 10 times normal **(Williams 1966).**

As a result of its enlargement it is sometimes liable to hypersplenism, causing all or any of the follwoing cytopenia: anemia, leucopenia or thrombocytopenia **(Trimble 1991).**

AIM OF THE WORK:

The aim of the work is to study the cause, pathology, pathogenesis and the role of different methods of diagnosis in diagnosing cases of huge splenomegaly.

REVIEW OF THE LITERATURE

ANATOMY OF THE SPLEEN

The spleen lies mainly in the left hypochondriac region of the abdomen , its posterior edge extending into the epigastric region. It is situated between the gastric fundus and diaphragm. In shape, it varies from a slightly curved wedge (if the colic impression is small) to a tetrahedron (if the colic impression is large). Its long axis lies in the plane of the tenth rib, its posterior border being about 3.5 - 4.0 cm from the mid-dorsal line at the level of the tenth thoracic spine and its anterior border reaching the mid axillary line. In is soft, friable, highly vascular and of dark purple colour (williams et al., 1989).

Relations : -

The spleen has diaphragmatic and visceral surfaces, superior and anterior borders and inferior and posterior extremities . The diaphragmatic surface is convex and smooth, faces posterosuperiorly and to the left, except at its posterior edge which faces slightly medial. It is related to the abdominal surface of the diaphram which separates it from the lowest part of the left lung and pleura and the nineth to eleventh left ribs. The pleural costodiaphragmatic recess extends down as far as its inferior border. The visceral surface, facing the abdominal cavity, presents gastric, renal, pancreatic and colic impressions . Near the inferior limit of the spleen is the hilum, along fissure pierced by several irregular apertures through which vessels and nerves of the spleen pass. The superior border, separating the diaphragmatic surface from the gastric impression, is usually convex and near its lateral end, has one or two notches indicating the lobulated form of the spleen in early fetal life. The border separates the renal impression from the diaphragmatic surface and lies between the

diaphragm and the upper part of the left kidney`s lateral border. More blunt and rounded than the superior border, it corresponds in position to the eleventh rib`s lower margin. The posterior extremity usually faces the rounded vertebral column. The anterior extremity is more expanded and cemmonly forms a margin connecting the lateral ends of the upper and lower borders. It is related to the left colic flexture and to the phrenicolic ligament.

The spleen is almost entirely covered by peritoneum, which adheres firmly to its capsule. Recesses of the greater sac separate it from the stomach and left kidney. It develops in the upper dorsal mesogastrium, remaining connecting to the posterior abdominal wall and stomach by two folds of peritoneum, respectively,the lienorenal ligament and the gastrosplenic ligament (williams et al ., 1989).

The size and weight of the spleen vary at different ages in different individuals and in the same individuals under different conditions. In the adults, it is usually about 12 cm in length , 7 cm in breadth and 3 - 4 cm in thickness , but tends to diminish in size and weight with age. Its average adult weight is about 150 grams, ranging between 80-300 grams, largely according to its content of blood .

It slowly enlarges during alimentary digestion and varies in size with state of nutrition, being large in well-fed animals and small in starved ones (Williams et al., 1989) .

HISTOLOGY OF THE SPLEEN

- General structure : -

The spleen is surrounded by a Capsule of dense connective tissue which sends out trabeculae that divide the parenchyma or splenic pulp into incomplete compartments. The medial surface of the spleen presents a hilum at the level of which the capsule gives rise to a number of trabeculae through which the nerves and arteries penetrate . the veins derived from the parenchyma and the lymphatic vessels that originate in the trabeculae leave through the hilum.

The splenic pulp has no lymphatic vessels **(Junqueira et al., 1988).**

- Splenic pulp: -

On the surface of a fresh or fixed slice cut through the spleen, one can observe white spots in the parenchyma with the naked eye. These are lymphatic nodules and are part of the so, called white pulp. These nodules appear within the dark red tissue , rich in blood, called the red pulp. Examination under a low-power microscope, reveals that the red pulp is composed of elongated structures, the splenic cords , which lie between the sinusoids. All of the splenic pulp supported by connective tissue containing reticular fibers. Fixed cellular elements of this tissue are the reticular cells and macrophages and the function of the reticular fibers is that of support. (Junqueira et al., 1988) .

- White pulp : -

The white pulp consists of lymphocyte-packed lymphatic sheaths and lymphatic nodules, that are arranged along the small arterial branches

emerging from the trabecular to supply the splenic pulp. In addition to having an abundant content of small lymphocytes, the white pulp is known to include antigen - presenting dendritic cells. The periarterial and periarteriolar lymphatic sheaths become densely populated with T-lymphocytes. In contrast , the lymphatic nodules of the white pulp become densely populated with B - lymhocytes. when there is a prolonged or secondary exposure of these cells to blood borne antigens, germinal centers appear within the nodules, proliferating and differentiating progeny of the activated B-Lymphocytes in primary and secondary lymphatic nodules become progressively displaced towards the red pulp, where their maturation into antibody secreting plasma cells is completed. Plasma cells are therefore generally quite prominent in the marginal zone and red pulp of the spleen (cormack 1987).

- Red pulp : -

The red pulp is a reticular tissue with a special characterstic ie : the presence of splenic cords of Billroth, The cords consist of all the cells between the sinusoids (Junqueira et al., 1988). The cords are continuous and of varying thickness according to the local distension of the sinusoids. Besides reticular cells, the splenic cords contain fixed and wandering macrophages, monocytes, lymphocytes, plasma cells and many blood elements (erythrocytes, platelets and granulocytes) .

The sinusoids of the spleen differ from common capillaries in 3 ways : (1) They have dilated large irregular lumen (2) Between their lining endothelial cells, are spaces that permit exchange between the sinusoids and adjacent tissues, and (3) The basal lamina-like material is not continous but forms barrel hoop-like rings around the endothelial walls . **(Junqueira et al., 1988) .**

Blood supply : -

The large tortous splenic artery, before reaching the spleen, divides in the lienorenal ligament into five or more rami entering the hilum to ramify in the trabeculae throughout the organ. likewise, the splenic vien forms in the ligament from five or more tributaries emerging from the hilum (Last 1978) .

Functions of the spleen :

The spleen is a lymphatic organ with special characteristics . Its best known functions are (1) formation of lymphocytes, (2) Destruction of erythrocytes (3) Defence of the organ against foreign particles that enter the blood stream., (4) Storage of the blood (Junqueira et al., 1988) .

1 - Production of blood cells : -

- The white pulp of the spleen produces lymphocytes that migrate to the red pulp and reach the lumens of the sinusoids, where they are incorporated into the blood that is present there. A constant flow of lymphocytes is observed from the splenic parenchyma to the blood stream as well as in the opposite direction. In the fetus, the spleen also produces granulocytes (neutrophil, basophils and eosinophils) and erythrocytes, but these activity ceases at the end of the fetal phase. In certanin pathologic conditions (e.g. leukemia) , the spleen may recommence the production of granulocytes and erythrocytes, thus, undergoing a process known as myeloid metaplasia (pathologic transformation of one kind of cell into another) .

2 Destruction of erythrocytes : -

The macrophages of the red pulp-in the red pulp cords -engulf entire pieces of the erythrocytes that frequently fragment in the extra cellular

spaces. The engulfed erythrocytes are altered and digested by lysosomes of the phagocytes. The hemoglobin they contain is broken down, forming a pigment, bilirubin which contains no iron and a protein ferritin , which does contain iron. These components are then returned to the blood.

3 - Defence : -

- Since it contains both B and T lymphocytes and macrophages,the spleen is important in body defense. In the same way that lymph nodes "filter" the lymph , the spleen is considered as a "Filter" for the blood. The T lymphocytes found in the periarterial sheath of the white pulp proliferate and enter the blood stream. They play a key role in cell-mediated immune mechanisms .Under the stimulus of antigens, splenic B lymphocytes proliferate and give rise to antibody-producing plasma cells. Of all the macrophagic cells of the organism, those of the spleen are most active in the phagocytosis of living particle (bacteria and viruses) and inert particles that find their way into the blood stream.

D - Blood Storage : -

Owing to the spongy structure of the red pulp , the spleen stores blood , which can be returned to the circulation to increase the volume of circulating blood. It has been demonstrated that in humans, blood storage capacity of the spleen is very small .

CAUSES OF SPLENIC ENLARGEMENT

There are various ways in which the different causes may be classified. **Asthens (1993c),** classified the various causes of splenomegaly according to their aetiology into inflammatory, congestive, hyperplastic, infiltrative and neoplastic causes. **DeGruchy in 1978** classified splenomegaly according to its size into slight, moderate and marked enlargement. **Taylor et al., (1980)** introduced their classification of splenomegaly according to the weight into massive splenomegaly (over 1000 grams), moderate splenomegaly (from 500 to 1000 grams), and minimal splenomegaly (less than 500 grams).

1- Causes of splenomegaly according to their aetiology (After Asthens 1993c):

I- Inflammatory Splenomegaly :

A- Acute and Subacute :

1- Acute splenic enlargement of various infections (typhoid, septicemia, ect.....)

2- Abscess of the spleen .

3- Infectious mononucleosis .

4- Subacute bacterial endocarditis .

B- Chronic :

1- Tuberculosis .

2- Syphilis especially congenital .

3- Felty's syndrome, rheumatoid arthritis .

4- Malaria .

5- Leishmaniasis .

6- Shistosomiasis .