Glomerulonephritis Associated With Sarcoidosis

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Clinical findings and structural alterations in the kidneys of 6 patients with sarcoidosis and an associated glomerulonephritis are described. Five of the 6 patients manifested the nephrotic syndrome during some phase of their illness. Additional clinical evidence of renal disease included persistent microscopic hematuria (5 patients), hypertension (4 patients) and progressive renal failure (3 patients). Glomerular pathology varied and included proliferative glomerulonephritis (3 patients), membranous glomerulonephritis (1 patient), and chronic glomerulonephritis (2 patients). In 2 patients sequential examination of the kidney was possible, with renal biopsies preceding autopsy examination by 3 and 6 years, respectively. Glomerular pathology had progressed in severity in each case. Immunofluorescent studies in 2 patients revealed patterns of glomerular antibody localization consistent with immune complex disease. Electron microscopic studies of 1 revealed membranous changes characterized by electron-dense subepithelial and intramembranous deposits. Totally unexpected were virus-like intraendothelial structures in the glomeruli identical to those previously reported in systemic lupus erythematosus. Since current evidence suggests that the pathogenesis of both membranous and proliferative types of glomerulonephritis is immunologic, it should not be surprising that sarcoidosis, a disease which quite possibly results from an immune response to a disseminated antigen(s), should occasionally include glomerulonephritis as a part of its histologic expression (Am J Pathol 68:339–358, 1972).

IMPAIRED RENAL FUNCTION in patients with sarcoidosis has generally been attributed either to hypercalcemia with nephrocalcinosis and renal calculi [1–4] or to direct invasion of the renal parenchyma by the granulomatous process.[5–7] Primary glomerular alterations are not generally considered to be associated with systemic sarcoidosis, although a few isolated cases of glomerular disease have been reported.[8–14] Descriptions of the histopathology of the glomerular lesions have varied considerably. Membranous glomerulonephritis has been reported in 4 patients[8–10] and a proliferative glomerulonephritis characterized by glomerular hypercellularity and an increase in the mesangial matrix has been described in 2 patients.[10–11] Correa reported 1 patient with a progressive proliferative glomerulonephritis, demon-

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strating epithelial crescent formation and neutrophilic infiltrates in glomerular tufts.[12] Early reports by Teilum emphasized the presence of hyaline and fibrinoid changes in glomerular capillaries and renal arterioles in a patient with sarcoidosis. He pointed out the similarity between that lesion and the renal lesion observed in systemic lupus erythematosus.[13,14]

Although proteinuria is occasional encountered in patients with sarcoidosis,[15,16] the nephrotic syndrome is exceedingly rare. To date this syndrome has been reported in 4 patients with sarcoidosis.[8–10] The present study describes the clinical and renal histologic features of 6 patients with sarcoidosis. In each there were significant renal glomerular alterations. In addition, 5 of the 6 patients developed the nephrotic syndrome during some phase of their illness.

Materials and Methods

The autopsy files at the Duke University Medical Center and the Durham Veterans Administration Hospital were reviewed for cases of systemic sarcoidosis. The diagnosis of sarcoidosis was based on histologic evidence of the disease in the absence of other demonstrated processes or etiologic agents known to cause granulomatous lesions. In addition, the surgical files of the two hospitals were reviewed for renal biopsies of patients with clinical and histologic evidence of systemic sarcoidosis. The clinical records of all patients identified were carefully evaluated for evidence of sarcoidosis.

Fifteen autopsy cases were identified in which adequate clinical and histopathologic evidence was available to support a diagnosis of systemic sarcoidosis. Of these 15, four had histologic evidence of associated renal glomerular disease. Two patients with glomerular disease underwent renal biopsy 3 and 6 years, respectively, before their deaths. In addition, biopsies with evidence of glomerular disease were available from an additional 2 patients with histologic diagnoses and clinical findings of sarcoidosis. Thus, a total of 8 specimens from 6 patients were available for evaluation.

Renal tissue for light microscopy was fixed in 10% buffered formalin and or Zenker's solution, embedded in paraffin and stained with hematoxylin and eosin (H and E), periodic acid-Schiff (PAS), periodic acid-methanamine silver-Masson trichrome (PAMM) and von Kossa calcium stains.

Tissue obtained for electron microscopy was fixed in 4% glutaraldehyde buffered with 0.1 M sodium cacodylate, postfixed for 1 hour in 1% osmium tetroxide and embedded in Epon epoxy resin. Thin sections cut on a Porter-Blûm ultramicrotome were stained with lead citrate and uranyl acetate and studied and photographed with an Hitachi HS-8 electron microscope.

When tissue was available for immunofluorescent evaluation, the unfixed specimen was frozen at −70 C in a gelatin matrix. Sections for immunofluorescent evaluation were cut at 4 μ, fixed in acetone, washed in phosphate-buffered saline, incubated for 30 minutes with fluorescein-labeled antibody preparations, washed again in phosphate-buffered saline and mounted with glycerin. Sections were examined with a Leitz Ortholux microscope equipped with an HBO-200W mercury vapor light source, a UG-1 exciter filter and a K-490 barrier filter. Antibody preparations included goat or rabbit antihuman 7S globulin, IgG, IgM, IgA, β1C-globulin, fibrinogen and albumin. The antibody preparations were tested

for specificity by immunoelectrophoresis. Sodium sulfate-precipitated immunoglobulin fractions were labeled with fluorescein isothiocyanate by the method of Marshall, Eveland and Smith.[17] Control preparations for immunofluorescent studies consisted of conjugates absorbed with specific antigen prior to incubation with tissue sections, and of tissue sections incubated first with unlabeled and then with labeled antibody preparations.

Clinical Material

Case 1

CM, a 47-year-old white male with sarcoidosis of 20 years' duration, initially diagnosed by lymph node and lung biopsy, first experienced recurrent nephrolithiasis and was found to be hypertensive 4 years after the onset of his disease. Fourteen years later, or 18 years after the onset of sarcoidosis, 3 to 4+ proteinuria and a 24-hour creatinine clearance of 54 ml/min were first noted. A few months before his death from progressive pulmonary insufficiency complicated by recurrent respiratory infections, the patient became nephrotic and developed peripheral edema, hypoalbuminemia, hypercholesterolemia and proteinuria of up to 4.0 g/24 hr. Microscopic hematuria was noted and the creatinine clearance fell to 25 ml/min shortly before death.

Case 2

LH, a 44-year-old black male with systemic sarcoidosis of 24 years' duration, initially diagnosed on lymph node biopsy, first manifested evidence of renal disease 13 years after the onset of his primary disease. Initially, signs and symptoms of renal involvement included microscopic hematuria, pyuria, proteinuria up to 1.5 g 24 hr and mild hypertension. Five years later, or 18 years after the onset of sarcoidosis, he became nephrotic, with hypoalbuminemia, hypercholestolemia and proteinuria up to 3.5 g 24 hr. Microscopic hematuria persisted while a 24-hour creatinine clearance was normal. A percutaneous renal biopsy was performed. During the 6 years preceding his death, the patient continued to manifest evidence of active renal disease with microscopic hematuria, proteinuria and a creatinine clearance severely reduced to 10 ml/min. The hypoalbuminemia (0.7 to 0.9 g 100 ml) persisted. At autopsy, noncaseating granulomata involved the lungs, lymph nodes, spleen, central nervous system and the right eye.

Case 3

AS, a 28-year-old black male, was found to have bilateral pulmonary infiltrates and right hilar adenopathy during an evaluation for severe headaches. A scalene lymph-node biopsy revealed a granulomatous lymphadenitis interpreted as compatible with sarcoidosis. Renal function was normal at the time. During the next 2 months the patient complained of a low-grade fever and night sweats followed by generalized mild arthralgias, ankle edema and orthopnea. There was no history of a preceding upper respiratory infection or a skin infection. Physical examination revealed mild hypertension and periorbital and ankle edema. Microscopic hematuria and red blood cell casts were noted. The patient excreted up to 3.5 g protein 24 hr and had evidence of hypoalbuminemia with a normal serum cholestrol. Blood urea nitrogen and serum creatinine remained normal. Extensive evaluation for a possible connective tissue or collagen-vascular disease was negative; a significant rise in ASO titer could not be documented. A percutaneous renal biopsy was performed. All signs and symptoms of renal disease cleared within 6 months. The patient was lost to further followup.

Case 4

DS, a 23-year-old black male was hospitalized for evaluation of asymptomatic hematuria and proteinuria of 2 years duration. The physical examination was unremarkable, but a chest x-ray revealed enlargement of the hilar and paratracheal lymph nodes and bilateral pulmonary infiltrates; these findings were interpreted as compatible with sarcoidosis. A percutaneous liver biopsy demonstrated noncaseating granulomata compatible with sarcoidosis. Urinalysis revealed both hematuria and proteinuria. The patient excreted up to 4.0 g protein 24 hr and manifested persistent hypoalbuminemia in the presence of a normal serum cholesterol. The blood urea nitrogen and creatinine clearance remained normal. Several LE cell preparations were negative and antinuclear antibodies could not be demonstrated. A percutaneous renal biopsy was performed. The patient was subsequently lost to followup.

Case 5

AA, a 30-year-old black male farm worker was initially evaluated for a foreign body in his right eye. Subsequently the eye was enucleated. At the time of hospitalization he was hypertensive and suffered from diabetes mellitus. He left the hospital against medical advice and received only sporadic medical care during the ensuing 4 years. He was then readmitted with malignant hypertension, azotemia, abdominal pain and severe dehydration. The admission chest x-ray revealed bilateral hilar and mediastinal adenopathy consistent with sarcoidosis. His total serum protein concentration was 4.1 to 4.5 g 100 ml with a serum albumin of 1.4 to 1.7 g 100 ml. With rehydration, pedal edema was noted. Urinalysis revealed 3+ proteinuria and microscopic hematuria with a fixed specific gravity. The patient developed staphylococcal septicemia and expired before more extensive renal evaluation could be completed. At autopsy, histologic changes in the hilar lymph nodes and lungs were compatible with sarcoidosis.

Case 6

EB, a 17-year-old black male was first suspected of having sarcoidosis on the basis of an abnormal chest x-ray, hypercalcemia, hypercalciuria and band keratopathy discovered during evaluation for congenital glaucoma. Qualitative proteinuria was evident at the time. One year later excisional biopsy of an anterior cervical lymph node revealed noncaseating granulomata consistent with sarcoidosis. Over the ensuing 2 years the patient developed progressive renal insufficiency with severe hypertension and continued to manifest hypercalcemia. Approximately 1 month before death, proteinuria increased to 4+, serum albumin fell to 1.6 g 100 ml and pedal and periorbital edema were present. The patient's blood urea nitrogen rose to levels greater than 200 mg 100 ml, and he underwent peritoneal dialysis. Shortly thereafter he died in terminal uremia and at autopsy generalized sarcoidosis involving the mediastinal lymph nodes, spleen, liver and lungs was found.

Results

Clinical Findings

The pertinent clinical findings in the 6 patients are presented in Table 1. All 6 were male; 5 were black and 1 was caucasian. The time relationship between the diagnosis of sarcoidosis and the diagnosis of

Table 1—Clinical Findings

Patient	Age Race Sex	Hyper-tension	Micro-hematuria	Urinary protein (g/24 hr)	Serum protein (g/100 ml) total / albumin	BUN	Creatinine clearance (cc/min)	Serum cholesterol (mg/100 ml)	Serum calcium (mg/100 ml)
CM	49 WM	—	+	4.0	5.7 / 2.3	120	25	420	9.6
LH	44 BM	+	+	3.5	7.9 / 2.4	15	115	312	9.6
AS	28 BM	+	+	3.5	6.2 / 2.6	15	ND†	170	ND
DS	23 BM	—	+	4.0	7.8 / 2.6	10	160	200	9.1
AA	30 BM	+	+	3+*	4.5 / 1.4	205	ND	226	4.7
EB	17 BM	+	—	2-4+*	7.0-4.5 / 2.8-1.4	200	8.3	410	11.9

* Semiquantitative determination only
† Not determined

renal disease varied considerably. In 2 patients (DS and AA) renal disease was noted when sarcoidosis was originally diagnosed, while in 1 patient (CM) the diagnosis of sarcoidosis preceded the onset of renal disease by 18 years. Four of the 6 patients (LH, AS, AA, and EB) were hypertensive, 5 had microscopic hematuria (CM, LH, AS, DS and AA), 3 (CM, AA and EB) eventually developed uremia and a fourth (LH) was mildly azotemic.

Five of the patients developed signs and symptoms of nephrotic syndrome during some phase of their clinical illness. The patients were edematous and had serum albumin levels below 3g/100 ml. Although the sixth patient (EB) may have been nephrotic terminally, as evidenced by hypoalbuminemia, hypercholesterolemia and qualitative proteinuria, other factors may have been at least partially responsible for the hypoalbuminemia; these factors include generalized sarcoid involvement of the liver, uremia with poor nutrition and peritoneal dialysis. In those patients in whom quantitative urinary protein determinations were obtained (CM, LH, AS and DS), all excreted 3.0 g or more protein/24 hr. In the 2 patients who did not have a quantitative urinary protein determination (AA and EB), qualitative values of 3 and 4+, respectively, were recorded. Three of the 6 patients (CM, LH and EB) had an elevated serum cholesterol. Four (LH, AS, DS and AA) did not receive steroid therapy, while 2 (CM and EB) were treated with prednisone; CM was treated intermittently for a period of 15 years and EB for 2 years. In the latter case, steroid therapy was initiated after the renal biopsy was performed.

Histopathology

Significant features of the renal histology in the 6 patients are summarized in Table 2; 3 of the 6 (CM, LH and AS) exhibited proliferative glomerulonephritis. The histologic features in Patient CM were characterized by a moderate increase in endocapillary cells and mesangial matrix material without prominent thickening of the glomerular capillary walls. Local accentuation of this proliferative process was marked in some glomeruli with segmental areas of sclerosis within individual glomerular tufts (Figure 1). Vascular lesions were characterized by mild to moderately severe intimal thickening and hyaline deposits in the small arteries and arterioles. The tubules and interstitium were normal except for small focal areas of calcium deposition in the medulla. Immunofluorescent studies in Patient CM revealed a diffuse linear localization of antihuman 7S globulin and IgG along the glomerular capillary walls and in the mesangial regions (Figure 2)

with segmental linear localization of antihuman IgM. There was no significant glomerular localization of antihuman IgA, β1C-globulin, fibrinogen or albumin. In Patient LH a renal biopsy was taken 6 years before his death and autopsy. In the initial biopsy proliferation of glomerular endocapillary cells and an increase in mesangial matrix material were moderate. Local sclerotic lesions were seen within the tufts of some glomeruli (Figure 3). A small fraction of the glomeruli were completely sclerotic. Hyaline deposits were present in an apparent subendothelial location in some of the glomerular capillaries as well as in a few of the small arteries and arterioles. In addition, exudative or fibrin-cap lesions were observed in some glomerular capillaries. At autopsy, 6 years later, the severity of the glomerular disease had increased with endocapillary cell proliferation, an increase in mesangial matrix material, hyaline deposits in the glomerular capillaries and segmental as well as generalized sclerosis of many of the glomerular tufts (Figure 4). There was diffuse interstitial fibrosis with focal interstitial calcification and tubular atrophy were noted.

Patient AS had an acute proliferative glomerulonephritis with an increase in glomerular endocapillary cells, narrowing of capillary lumens and neutrophilic infiltrates in glomerular tufts (Figure 5). Interstitial edema was mild. The tubules and vasculature were unremarkable.

Patient DS had a membranous glomerulonephritis with diffuse and generalized thickening of the glomerular capillary walls. Special stains revealed silver-positive spikes projecting from the epithelial side of the capillary walls. There was mild proliferation of endocapillary cells of glomerular tufts and an associated mild increase in mesangial matrix material (Figure 6). In focal areas the tubules were atrophic, with thickening of the tubular basement membranes. The vessels were unremarkable. Immunofluorescent studies revealed that antihuman 7S globulin, IgG and β1C-globulin were localized in a diffuse granular pattern (Figure 9) and antihuman IgM in a segmental granular pattern along the glomerular capillary walls. Electron microscopy confirmed membranous alterations consisting of electron-dense deposits located on the subepithelial side of the basement membrane (Figure 7). There was villous transformation of the epithelial cells and loss of the epithelial foot processes with sheets of epithelial cytoplasm overlying the irregular external surface of the glomerular basement membrane. The mesangium was prominent: both the matrix material and the cytoplasmic processes were increased. In addition, microtubular or virus-like structures were present in rough surfaced endoplasmic reticulum of swollen endothelial cells (Figure 8). These

Table 2—Summary of Histopathologic Findings

Patient and source	Histologic diagnosis*	Glomerular alterations								
		Tuft cellularity	Basement membrane	Mesangial matrix increase	Adhesions	Sclerosis	Neutrophilic infiltrates	Vessels	Interstitial fibrosis	Calcinosis
CM										
autopsy	PGN	++ F,L	N	+++ F, L	+	++ F, L	0	+ intimal hyaline	F	+
LH										
biopsy	PGN	++	++ local subendothelial deposits	++	+	+	0	+ intimal hyaline	F	0
autopsy	PGN	+++	++++ local subendothelial deposits	+++	++	++	0	++ intimal hyaline	D	+
AS										
biopsy	PGN	++	N	+	0	0	+++	N	N	0

DS biopsy	MGN	+	subepithelial deposits silver-positive spikes	+	0	+	0	N	N	0
AA autopsy	CGN	++	+++ local subendothelial deposits	+++	++	++++	++	+++ intimal hyaline	D	0
EB biopsy	PGN	+	N	+	++	++	0	+ intimal proliferation	F	0
autopsy	CGN	++	+++ local subendothelial deposits	++	++	+++	0	++++ intimal proliferation and hyaline	D	0

* PGN = proliferative glomerulonephritis; MGN = membranous glomerulonephritis; CGN = chronic glomerulonephritis
F = focal; L = local or segmental; N = normal; 0 = absent; D = diffuse

structures were identical in appearance to those previously observed in systemic lupus erythematosus.

The 2 patients with clinical evidence of the most severe renal disease (AA and EB) had a chronic glomerulonephritis with complete sclerosis of most of the glomeruli. Those that were not completely sclerotic were hypercellular and contained increased numbers of endocapillary cells (Figure 10). In segmental areas, the glomerular capillary walls were markedly thickened by eosinophilic deposits (Figure 11), and occasional exudative or fibrin-cap lesions were found in both patients in the glomerular capillaries. Glomerular capsular adhesions were prominent as was pseudotubule formation within the parietal epithelium of Bowman's capsule. In neither of these cases were there nodular glomerular lesions of the type seen in diabetic glomerulosclerosis. Interstitial fibrosis and tubular atrophy were extensive in one patient and mild in the other. Arteries and arterioles from both patients revealed intimal thickening and hyaline deposits. The kidney of Patient TB had been biopsied 3 years before his death. Parenchymal alterations in that specimen were similar, though less severe, than those observed at autopsy.

Discussion

The occurrence of glomerulonephritis in patients with sarcoidosis immediately raises the question of whether the relationship between these conditions is causal or fortuitous. Although the etiologic agent(s) responsible for generalized sarcoidosis have not been identified, it is believed that this granulomatous reaction represents a type of immunologic hypersensitivity. Waksman [18] concluded that lesions of the sarcoid type are immunologic reactions to more or less widely disseminated antigens which either have a low solubility or cannot be metabolized. Scadding [19] suggested that the clinical findings of hyperglobulinemia, positive precipitins to certain antigens and positive tests for rheumatoid factor indicated that the normal immunologic mechanisms were altered in sarcoidosis. Since present evidence, drawn from studies of human disease as well as from experimental models, suggests that both membranous and proliferative types of glomerulonephritis have an immunologic or hypersensitivity pathogenesis, it should not be surprising to find that generalized sarcoidosis, a disease which quite possibly results from an immune response to a disseminated antigen, should occasionally include, as a part of its histologic expression, either a proliferative or membranous type of glomerulonephritis.

The type of glomerular lesions observed in both the autopsy material and the renal biopsies varied considerably. Similar observations have been made in the few scattered reports of glomerulonephritis associated with sarcoidosis (Table 3). This situation is not unlike that which prevails in systemic lupus erythematosus, the human prototype of immune complex nephritis. The nephritis associated with systemic lupus erythematosus may be either membranous, proliferative or a combination of both.[20] It may be either generalized and diffuse or focal and segmental. Teilum [13,14] emphasized the similarity between certain glomerular and renal arteriolar lesions in sarcoidosis and those observed in lupus nephritis. The results of the present study are very similar. Local and diffuse proliferative lesions, diffuse membranous alterations, and local as well as diffuse glomerular sclerosis were observed in the kidneys of patients included in this present study. Arteriolar hyaline deposits of the type described by Teilum were observed in the kidneys of 4 of the 6 patients. In addition, glomerular subendothelial deposits of the type often seen in lupus nephritis were noted in the same 4 patients. The histologic similarity between the two conditions was further evidenced by the findings in the kidney biopsy of Patient DS—the glomeruli exhibited a diffuse membranous glomerulonephritis, a lesion frequently seen in lupus nephritis. In addition, electron microscopy revealed microtubular or virus-like intraendothelial structures identical to those commonly observed in kidneys of patients with systemic lupus erythematosus.[21,22] Unfortunately, glomerular ultrastructure was not available in the other cases of sarcoidosis in the present study. However, glomerular ultrastructure in 2 additional patients with sarcoidosis but without clinical or histologic renal abnormalities who were not included in the present study revealed no such microtubular structures.

Table 3—Sarcoidosis with renal glomerular disease

Source	Description
Berkman **et al** [9]	Two cases of membranous glomerulonephritis with nephrotic syndrome
Falls **et al** [10]	One case of membranous glomerulonephritis with nephrotic syndrome; 1 case of proliferative glomerulonephritis
Laroche **et al** [5]	One case of membranous glomerulonephritis with nephrotic syndrome
Plattner **et al** [11]	One case of proliferative glomerulonephritis
Correa [12]	One case of rapidly progressive glomerulonephritis
Teilum [13]	One case with glomerular hyaline lesions

In those patients evaluated by immunofluorescence, the results differed. In Patient DS, a diffuse granular localization of antihuman immunoglobulins and β1C-globulin was similar to that usually observed in diffuse membranous glomerulonephritis. On the other hand, in Patient CM a diffuse linear localization of antihuman IgG was observed in the glomerular capillary walls, the exact significance of which is not apparent in this situation. Diffuse linear glomerular capillary localization of antihuman immunoglobulins is most often associated with antiglomerular basement membrane disease, such as is seen in Goodpasture's syndrome and other rare forms of rapidly progressive glomerulonephritis.[23,24] In Goodpasture's syndrome, antihuman β1C-globulin is also localized in an identical pattern. However, in the present case antihuman β1C-globulin localization was not observed. Diffuse linear localization of antihuman immunoglobulin without similar β1C-globulin localization has been observed in systemic lupus erythematosus,[25,26] as well as in rare cases of diabetes mellitus[26] and in certain unclassified forms of renal disease.[24] Thus, though the patterns of immunoglobulin localization in the two patients differed, both patterns have been associated with immune complex disease, specifically lupus nephritis.

Patient AA, in this series, had diabetes mellitus. The question must be raised as to whether clinical findings of the nephrotic syndrome—hypertension and renal failure—as well as the renal histologic alterations might be ascribed to diabetic glomerulosclerosis. Certainly many of the clinical findings could be explained on the basis of diabetic nephropathy. However, histologic evaluation failed to reveal the typical nodular lesions of diabetic glomerulosclerosis. Endothelial and mesangial hypercellularity of the extent seen in this patient is not characteristic of diabetic nephropathy, although some degree of cellular proliferation may accompany the less specific diffuse intercapillary type of glomerulosclerosis. The fibrin-cap lesion present in 3 patients in this report, though often associated with diabetic glomerulosclerosis, is not a specific lesion. It has been observed in arteriosclerotic kidneys, in various types of glomerulonephritis[27] and in animals treated with steroids.[28] In the present study 2 of the 3 patients whose kidneys contained this lesion did receive steroids. However, whether such a renal lesion occurs in humans treated with steroids is uncertain.[29]

The cases reported here should not be confused with Wegener's granulomatosis, although both conditions represent forms of granulomatous disease. Wegener's granulomatosis[30] is characterized by granulomatous lesions in the upper respiratory tract and lungs and

by a florid form of glomerular disease. The upper respiratory symptoms are usually prominent and the progression of renal disease is usually rapid, with renal failure and uremia occurring in months. Histologically, the granulomatous inflammation has a necrotizing component which serves to distinguish it from sarcoidosis. In addition, there is frequently an associated polyarteritis in Wegener's granulomatosis which was not observed in any of the cases reported here. Furthermore, the glomerular lesions in Wegener's granulomatosis are usually characterized by a rapidly progressive process with prominent parietal epithelial cell proliferation (crescent formation) and fibrinoid necrosis involving the glomerular tufts. Such glomerular changes were not observed in any of the present cases.

This report of 6 patients with sarcoidosis and concommitant renal glomerular disease does not answer the question of causal relationship. Certainly the association of these conditions in 4 of 15 autopsies is greater than would be expected by chance alone. Considering the elusive nature of the inciting antigen, if indeed such exists in sarcoidosis as well as in most types of glomerulonephritis, the establishment of a causal relationship through an etiologic agent may not be imminent. However, awareness of the association may help to clarify the nature of this relationship.

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[*Illustrations follow*]

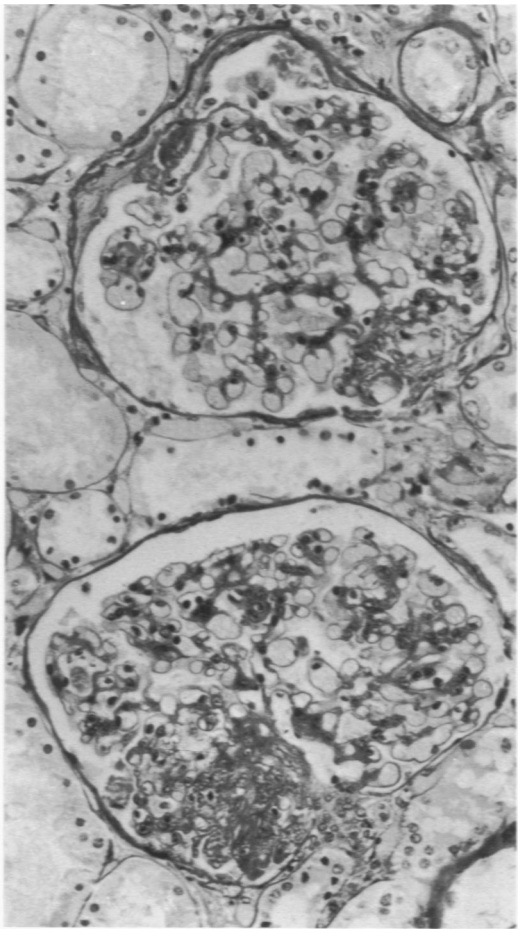
Legends for Figures

Fig 1—Glomeruli from the kidney of patient CM revealing localized proliferation and sclerosis of a glomerular tuft. A capsular adhesion is present in the lower glomerulus (PAS, × 225).

Fig 2—Glomerulus from patient CM showing localization of antihuman IgG in a diffuse linear pattern along the capillary walls and in the mesangial regions (× 265).

Fig 3—Glomerulus from the biopsy of patient LH showing localized mesangial cell proliferation with segmental sclerosis of the glomerular tuft and a capsular adhesion (H&E, × 375).

Fig 4—Glomerulus from the autopsy kidney of patient LH obtained 6 years after the biopsy illustrated above. Note the subendothelial deposits and hyaline thrombi in the glomerular capillaries. A capsular adhesion with pseudotubule formation and a single exudative capsular drop lesion along the basement membrane of Bowman's capsule is demonstrated (H&E, × 375).



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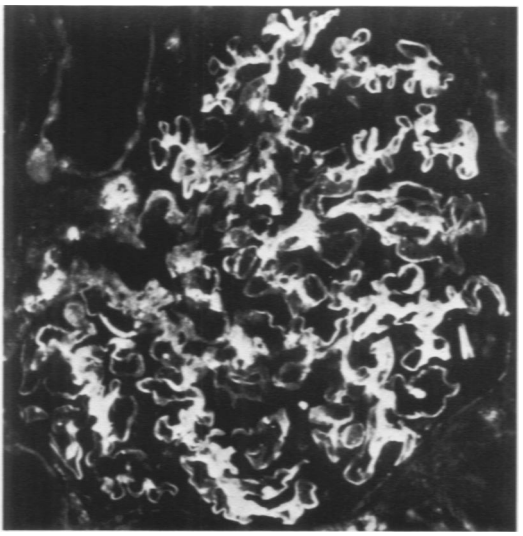

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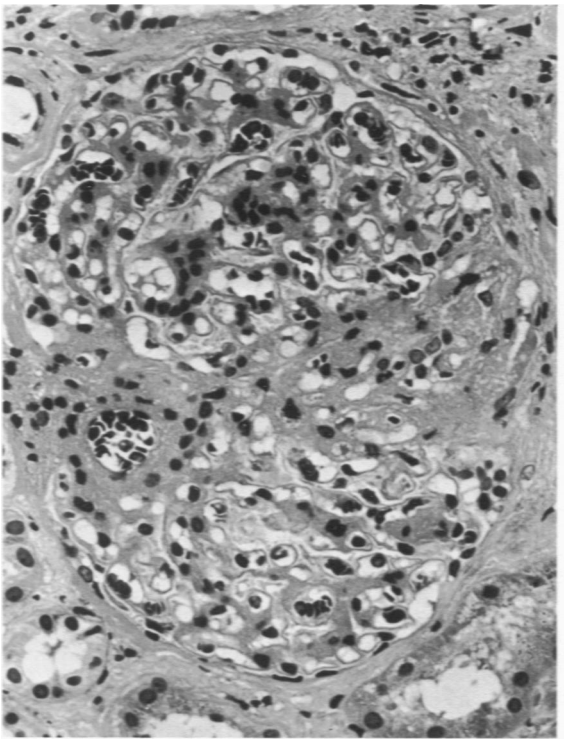

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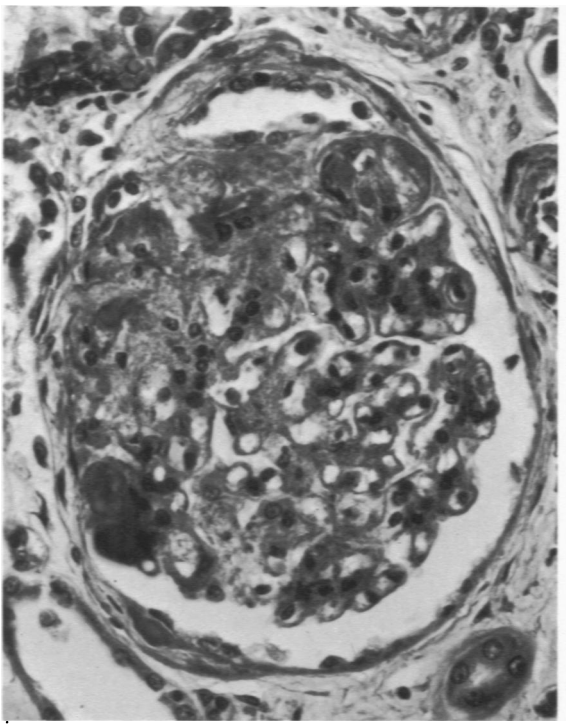

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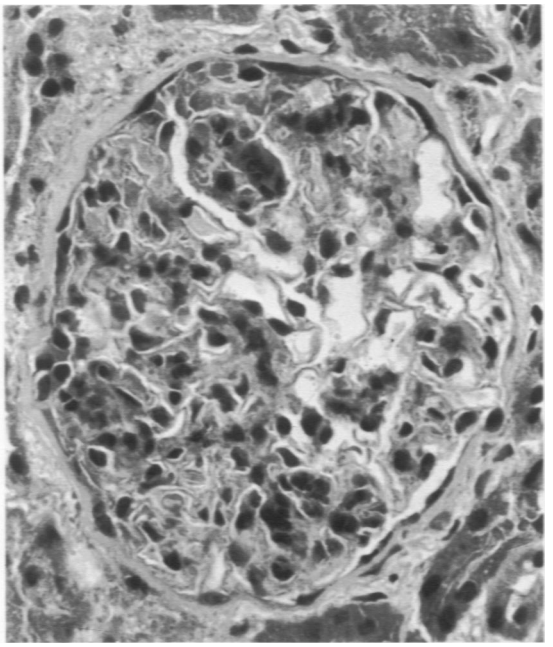
Fig 5—Glomerulus from the biopsy of patient AS revealing segmentally accentuated proliferation of endothelial and mesangial cells with neutrophilic infiltration of the glomerular tuft (H&E, × 315).

Fig 6—Glomerulus from the biopsy of patient DS revealing diffuse thickening of the glomerular capillary walls with marked segmental increase in the mesangial matrix and adhesion of the tuft to Bowman's capsule (PAMM, × 315).

Fig 7—Electron micrograph from a glomerulus of patient DS revealing subepithelial and intramembranous electron-dense deposits along the capillary basement membrane. Epithelial foot processes are retracted, leaving sheets of epithelial cytoplasm overlying the electron-dense deposits and basement membrane (× 11,980).



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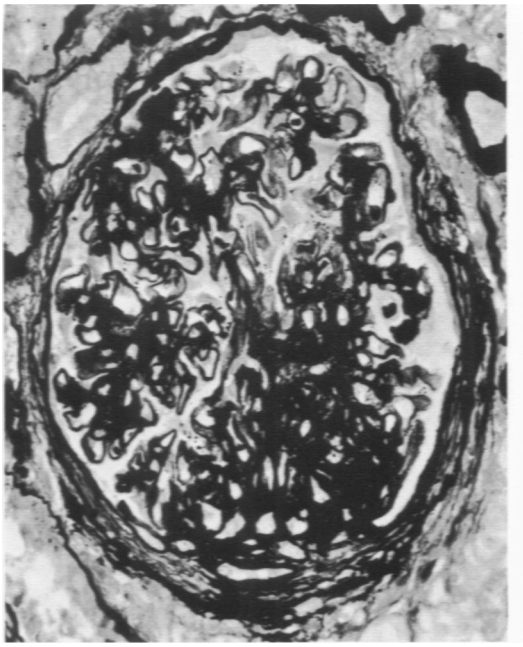

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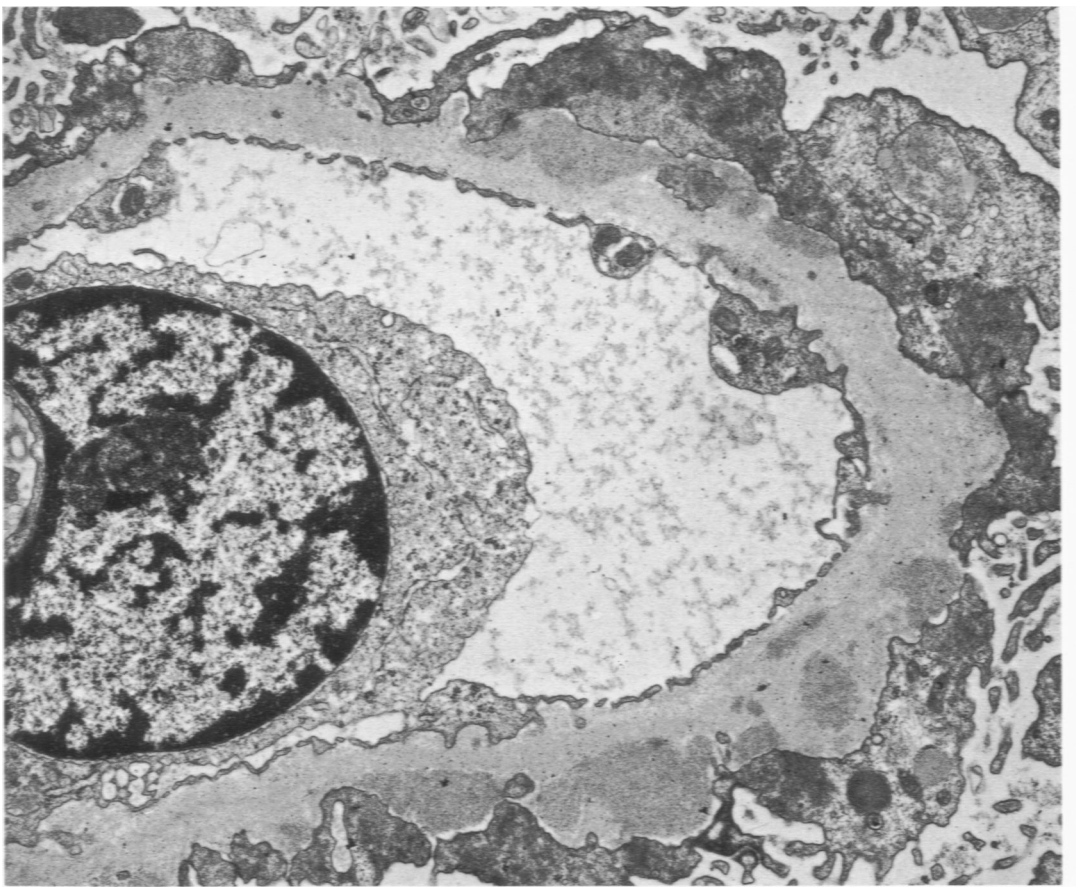

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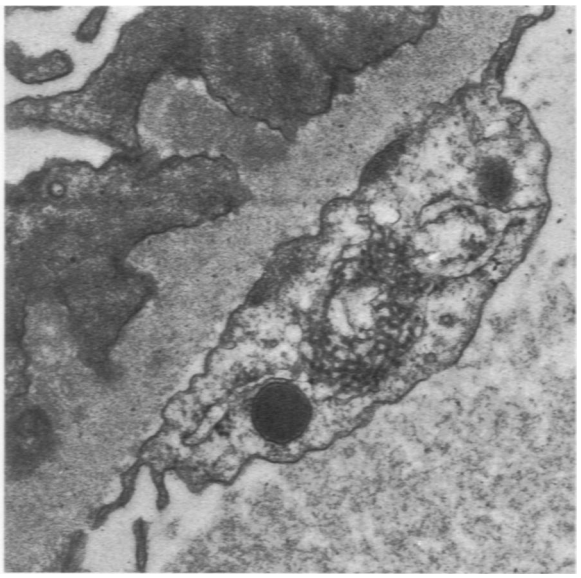

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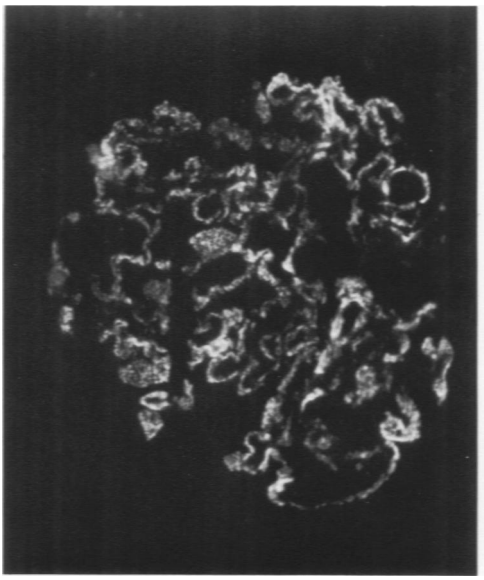

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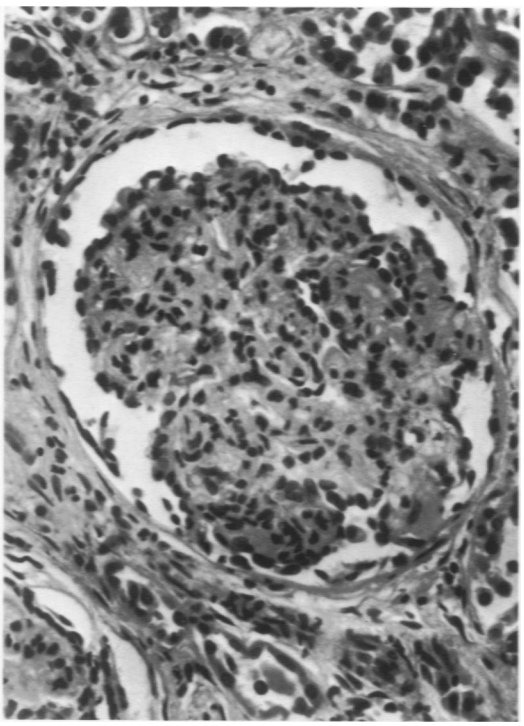

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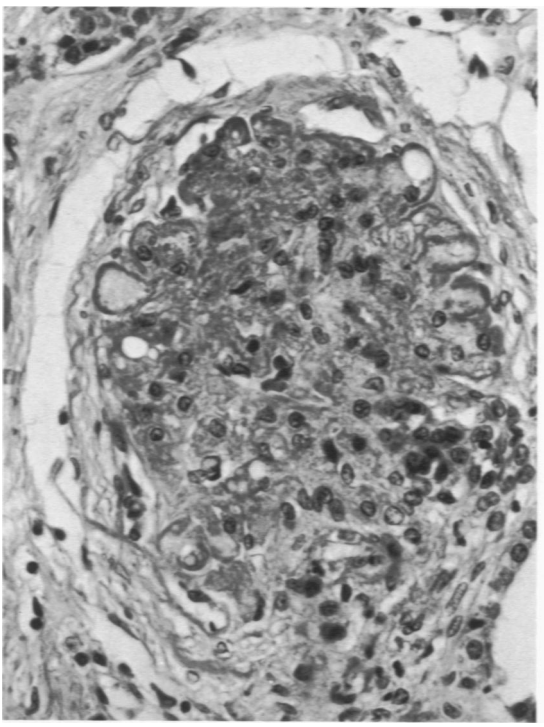

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Fig 8—Electron micrograph from glomerulus of patient DS showing a collection of virus-like particles in the endoplasmic reticulum of a capillary endothelial cell. Subepithelial electron-dense deposits are present along the basement membrane (× 23,100). **Fig 9**—Glomerulus from patient DS showing localization of anti-human 7S globulin in a diffuse granular pattern along the glomerular capillary walls (× 265). **Fig 10**—Glomerulus from patient AA demonstrating endothelial and mesangial hypercellularity (H&E, × 375). **Fig 11**—Glomerulus from patient EB showing solidification of the glomerular tuft with marked thickening of several peripheral capillary walls (H&E, × 375).