Medical History

Histological Reassessment of Three Kidneys Originally Described by Richard Bright in 1827-36

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Summary

Portions of kidney from three patients with renal disease that were originally described by Richard Bright between 1827 and 1836 have been preserved in the Gordon Museum at Guy's Hospital. Histological study has shown that two cases fall into the current diagnostic category of mesangiocapillary (membranoproliferative) glomerulonephritis. One of these patients had a five-year clinical history and died with chronic renal failure and uraemia. The other patient died after three to four months with a severe nephrotic syndrome. The third patient was a young woman with chronic "phthisis pulmonalis" and renal amyloidosis.

Introduction

Richard Bright was physician to Guy's Hospital from 1820 until 1843. During this time he wrote clinical accounts of many diseases[1], but is probably best remembered for his descriptions of renal disease. There are many beautifully coloured illustrations of the gross appearances of kidneys from his patients, but only three actual specimens have been preserved. The histology of these kidneys, now over 140 years old, has been described by Osman[2] and by Cavanagh.[3] Since these accounts were published there have been appreciable advances in the methods of study of renal disease. The main purpose of the present account, therefore, is to discuss the three cases in the context of current views of renal pathology.

Material and Methods of Tissue Preparation

The renal vessels in all three cases were injected with red mercuric salts and the specimens were probably fixed in spirit. They were, however, transferred to formalin at the outbreak of the first world war as a precaution against air attacks.[2]

Thin slices of cortex and medulla were taken from each kidneys and cleared in cedar wood oil for direct transillumination of the injected vasculature. Further pieces were embedded in paraffin and the sections stained with haematoxylin and eosin, periodic-acid Schiff, hexamine silver, congo red, and thioflavine T. Small blocks of tissue were fixed in 1% buffered osmium tetroxide, dehydrated in alcohol, and embedded in araldite. Sections one-micron thick were cut on an LKB Ultrotome and stained with 1% toluidine blue.

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Clinical and Pathological Observations

The clinical histories of all three cases have been published previously[2 4 5] and are summarized below.

CASE 1 Mary Brooks (GM 1611) was 24 years old and had a five-year history of repeated episodes of severe anasarca. During this time her urine was coagulated by heat whenever tested and contained some 1% protein. The specific gravity of her serum was low and the protein level was reduced. Her blood urea was 15 grains per 1,000 grains of serum and towards the end of her life she suffered from epilepsy. Following such a fit she remained unconscious and died.

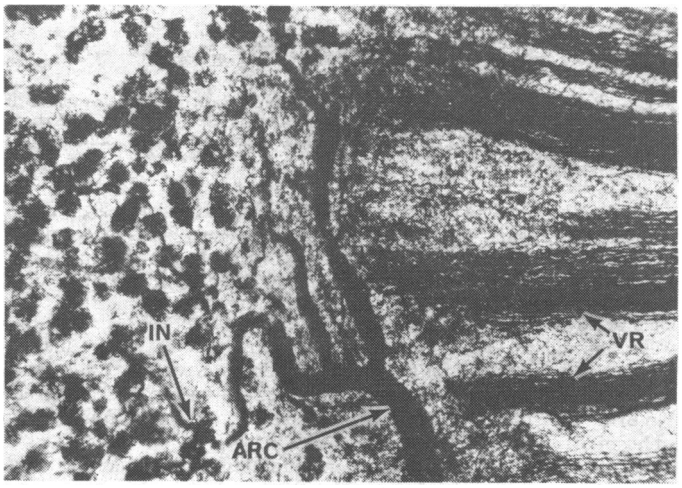

FIG. 1—Transilluminated slice of kidney from Mary Brooks. The arteries are outlined by red mercuric salts; arcuate artery (ARC), interlobular artery (IN), vasa recta (VR). (×10)

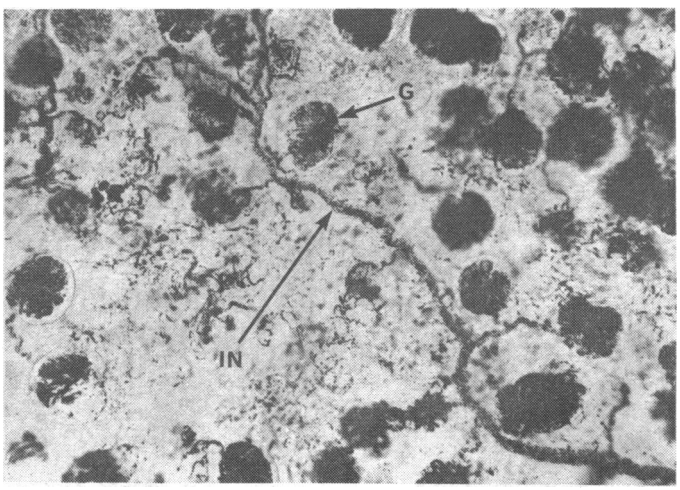

FIG. 2—Same specimen as Fig. 1 showing an interlobular artery (IN) and its branches to glomeruli (G). (×25.)

Necropsy showed some increase in subarachnoid fluid and injection of the brain. The heart was not enlarged and there was little atherosclerosis recorded. Her kidneys were small, granular, firm, and light in colour with a reduced cortical width and fetal lobulation.

Histology.—Transillumination of kidney slices reveals a well-injected arterial system. Fig. 1 shows an arcuate artery and several interlobular arteries; groups of vasa recta are seen in the medulla. Details of the afferent arterioles supplying individual glomeruli are also well visualized in this specimen (Fig. 2). Paraffin and araldite sections of the kidney show considerable tubule loss and interstitial scarring. The cellular detail is poorly preserved and there is a total lack of nuclear staining. Nevertheless, the overall glomerular morphology is readily discernible. There is wide variation in glomerular size and shape; some are very large and lobulated (Fig. 3), with a marked increase in mesangium and thickened, irregular capillary

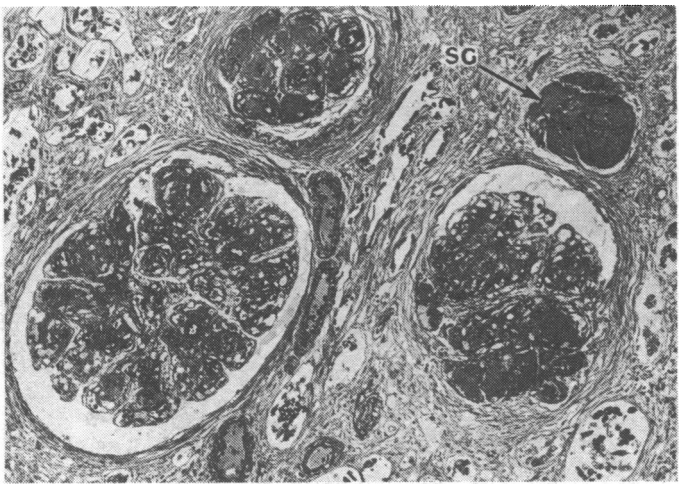

FIG. 3—Section of renal cortex from Mary Brooks showing lobular glomeruli with mesangial proliferation. Sclerosed glomeruli (SG) are seen and there is considerable interstitial fibrosis. One-micron araldite section stained with 1% toluidine blue. (×100.)

walls. Many glomeruli are sclerosed and there is extensive periglomerular and subcapsular fibrosis. The arcuate vessels show only minor intimal thickening and some duplication of the elastica. Evaluation of the smaller vessels is difficult as they are filled with mercuric salts.

CASE 2 Edward M. (GM 1605) was a sailor about 25 years old. He was admitted to Guy's Hospital in September 1827 with a history of generalized anasarca for three to four months. Severe breathlessness developed when he lay down and frequent vomiting was observed. No urine specimen was obtained and he died 10 days after admission to hospital.

Necropsy showed pleural effusions and ascites. Both kidneys were large, plump, smooth, and very pale, almost white in colour.

Histology.—The half kidney that remains from this case is moderately well preserved and shows good nuclear staining. There is

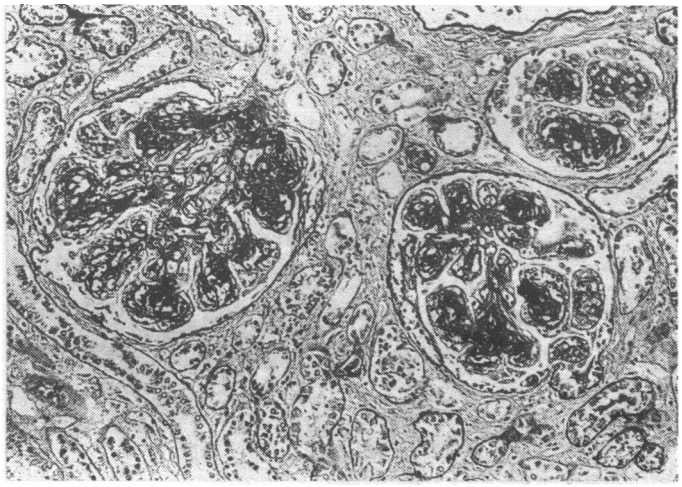

FIG. 4—Kidney from Edward M. showing lobular glomeruli. There is some increase in interstitial fibrous tissue but many of the tubules are well preserved. Paraffin section stained with P.A.S. (×100.)

very much less tubule atrophy and interstitial fibrosis than in Case 1 and there are fewer sclerosed glomeruli. Well-marked mesangial proliferation is seen in all the glomeruli which results in varying degrees of lobularity (Fig. 4). There is little periglomerular fibrosis and a few subcapsular cresents are observed. Examination of the glomeruli at higher power shows that there is an increase in mesangial substance with cells set within it (Fig. 5). The capillary basement membranes are well preserved and, for the most part, they are not

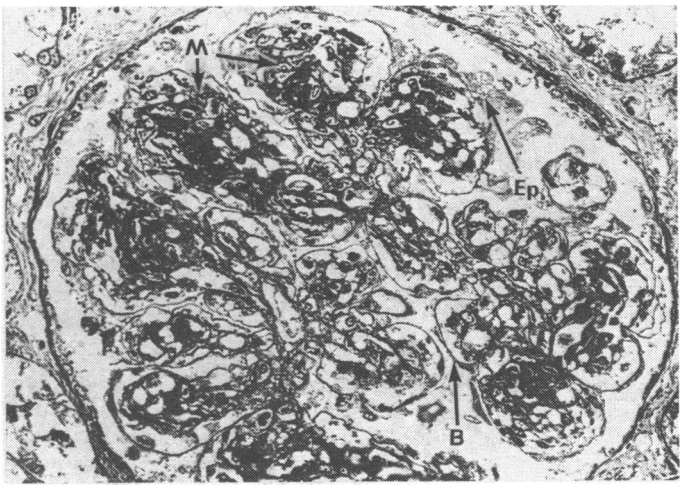

FIG. 5—High magnification of glomerulus from Edward M. Proliferation of mesangial substance and cells (M) expands the glomerular tufts to produce a lobular pattern. Basement membrane (B). Epithelial cells (Ep). One-micron araldite section stained with 1% toluidine blue. (×249.)

greatly increased in thickness. As the endothelial cells are not always visible it is difficult to comment on the capillary lumina but they do appear patent. Many epithelial cells and Bowman's capsule lining cells are preserved.

CASE 3 May Sallaway (GM 1606) aged 25 years was admitted to Guy's Hospital in November 1826 with a two-month history of swelling of the legs and face. She had a long-standing cough and a pleural effusion was suspected clinically. Her urine coagulated when heated. She died early in January 1827.

Necropsy showed a left pleural effusion and ascites. Cavitating tuberculosis was seen in the right lung and less advanced tubercular lesions were present in the left lung. Both kidneys were normal in size. The capsules were adherent and white patches were observed on the renal surface. Injection of the vessels with mercuric salts was not complete and the cut surfaces of the kidneys were yellow with small opaque spots (see Plate II, Osman,[2] p. 12).

Histology.—The histological picture of the kidney is not very well preserved although some nuclear staining does remain. A moderate

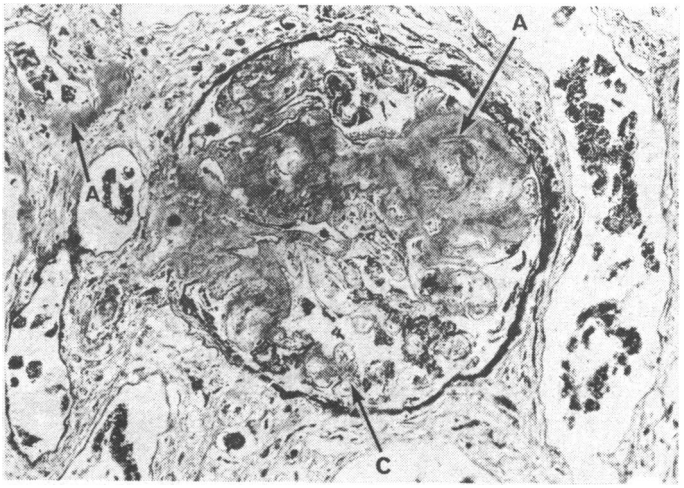

FIG. 6—Section from the kidney of Mary Sallaway. The amorphous areas (A) in the glomerulus and around tubules are congophilic and stain for amyloid with thioflavine T. Some segments of the glomerulus show normal capillary loops (C). One-micron araldite section stained with 1% toluidine blue. (×249.)

amount of tubule loss is observed and there is some interstitial fibrosis. The injected salts have filled most of the vessels and have burst through into the urinary space of many of the glomeruli. Large irregular lakes of amorphous material are seen in the mesangial regions of all the glomeruli (Fig. 6). Congo red and thioflavine T staining show amyloid deposits within the glomeruli and in the tissue between the tubules. The larger blood vessels appear normal and no amyloid is detectable within their walls.

Discussion

Cases 1 and 2 fit into the current diagnostic category of mesangiocapillary (membranoproliferative) glomerulonephritis. This disease is characterized histologically by an increase in the mesangium and thickening of the capillary walls;[6 7] when the mesangial increase is extensive the glomeruli have a lobular appearance. Immunofluorescence studies on renal biopsy specimens from patients with this disease show deposits of complement and variable amounts of IgG associated with the basement membrane.[8] Such deposits stain densely with osmium and can be seen with the light microscope in one-micron Araldite sections and in electron micrographs.[7 9]

The differences that do exist between the histology in Cases 1 and 2 probably reflect the different clinical courses of the disease in the two patients.

Case 1 has a long history of oedema terminating in chronic renal failure. Her fits may have been due to uraemia. Histologically the kidneys show severe glomerular sclerosis and extensive tubule loss. Case 2, on the other hand, died after a comparatively short nephrotic illness, and although there are well-marked glomerular changes, there is very little tubule loss or glomerular sclerosis.

Such differences in histological appearances may largely be explained by the length of the illness in each case. We have observed patients with mesangiocapillary glomerulonephritis who have shown very little tubule loss on biopsy soon after the onset of nephrotic symptoms, but on subsequent biopsy or necropsy they show considerable tubular atrophy.

The diagnosis of Case 3 presented no difficulty to either Osman[2] or Cavanagh[3] and we have merely confirmed the diagnosis of renal amyloidosis.

We are grateful to Mr. John Maynard, curator of the Gordon Museum, for permission to study the kidneys and to his staff for their help. We would also like to thank Mr. R. Francis and Miss J. Clare for their technical help. Mrs. Elizabeth Abdulla performed the qualitative inorganic analysis of the kidneys.

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Any Questions?

We publish below a selection of questions and answers of general interest

Survival of Pathogenic Viruses in River Water

Is there any definite knowledge about the length of time that viruses pathogenic to man can survive in river water? Are such viruses killed or inactivated by chlorination in the concentration usually employed by water authorities?

The survival of viruses in river water is governed by such factors as their initial concentration when introduced, the subsequent dilution, the temperature and pH of the water, how long the water is stored, whether it is filtered, and the concentration of chlorine added. The results of repeated sampling of water from the rivers Thames and Lee over an 18-month period have been reported.[1] Enteroviruses including polioviruses, Coxsackie, and echoviruses were isolated with some frequency particularly during the colder months. Experimentally also, virus survival was affected by the temperature of the water. At 5-6°C more than nine weeks were necessary for inactivation but at 22° this was virtually complete in 11 days. Kelly and Sanderson[2] showed that at 25° and a pH of 7 enteroviruses needed to be in contact with 0·5 p.p.m. chlorine for more than seven hours for complete inactivation. Indirect evidence of the effectiveness of chlorination suggests that though some outbreaks of infectious hepatitis have been reported as waterborne, this route of transmission cannot be blamed when water supplies are properly treated.

1 Poynter, S. F. B., *Water Treatment and Examination*, 1968, **17**, 187.
2 Kelly, S., and Sanderson, W. W., *American Journal of Public Health*, 1960, **50**, 14.

Oral Contraceptives after Infectious Jaundice

A woman of 30 had a six-week attack of infectious jaundice two years ago. Is it safe for her to start taking oral contraceptives?

An attack of infectious hepatitis two years previously is not a contra-indication to oral contraceptive use provided that there is no reason to suspect residual liver damage. If there are doubts about hepatic function it might be wise for the woman to have liver function tests done before she starts on oral contraceptives. Among the tests most likely to be useful in these circumstances would be bromsulphalein retention, serum transaminase, and serum bilirubin determinations.

Anti-influenza Vaccination during Steroid Therapy

Is there any contraindication to giving an anti-influenza vaccine to a patient with asthma (subject to periodic attacks of bronchitis) during prednisone therapy or should vaccination be deferred until the course has finished?

There is no evidence that maintenance doses of prednisone, as used in asthmatic patients, will render the administration of *inactivated* influenza vaccine hazardous or seriously interfere with its efficacy. It is assumed that the vaccine would not be administered during one of the periodic attacks of bronchitis.