CORRELATION BETWEEN CLINICAL AND IMMUNOLOGICAL FINDINGS IN CASES OF NEPHROPATHIES

THESIS

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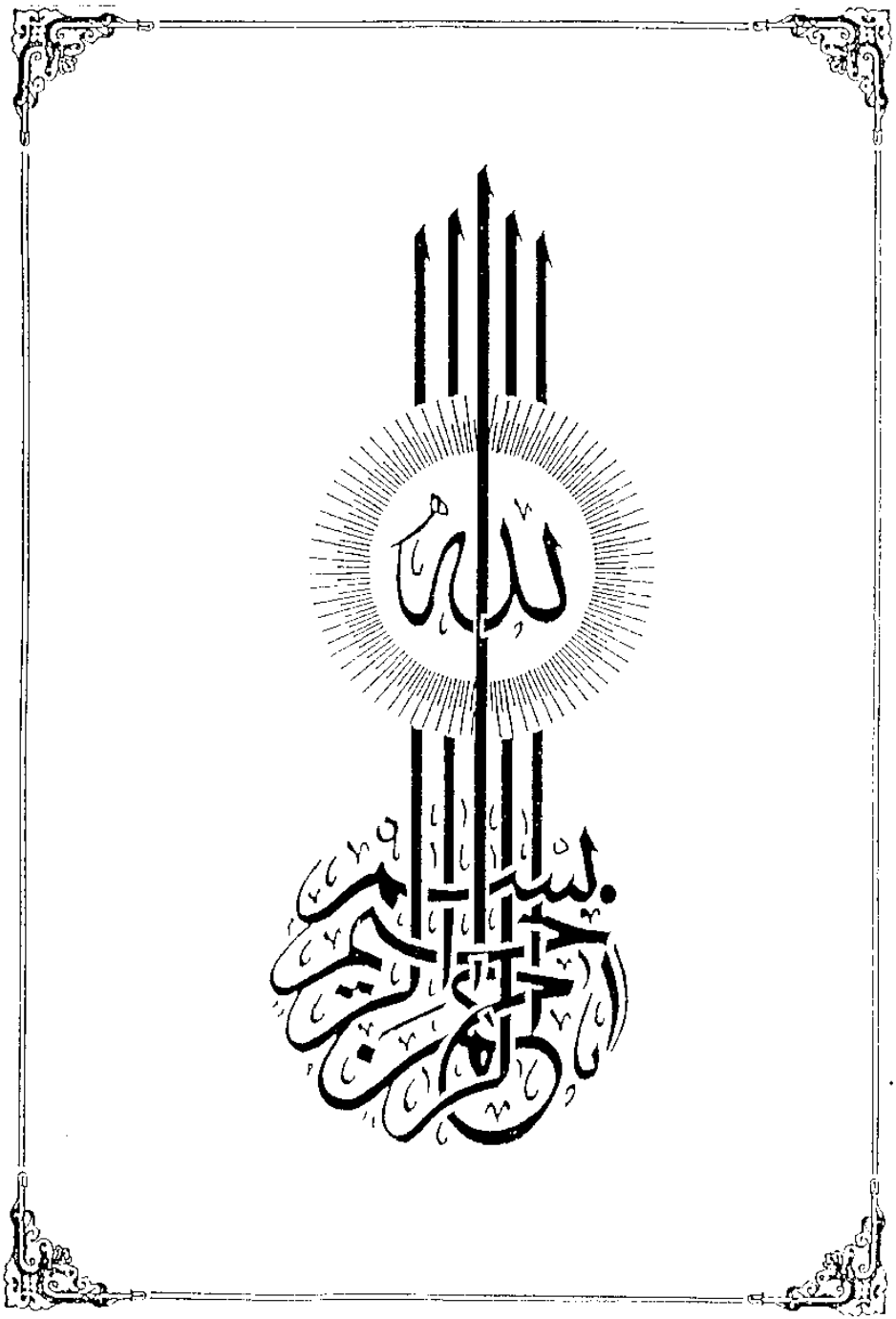

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I extend my thanks to all my colleguee in our unit of Pediatrics for their cooperation and encouragement.

Finally I am very greateful to my little patiente my God cure them all.

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INTRODUCTION

INTRODUCTION AND AIM OF WORK

Until recent years, glomerular kidney diseases remained poorly understood, even though many of their features as generalised oedema and albuminemia, were described by Bright as early as 1827.

The lack of progress in this field was mainly due to the absence of clinico-pathological correlations especially in early and less severe cases, where histologic examination of renal tissue was difficult to perform.

The popularization of percutaneous renal biopsy and the application of new techniques for the study of biopsed tissue, mainly immunofluorescence and electron microscopy, have been a step that has revolutionized the considerations with regards kidney pathology. It helped establishing an accurate diagnosis which is essential for the choice of the appropriate line of treatment and for assessing the prognosis in each case. The importance of renal biopsy as an indispensable tool for the diagnosis of the various glomerulopathies is strongly emphasized. Biopsy of the kidney is, however, quite hazardous and frequently unsuccessful in the young age groups.

If a precise correlation could be established between the different histopathologic lesions encountered in the glomerulopathies and the various clinical and

laboratory data, then one of the major purposes of renal biopsy would be achieved and eventually this procedure could be abandoned.

This work mainly aims at assessing the possibility of putting down a formula from clinical and laboratory criteria which might enable the clinician to predict the histopathologic type of glomerular disease without resorting to histopathologic investigation of renal tissue obtained by biopsy. We attempted at establishing an accurate diagnosis in the various types of nephropathies in children at time of presentation, through correlating the clinical and laboratory findings and the immunologic changes that may develop in the patient's serum with the actual pathology in the kidney as revealed by light microscopic and immunofluorescent investigation of tissue obtained by percutaneous needle biopsy.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Anatomical Consideration

The kidneys are retroperitoneal organs situated at the level of the first to fourth Lumbar vertebrae. Each kidney has eight to twelve pyramid shaped lobes. Each lobe consists of two principal zones: The cortex or outer zone, where the glomeruli, the proximal and distal convoluted tubules are located; and the medulla or inner zone where the vasa recta, descending and ascending limbs of loop of Henle, and collecting ducts are located.

Normal Histology of the Kidney as revealed by kidney biopsy (Brewer, 1973):

If a biopsy is taken to describe the normal renal architecture, there will be successively along the length of the biopsy the following layers:

1. Renal capsule
2. Cortex
3. Medulla.

The parenchymatous tissue in the cortex and medulla are held together by a minimal amount of interstitial tissue, that is rarely visible in the renal cortex under normal conditions. Blood vessels that are likely to be included in the biopsy usually do not exceed the size of small arteries and veins.

A. The cortex: Consists essentially of renal corpuscles, each formed of a glomerulus the Bowman's capsule, and the proximal and distal convoluted tubules.

The glomerulus: Is a complex structure made up of a tuft of complexly interwined thin walled capillaries formed from branching of an afferent arteriole and combining to form the efferent arteriole. The capillaries rarely appear circular in cross-section in normal glomeruli even when cut transversly. Many capillaries are cut obliquely so they appear as irregularly curved and sometimes branched structure outlined by the glomerular basement membrane, which is also irregularly curved and infolded.

The glomerulus consists of glomerular epithelial cells over the outer surface of the basement membrane of the glomerular capillaries, and endothelial cells and mesangial cells within the glomerular basement membrane. As can be demonstrated by electron microscopy, the glomerular epithelial cells have a complex structure of branching cytoplasmic processes embedded in the basement membrane, and hence the name podocytes. It is not always possible by the light microscope to identify certainly every cell within the glomerular bassment membrane. Cells which have the nucleus and cytoplasm immediately adjacent

to a capillary lumen are endothelial cells. Other cell nuclei are seen in the centre of lobules where small groups of capillaries meet. Most of these cells do not line capillaries and they are the mesangial cells. These latter cells often proliferate in disease and become surrounded by basement membrane like material.

Although mesangial cells differ in many respects from endothelial cells it is important to realize that they also are situated within the glomerular basement membrane. The glomerular basement membrane is pinched in at these points and does not in fact completely surround the glomerular capillary. The epithelial cells lining Bowman's capsule normally form a very flat incospicuous layer in the human, they overlie a basement membrane continuous at the root of the glomerulus with the glomerular basement membrane and are separated from the glomerulus by the capsular space.(Fig. No. 1).

Proximal convoluted tubules:

The normal proximal convoluted tubules can readily be distinguished from distal convoluted tubules. The cells of proximal convoluted tubules have more cytoplasm than those of the distal tubules. They also stain rather more deeply within eosin. The nuclei in the proximal

convoluted tubules are more widely spaced than those of the distal tubules so that fewer are seen in a cross-section. Other features of the cells of proximal convoluted tubules are a rather indefinite basal striation due to the orderly arrangement of the mitochondria and a brush border on the lumenal border of the cell.

The cells stain brightly with PAS stain and also contain a high concentration of alkaline phosphatase. They commonly appear to have rather a frayed edge on their lumenal border, with fine loose debris apparently derived from them in the lumen of the tubule, this sort of appearance is due in part to the formation along the brush border of spherical bodies derived from the cell cytoplasm.

The characteristic features of the proximal convoluted tubules are often not present in diseased kidneys. This is particularly so when the tubules regenerate after previous damage. In these circumstances it may not be possible certainly to identify the proximal convoluted tubules. They can sometimes only be suspected from their number and position. In such regenerating tubules mitotic figures may also be found.

Distal convoluted tubules

The distal convoluted tubule arises from the

ascending limb of loop of Henle returning to the glomerulus, it is adherent to the vascular pole of the glomerulus. The distal tubules are readily recognized from normal proximal convoluted tubules as they are lined by smaller cells with paler cytoplasm. More nuclei are present in cross-sections of distal tubules than proximal tubules. The distal tubules also have no brush border.

At the point of attachement of the distal tubule to the vascular pole of the glomerulus, the arrangement of the tubular cells alters. They become more closely grouped on the side of the tubule adjacent to this attachement so that the nuclei are more crowded than normal. This area is referred to as the macula densa. (Fig. No. 1).

B. Medulla

The loop of Henle:

This hair-pin shaped loop consists of 3 parts, the first part is the straight portion of the proximal convoluted tubule. Quite suddenly the descending limb of the loop of Henle changes in character; its lumen becomes narrower and its lining cells very flat that they might be mistaken for endothelium and the tubule for a capillary. The extent of this thin portion of the loop varies but it changes again abruptly to the thick portion of the ascending limb lined by cells similar to those lining the distal convoluted tubules.

The Collecting tubule:

Is formed by junction of two or more terminal segments of distal convoluted tubules and receives additional branches through its course in the medullary papilla.

It is lined by cubical or columnar cells with sharply defined cell borders and clear cytoplasm. They are often not present in biopsy material.

C. The Interstitium

The interstitial space and its cells increase as the papilla is approached. The space itself is filled with a flocculent material of low electron density. Several types of interstitial cells are recognized. Type I cells are the most numerous, they resemble fibroblasts. Type II cells have the characteristics of mononuclear cells and have a phagocytic activity. Type III, the pericyte, is found adjacent to the vasa recta.

D. Arteries and veins:

The intrarenal arteries have a single internal elastic lamina. Normally the intima is so thin to be hardly detectable.

A striking change occurs in the media of the afferent arteriole as it approaches the glomerulus.