MEDICAL PRACTICE

Hospital Topics

Value of renal biopsy in acute intrinsic renal failure

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Summary

Eighty-four patients presented with acute renal failure and features suggesting a diagnosis of intrinsic renal disease other than "acute reversible renal failure." Renal biopsy proved valuable in establishing the diagnosis, in indicating the reversibility of the lesion, and in helping to decide on treatment.

Introduction

Acute renal failure is a problem common to many medical specialties, and its investigation has become more important since the advent of successful palliative treatment, especially haemodialysis and renal replacement. Acute renal failure may be defined as a sudden reduction in renal function with a consequent rise in blood urea and creatinine levels, usually associated with anuria or oliguria of less than 400 ml/24 h/1·73 m^2. The first steps in diagnosis are to exclude prerenal and postrenal causes as well as acute or chronic disease, but these aspects are not discussed here.

Acute renal failure due to intrinsic renal disease may be vascular, glomerular, or tubulointerstitial in origin. The most common cause is so-called acute tubular necrosis (ATN), better called acute reversible intrinsic renal failure,[1] which has received most attention in reports. When a patient presents in acute renal failure apparently due to causes in the kidney the origin of the disorder may not be apparent. If none of the usual precipitating factors of ATN are present or there are features to suggest a different cause a precise diagnosis is essential for better management.

Clinical features and laboratory examination of blood and urine may help in defining further possible causes, but ultimately renal biopsy is the best method of diagnosing the origin of acute renal failure, deciding on further treatment, and assessing prognosis. When the history and clinical features strongly suggest a diagnosis of ATN renal biopsy may be considered only if oliguria is prolonged or acute cortical necrosis is suspected. If there is doubt about the precipitating factors or there are features to suggest a different cause for the syndrome biopsy should be performed.

Renal biopsy carries a higher morbidity in acute uraemia,[2] so its value must be assessed against this risk. The value of renal biopsy in diagnosing glomerulonephritis was mentioned by Sharpstone,[3] but other treatable conditions, such as drug-induced instertitial nephritis, polyarteritis nodosa, and systemic lupus erythematosus, have received little attention. Basløv and Jørgensen[4] performed 37 biopsies in a series of 104 patients with other renal diseases presenting in acute renal failure and stressed the importance of biopsy in deciding whether to continue with supportive dialysis. Thomson[5] mentioned the value of biopsy in acute renal failure, especially when the kidneys are radiographically of normal size. Sraer *et al*[6] analysed the results of biopsy in 12% of patients presenting in acute renal failure who had prolonged anuria, signs suggestive of a primary renal disease, or other features to indicate a diagnosis other than ATN.

We aimed to assess by means of a retrospective study the value of performing renal biopsy on patients with acute renal failure when various features suggested that ATN was not responsible for the syndrome.

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Patients and methods

During 1964-74, 84 patients underwent biopsy in the renal unit. Their ages ranged from 2 months to 82 years, with an average of 37 years. Two specimens were taken at operation, and the remainder were obtained by percutaneous needle biopsy. During the decade some 650 patients were seen with acute renal failure. Patients who did not undergo biopsy but in whom prerenal and postrenal causes were excluded were presumed to have ATN. Of those who did not recover (54%,) most came to necropsy, and in only two (both with amyloid infiltration of the kidneys) was the initial diagnosis incorrect. In both cases there were adequate reasons for a diagnosis of ATN. One was a woman of 68 who became oliguric when in shock after a cholecystectomy. The other, a woman of 72, became oliguric when she developed a Gram-negative septicaemia while being treated for perforated diverticulitis.

All the biopsy specimens were examined by light microscopy. A piece of each of the 17 most recent specimens was fixed in glutaraldehyde, embedded in Araldite, cut at 1 μm, and stained with toluidine blue. Electron microscopy was performed on selected material. The cause of the acute renal failure in each case was determined from the histopathological diagnosis considered in conjunction with the clinical features and laboratory findings.

We (*a*) sought the reason for biopsy in each case, (*b*) compared the clinical and histopathological diagnoses, and (*c*) assessed the effect of biopsy on management.

Results and discussion

Of the 84 biopsies, 53 were performed to establish a diagnosis, 14 to confirm the diagnosis (nine cases confirmed), and 17 to assess the prognosis. Features suggesting a cause other than ATN were the absence of any of the usual precipitating factors or the presence of factors suggesting vasculitis (purpuric rash, acute haemolytic anaemia), tubulointerstitial disease (drug reaction), glomerular disease (profuse proteinuria), or systemic disease (bone pain and hypercalcaemia), or both.

Table I shows the histological diagnoses and causes of the renal disease. Only 14 patients had a histopathological appearance consistent with ATN, while most had glomerular disease. Proliferative glomerulonephritis with crescents (often referred to clinically as rapidly progressive glomerulonephritis) was found in 21 patients (fig 1). Various clinical causes for this appearance were noted, including systemic lupus erythematosus, polyarteritis nodosa, mesangiocapillary glomerulonephritis, and Schönlein-Henoch purpura. All the patients with focal proliferative glomerulonephritis and crescents had a systemic arteritis of one type or another.

TABLE I—*Histopathological diagnosis in the 84 patients with renal failure*

Diagnosis	No of patients		No in whom biopsy findings agreed with clinical diagnosis	
Vascular				
Hypertension/ischaemia	4			
TTP/HUS	10		2	
Acute cortical necrosis	1		1	
Tubulointerstitial				
ATN	14		7	
Interstitial nephritis*	9			
Myeloma kidney	2		2	
Glomerular				
Minimal-change nephropathy†	4			
Focal glomerulosclerosis†	1			
Membranous nephropathy†	2			
Mesangial proliferative glomerulonephritis	1			
Acute diffuse endocapillary proliferative glomerulonephritis	9		3	
Acute diffuse proliferative glomerulonephritis with crescents‡§	13	Crescentic nephritis 21	5	7
Focal proliferative glomerulonephritis with crescents‡§‖	6		2	
Mesangiocapillary glomerulonephritis with crescents	2			
Focal proliferative glomerulonephritis‖	3			
Amyloid	1		1	
Diabetic nephropathy	1		1	
Cryoglobulinaemia	1			

TTP = Thrombotic thrombocytopenic purpura. HUS = Haemolytic-uraemic syndrome.
*One patient with interstitial nephritis had multiple myeloma.
†Patients with minimal-change focal glomerulosclerosis and one with membranous nephropathy presented with nephrotic syndrome and oliguria (presumably secondary ATN).
‡Two patients with diffuse proliferative glomerulonephritis with crescents had Schönlein-Henoch purpura.
§Two patients with diffuse poliferative glomerulonephritis and crescents and three with focal proliferative glomerulonephritis with crescents had polyarteritis nodosa.
‖One patient with focal proliferative glomerulonephritis with crescents and two with focal proliferative glomerulonephritis had systemic lupus erythematosus.

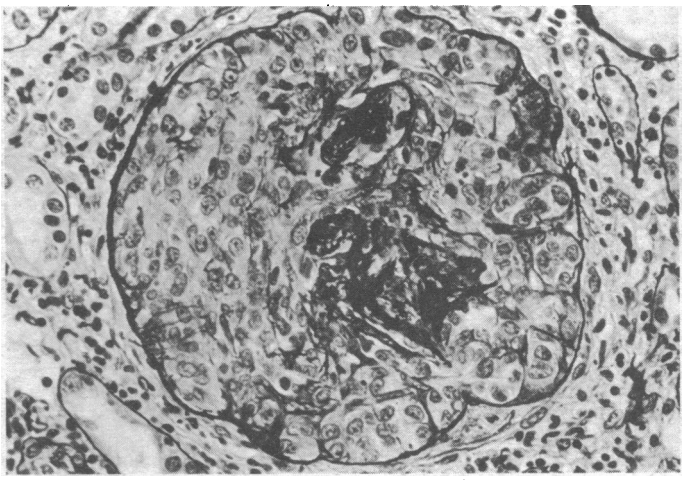

FIG 1—Glomerulus with large epithelial crescent. From patient with polyarteritis nodosa with 70% crescents. (Silver with haematoxylin and eosin. ×189.)

TABLE II—*Diagnostic categories in which patients recovered renal function*

Diagnosis	Total	Proportion who recovered renal function		No who recovered after dialysis
		No	%	
ATN	14	8	57·1	8
Interstitial nephritis	9	8	88·9	7
Myeloma kidney	2	2	100·0	2
Hypertension/ischaemia	4	1	25·0	1
TTP/HUS	10	1	10·0	1
Nephrotic (secondary ATN)*	5	4	80·0	3
Mesangial proliferative glomerulonephritis	1	1	100·0	1
Acute diffuse endocapillary proliferative glomerulonephritis	9	6	66·7	5
Diffuse proliferative and mesangiocapillary glomerulonephritis with crescents	15	4	26·7	3
Focal proliferative glomerulonephritis with crescents	6	1	16·7	1
Total	75	36	48·0	32

TTP = Thrombotic thrombocytopenic purpura.
HUS = Haemolytic-uraemic syndrome.
*Includes the four patients with minimal-change nephropathy and one of the two patients with membranous nephropathy.

The nephrotic patients who presented with oliguric renal failure, presumably due to secondary tubular damage from hypovolaemia, were all misdiagnosed. Usually severe glomerular disease was suspected clinically, whereas all were shown to have a lesion that was potentially reversible. Attention to this complication of the nephrotic syndrome was drawn by Chamberlain *et al*,[7] and to the reversibility of renal failure in minimal-change nephropathy by Conolly *et al*[8] and Meadow *et al*.[9]

The overall mortality in acute renal failure from all causes has varied in different series from 32% to 57%,[10 11] the former figure being among patients treated with intensive prophylactic haemodialysis. In our selected group of patients 36 died and 12 needed regular dialysis or transplantation, representing 57% who failed to recover adequate renal function. A higher mortality might have been expected, however, since most patients with acute renal failure have ATN.

Of the 36 patients who recovered at least some renal function 32 had undergone dialysis (table II). Failure to recover renal function varied greatly between the various histological groups, and thus treatment may be planned according to whether return of function is expected or not. In particular, all the five nephrotic patients with minimal focal or mesangial lesions recovered, four needing prolonged dialysis. Eight of the nine patients with interstitial nephritis (fig 2)

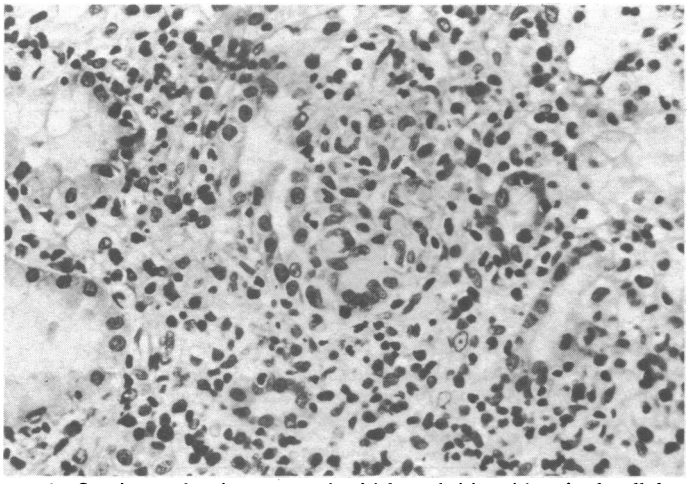

FIG 2—Specimen showing severe institial nephritis with mixed cellular infiltrate separating renal tubules. From child who presented with acute renal failure after apparent recovery from attack of measles eight weeks before. (Silver with haematoxylin and eosin. ×189.)

recovered; in none of them was the diagnosis suspected clinically before biopsy. It was then possible to incriminate and avoid the offending drug, and three patients were treated with corticosteroids. Two-thirds of the patients whose diffuse proliferative glomerulonephritis was confined to the glomerular tuft (fig 3) recovered renal function. In contrast, only one out of 10 patients with thrombotic thrombocytopenic purpura or the haemolytic-uraemic syndrome and four out of 21 with extensive crescents showed a return of useful function. Major problems are presented to medical services, the patient, and the family when sudden acute renal failure appears and persists, and the earlier planning can begin the better.

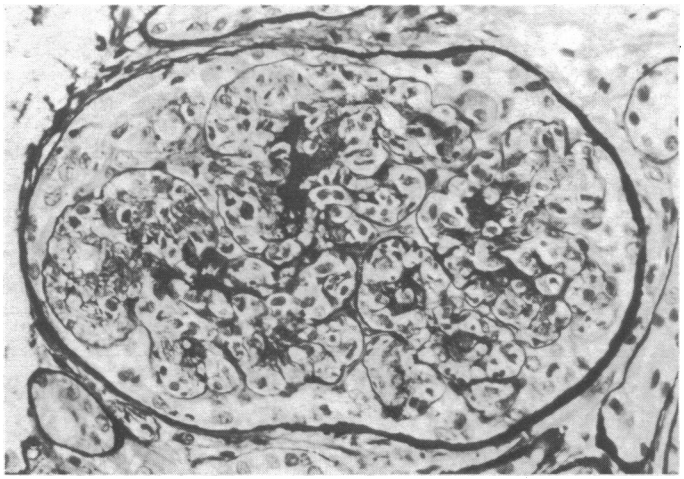

FIG 3—Hypercellular glomerulus containing many neutrophil polymorphs within capillary lumina. From child with poststreptococcal glomerulonephritis who developed acute renal failure. (Silver with haematoxylin and eosin. ×189.)

The effect of the biopsy information on specific treatment was smaller but significant. The two patients with myeloma (fig 4) had not been diagnosed before they presented with acute renal failure; confirmation of myeloma kidney allowed intensive treatment of the primary disease with cyclophosphamide, prednisone, and allopurinol with recovery of function as noted by others.[12] In only two out of 10 patients whose biopsies showed afferent arteriolar and capillary thrombi had the diagnosis been made from the initial blood smear. Treatment with heparin in the haemolytic-uraemic syndrome remains controversial, but if it is to be given then patients requiring dialysis are one group in which it should be considered. Thrombolytic treatment may also be tried, although the outlook remains poor for adults and older children.[13] The treatment of interstitial nephritis has already been mentioned. In patients with extensive crescent formation treatment with combined immunosuppressants and anticoagulants has been tried,[14 15] although we have had no success in patients already anuric and requiring dialysis. Kincaid-Smith,[16] however, has reported recovery of function during similar treatment. Finally, the recognition that some patients had a minimal-change lesion and not the severe nephritis suspected clinically enabled their treatment with high-dose corticosteroids to be begun during the oliguric phase, and the profuse proteinuria during their diuresis was thereby limited.

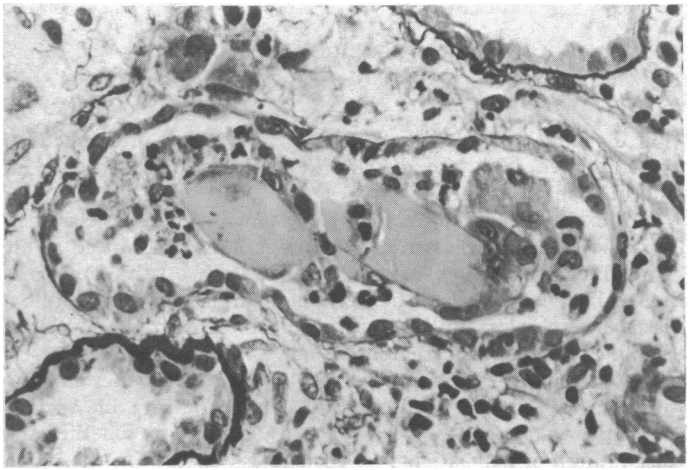

FIG 4—Renal tubule containing eosinophilic "myeloma" cast. From patient with multiple myeloma. (Silver with haematoxylin and eosin. ×304.)

Conclusions

Renal biopsy is of value in selected patients who present with acute uraemia. It may be indicated to assess prognosis, confirm a clinical diagnosis, or form a basis for attempting treatment. One indication for biopsy is prolonged oliguria when ATN has been suspected, although acute cortical necrosis is better excluded by angiography or dynamic scintigraphy. If the clinical features suggest a lesion other than ATN an early biopsy, bearing in mind the increased morbidity in this condition, permits better appreciation of the probable outlook and treatment of some lesions.

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