Role Of Renal Biopsy In Acute Renal Failure

Thesis

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Abstract

Acute renal failure (ARF) is common problem in pediatrics which continues to have a poor prognosis despite advances in renal replacement therapy. When one considers the future field of acute renal failure, the renal biopsy would be considered as the most important diagnostic modality because most of important therapeutic issues depend on a modern understanding the pathology of acute renal failure. A biopsy provides a definitive diagnosis and alter the management of acute renal failure .

The aim of this study is to evaluate the value of renal biopsy in diagnosing the etiology of ARF , to give information about the most common cause of ARF in children and to correlate between the clinical diagnosis and pathological diagnosis and its impact on prognosis.

The result of the biopsy had confirmed the clinical diagnosis in 47% of cases, altered the clinical diagnosis in 53% of cases and resulted in change the therapeutic management in 71%of cases.

From the study, the renal biopsy provides clear guidelines which aid the diagnostic evaluation and subsequent proper management.

Key words:

ARF: acute renal failure.

Renal biopsy.

CONTENTS

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Dedication

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INTRODUCTION

Acute renal failure is a life threatening condition in children with significantly increased morbidity and mortality rates. Early detection and appropriate treatment can provide complete recovery and a major goal of acute renal failure therapy. **(Vachvanichsanong et al; 2006)**

When one consider the future field of ARF the renal biopsy is everything and nothing. Nothing because there are virtually no research studies currently involving biopsies in ARF anywhere in the world. Everything ,because most of the important therapeutic and treatment issues currently depend on a modern understanding of the pathology of ARF. (**Ronco et al; 2001)**

Percutaneous ultrasound (US)-guided renal biopsy is the gold standard in the evaluation of renal diseases, reliable, easy, highly successful, time saving and with low incidence of severe side-effects.

(Gesualdo et al; 2007)

The renal biopsy was a significant support for many of the great advances seen in the understanding of renal diseases during the last 50 years and continues to play an important role. Accurate diagnosis and classification of renal diseases has also led to the development of more specific and superior therapy. **(Kretzler et al; 2002)**

The percutaneous renal biopsy is a fundamental investigation in the diagnostic procedure for renal diseases. The introduction of the kidney localization by real-time ultrasounds made the procedure more effective and safe. The automated ultrasound-guided procedure is a feasible and reliable technique for percutaneous renal biopsy. It gives a greater yield of diagnostic tissue without increasing the rate of clinical complications. **(Aimino et al; 2001)**

AIM OF WORK

This work aims:

1-To evaluate the value of renal biopsy in diagnosing the etiology of ARF and to give information about the most common cause of ARF in children.

2-To correlate between the clinical diagnosis and pathological diagnosis and its impact on prognosis.

BASIC RENAL LESIONS

☒ Normal

The normal *glomerulus* consists of a complex branching network of capillaries originating at the afferent arteriole **a**nd draining into the efferent arteriole. The glomerulus contains three resident cell types: mesangial, endothelial, and epithelial cells. The epithelial cells cover the urinary surface of the GBM with pseudopod-like extensions called *foot processes* with intervening infiltration slits.

Endothelial cells are opposed to the inner surface of the (GBM and are fenestrated. At the stalk of the capillary the endothelial cell is separated from the mesangial cells by intervening mesangial matrix. Because the endothelial cell nucleus most often lies in this stalk region. it may be difficult to distinguish from the mesangial cell nucleus by LM - The term ***endocapillary*** is used to describe proliferation filling up the capillary lumen, contributed to by proliferation of mesangial, endothelial, and infiltrating inflammatory cells. In contrast, *extracapilary proliferation* refers to proliferation of the parietal epithelial cells that line Bowman's capsule.

The mesangial cell is a contractile cell that also has phagocytic properties. It lies embedded in the mesangial matrix in the stalk region of the capillary loops, attached to anchor sites at the ends of the loop by thin extensions of its cytoplasm. The basement membrane consists of three layers distinct by EM, the central broadest lamina densa, and the less electron-dense zones of lamina rara externa and interna. Thickening occurs with maturational growth. It was found a range of GBM thickness in children with normal kidneys from approximately 110 nm at 1 year of age to 222 ± 14 nm at 7years of age. (**Fogo;2004**)

The glomerulus is surrounded by Bowman's capsule, which is lined by parietal epithelial cells. These are continuous with the proximal

tubule, identifiable by its PAS positive brush border. The efferent and afferent arterioles can he distinguished morphologically in favorably oriented sections or by tracing their origins on serial sections. Segmental. interlobular, and arcuate arteries may also be present in the renal biopsy specimen. The cortical biopsy also allows assessment of the tubulointerstitium. Proximal tubules are readily identified by their PAS-positive brush border lacking in the distal tubules. Collecting ducts show cuboidal, cobblestone like epithelium. The medulla may also be included in the biopsy. (**Fogo ;2004**)

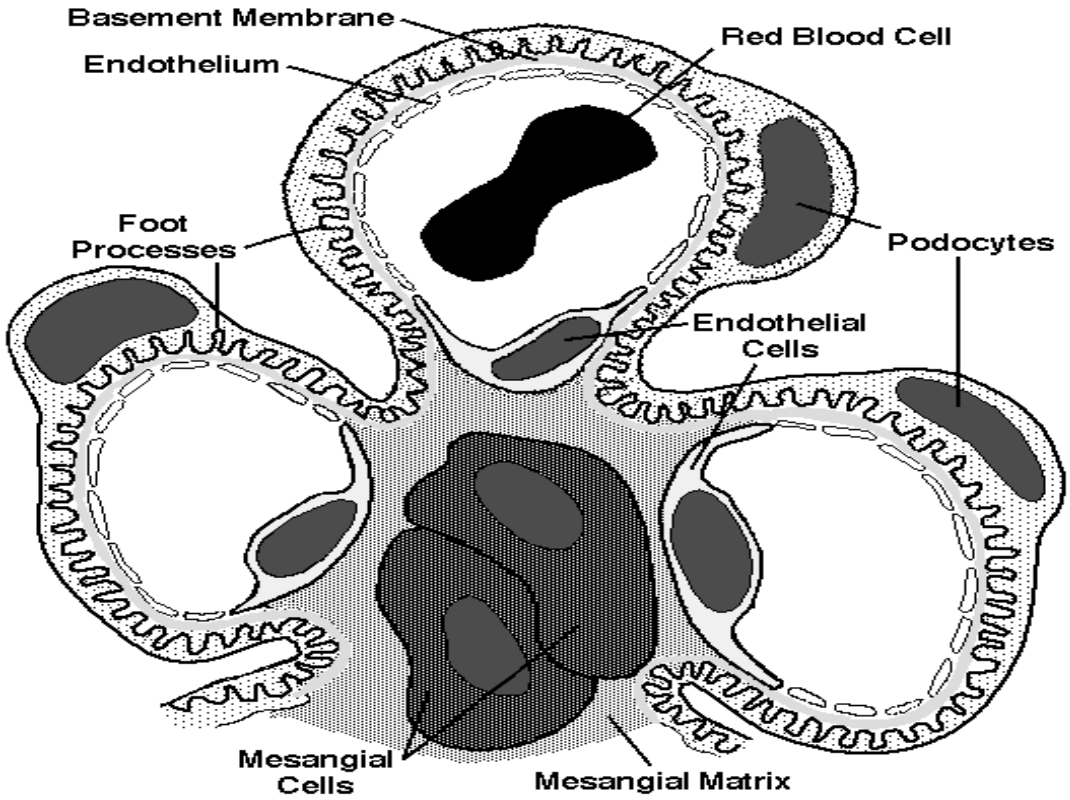

Figure (1):A normal glomerulus is shown diagrammatically. *Note the relationship of the capillary loops to the mesangium. About 15% of glomerular filtration occurs through the mesangium, with the remainder through the fenestrated epithelium. The normal anionic charge barrier of slit pores in overlying podocyte cytoplasm. The normal mesangium contains about 2 to 4 mesangial cells, which have a macrophage-like.* ***(Internet 1)***

☒ Overall Pattern

Assessment of the biopsy specimen must include inspection of all sections from different levels because additional glomeruli may be

sampled on deeper cuts of the biopsy core and many diseases are characterized by focal lesions. Assessment of severity and patterns of lesions is made, norma1 and affected glomeruli are counted.

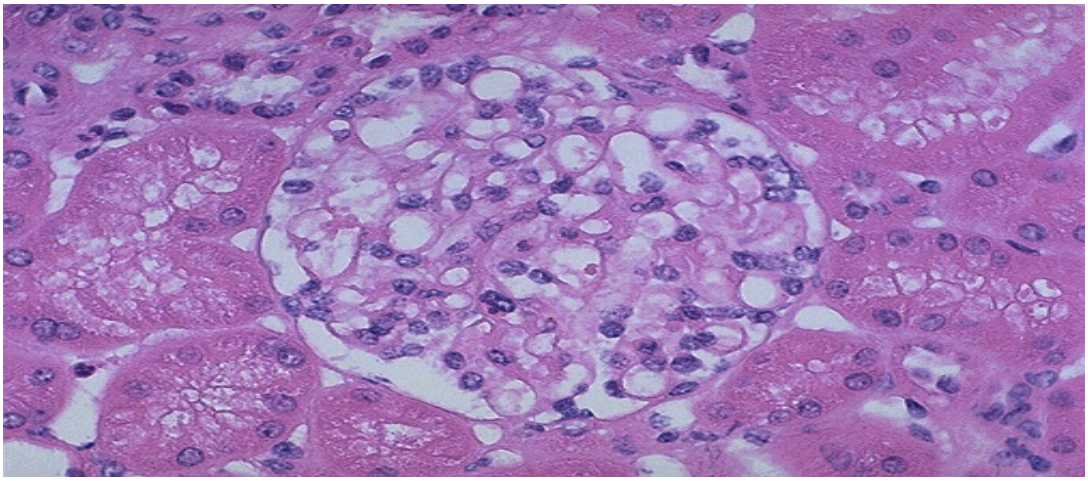

Figure (2)The normal glomerulus is shown by light microscopy. *The glomerular capillary loops are thin and delicate. Endothelial and mesangial cells are normal in number. The surrounding tubules are normal.*

(*Internet,2*)

Table (1):Definitions of common morphological terms.

Term	Definition
Light microscopy	
Focal	Involving some glomeruli
Diffuse	Involving all glomeruli
Segmental	Involving part of glomerular tuft
Global	Involving total glomerular tuft
Lobular	Simplified, lobular appearance of capillary loop
Nodular	A cellular areas of mesangial matrix
Sclerosis	Collapse and scarring of capillary loop
Crescent	Proliferation of parietal epithelial cells
Spikes	Projections of GBM intervening between subepithelial immune deposits
Endocapillary proliferation	Increase in mesangial or endothelial cells
Hyaline	Desciptive of glassy ,smooth appearing
Hyalinosis	Hyaline appearing insudation of plasma proteins

Mesangium	Stalk region of capillary loop with mesangialcell surrounded by matrix.
Subepithelial	Between visceral epithelial cell &GBM.
Subendothelial	Between endothelial cell and GBM.
Tram-track	Double contour of GBM.
Wire loop	Thick, rigid appearance of capillary loop due to subendothelial deposit.
Activity	Score of possible treatment-sensitive Lesion.
Chronicity	Score of probable irreversible lesion.
Immunoflourescence	
Granular	Discontinuous flecks of staining along capillary loop
Linear	Smooth continuous staining along capillary loop.
Electron microscopy	
Food process effacement	Flatting of food process
Microvillus transformation	Small extensions of visceral epithelial cell (villus like appearance).
Circmferential mesangial interposition (CMIP)	Extension of mesangial cell cytoplasm with interposition between endothelial cell cytoplasm and basement membrane.
Reticular aggregates	Organized arrays of membrane particle within endothelial cell
Immunotactoid glomerulopathy	Large, organized microtubular deposit
Fibillary glomerulopathy	Fibrils 14-20 nm in diameter without organization

(**Fogo;2004**)

☒ Specific Glomerular Cells

Podocytes

The podocytes (glomerular visceral epithelial cells) may show vacuolization in various diseases with severe proteinuria. Although more extensive vacuolization of podocytes has been seen in FSGS , hence

changes are seen only after established sclerotic lesions are identifiable by LM. (**Chiang et al;1988**)

Mesangial Cells

Hyperplasia of mesangial cells is recognized by LM when more than three mesangial cell nuclei are present per mesangial region. Increased mesangial prominence may be due to increased cellularity, increased matrix, deposits, or a combination. Large mesangial deposits appear on Jones' stain as pinkish areas surrounded by the light silver-staining areas of mesangial matrix. So-called mesangial interposition results when the monocyte or mesangial cell cytoplasm extends outward between basement membrane and endothelial cells and new matrix accumulates between the mesangial and endothelial cell bodies.

(**Fogo;2004**)

Endothelial Cells

Extreme proliferation and swelling of endothelial cells can obliterate capillary lumina in conditions characterized by abnormalities of coagulation. Endothelial cells usually contain characteristic reticular aggregates in lupus nephritis. Endocapillary cell proliferation is characteristic of, for example, diffuse proliferative lupus nephritis and MPGN type I**.** **(Furness and Boyd;1996)**

Crescents

Crescents consist primarily of proliferating parietal epithelial cells with some infiltrating macrophages and are a manifestation of severe glomerular injury. The name reflects the often crescent-shaped sheet of cells filling their part or nearly all of Bowman's space. Crescents result from injuries that break the GBM, leading to exudation of plasma protein and formation of fibrin within Bowman's space, which then induces proliferation of the parietal epithelial cells and infiltration of

macrophages. When crescents are a prominent histological feature, the patient most often presents clinically with a rapidly progressive glomerulonephritis. Crescents may occur in a variety of diseases. Diseases with crescents as a primary manifestation include antibody-mediated injury (anti-GBM antibody disease), immune-complex diseases (e.g., lupus nephritis), and nonimmune diseases.

(Jennette et al. ;1996)

In addition, crescents were divided into *cellular. fibrocellular,* or *fibrous* categories according to their histopathologic appearances and were further subcategorized according to other criteria, including changes in the glomerular tuft, immunochemical staining, and clinicopathological correlations. (**Dillon;2004)**

Renal biopsy is, therefore, critical for accurate diagnosis. Diagnosis and appropriate treatment must occur rapidly in this clinical situation to optimize chances of recovery of renal function. The early lesion of cellular crescents is responsive to cytotoxic therapy. Biopsy indications of irreversible renal damage include breaks of Bowman's capsule and fibrous transformation of the cellular crescents, periglomerular fibrosis, and scarred glomeruli and tubulointerstitium. (**Fogo;2004**)

☒ **Glomerular Basement Membrane**

GBM abnormalities are best evaluated by EM. In children, the diagnosis of thin basement membranes is more difficult than in adults because GBM increases in thickness with normal maturation. GBM thickness should be compared with normal for age and sex. Immune deposits may localize on either side of the GBM. (**Morita etal;1988**)

☒ **Tubules**

Tubules are atrophied with dilation and flattened epithelium in chronic renal disease although inherent interstitial factors may also be involved in

these changes. Tubular atrophy is also present in primary tubulointerstitial diseases. (**Heptinstall;1992**)

☒ **lnterstitium**

Interstitial edema is a nonspecific change present, for example, renal vein thrombosis, or inflammatory processes. Identification of eosinophils in an infiltrate is suggestive of drug-induced interstitial nephritis, although eosinophils are also present in some cases of idiopathic interstitial nephritis. Fibrosis results in increased spacing of tubules because of the accumulation of PAS-positive collagenous material. The connective tissue also stains specifically blue with Masson's trichrome stain.

(**Hawkins et al;1989**)

☒ **Vessels**

Larger vessels typically are not sampled by a biopsy; and diseases that affect these large vessels are, therefore, best evaluated by other methods (e.g., arteriography). Intimal fibrosis and medial thickening with hyperplasia and hypertrophy of media are characteristic of hypertensive injury. Fibrin thrombi, when present in glomeruli or arterioles, are the essential lesions of the thrombotic microangiopathies (e.g., HUS).

(**Fogo;2004**)

ACUTE RENAL FALIURE

Definition

First, well over 20 definitions for acute renal failure have been have been used in published studies ranging from dialysis requirement to subtle increase in serum creatinine**.** **(Mehta and Chertow; 2003)**

Acute renal failure (ARF) represents a sudden reduction in kidney function to a level insufficient to adequately filter and excrete solute and water and maintain fluid and electrolyte balance. In spite of many years of clinical recognition, intervention, and research, a precise definition of ARF remains elusive, and commonly used definitions, including oliguria and azotemia, have shortcomings in pediatric practice.

(Benfield and Bunchman;2004)

Acute renal failure is characterized by abrupt and sustained decline in glomerular filtration rate which lead to accumulation of urea and other chemicals in the blood. Most studied define it biochemically as a serum creatinine of 2 to 3 mg per dl (180 to 270 μmol per L), an elevation of more than 0.5 mg per dl (40μmol per L) over a baseline creatinine below 2 mg per day, or a twofold increase of baseline creatinine. An international interdisciplinary, consensus panel has classified acute renal failure according to change from baseline serum creatinine or urine output. The classification begins with risk, defined by a 50 percent increase in the serum creatinine or a urine output of less than 0.5 ml per kg per hour for at least six hours; and it concludes with failure, defined by a threefold increase in serum creatinine or a urine output of less than 0.3ml per kg per hour for 24 hours. **(Bellomo et al.; 2004)**

Acute renal failure is characterized by an abrupt increase in the blood concentration of creatinine and nitrogenous waste products a decrease in the glomerular filtration rate (GFR), and the inability of the kidney to appropriately regular fluid and electrolyte homeostasis.