Virchows Arch. A Path. Anat. and Histol. 363, 359—362 (1974)

Case Reports

Segmental Disorganizing Glomerulonephritis in a Wegener's Granulomatosis

H. Shigematsu, H. Ohtsu, and M. Matsuba

Departments of Pathology and Dermatology, School of Medicine, Chiba University, Chiba, Japan

Received May 4, 1974

Summary. The disorganizing process of glomerular lesions in a Wegener's granulomatosis was analyzed. Intracapillary damage of mesangial disintegration (mesangiolysis) was followed by extracapillary extension of the injury (crescent formation and granulomatous reaction) in which a rupture of the glomerular basement membrane was observed.

The glomerular lesions involved in Wegener's granulomatosis are characterized by necrotizing, thrombotic, crescent forming and often granulomatous glomerulonephritis in local or segmental distribution (Wegener, 1939; Godman and Churg, 1954; Altmann and Schicke, 1959). The course or development to this disorganizing glomerulonephritis, however, has not been fully understood. The presence of glomerular damages such as ruptures or gaps of the glomerular basement membrane (GBM) as well as mesangiolysis have been reported recently in human and experimental glomerulonephritis of progressive and irreversible clinical course (Kondo *et al.*, 1972; Stejskal *et al.*, 1973; Morita *et al.*, 1973; Shigematsu and Kobayashi, 1973). In this report we deal with an analysis of the disorganizing process of glomerulonephritis in a Wegener's granulomatosis.

Case History Outline and Pathological Findings

The patient (63–1969) was a 22 year old man who was admitted in October 1968 stating that he had been complaining of facial swelling with red macules, paples, erosions and crust formations of the face and lips. On admission severe edema was observed in the face resulting in inability of opening the left eyelid. Erosions and crust formations were observed on the upper lip and orobuccal mucosa. The skin biopsies from the ulcerative lesions of the face and lip revealed marked infiltration of eosinophils, neutrophils, mononuclear cells and plasma cells beneath the ulcer as well as vasculitis involving arteriole, venule and capillary. The cell infiltration extended deep into the fatty tissue with a proliferation of reticulum cells. The treatment consisted of corticosteroids and antibiotics. Three months after the disappearance of the edema and skin eruptions, similar symptoms reappeared, accompanied by fever, in the middle of February 1969. In the middle of March jaundice set in along with swelling of the liver. The SGOT and SGPT were 710 and 235 Karmen units respectively. In addition urinalysis showed many red cells with occasional granular casts and 3+ protein. The BUN was 110 mg per 100 ml. Blood pressure was within the normal range. The patient succumbed to severe jaundice and paralytic ileus on 26. March 1969.

A postmortem examination revealed formations of granulomatous lesions with necrotizing vasculitis in various organs. Ulceration with submucosal infiltration of eosinophils, neutrophils, mononuclear cells, macrophages and plasma cells was found in the nasal cavity.

Fibrinoid necrosis in the intima was seen with cell infiltration involving the whole thickness of the deep submucosal arterioles. In the liver granulom formations with necrotizing vasculitis were observed in the Glisson's sheath. Scattered foci of hepatic cell necrosis were observed with neutrophil and mononuclear cell infiltration. In the spleen fibrinoid necrosis with massive intimal accumulations of mononuclear cells and neutrophils was seen in the trabecular and follicular arteries, some showing complete destruction of vascular walls. Necrosis with plasma exudation was found in some lymphatic follicles. Segmental necrotizing and granulomatous glomerulonephritis was found to be generally distributed. Hemorrhagic pneumonitis was associated with tracheobronchitis. These findings were in general consistent with those of Wegener's granulomatosis (Wegener, 1939; Godman and Churg, 1954; Anthony and Wolff, 1973).

Glomerular Histopathology

Extracapillary crescent-forming glomerulonephritis was seen in generalized distribution, sometimes with granulomatous reaction from the interstitium. Analysis using serial sections stained with Periodic Acid Shiff (PAS) or Periodic Acid Methenamine Silver (PAM) elucidated that the glomerular damage could be initially seen in local and segmental portions of individual glomeruli. It was characterized by the disintegration of the mesangium (mesangiolysis), resulting in the balooned and globular appearance of the glomerular tuft (Fig. 1). The lumen of the dilated and simplified tuft was filled with mononuclear cells, macrophages, neutrophils and other undifferentiated cells, often intermingled with cell debris and materials of fibrin-staining property. The stainability of mesangium was decreased and fragments of PAS or PAM positive materials, probably of mesangium origin, were seen within the lumen. The interruption or rupture of the GBM was seen in these expanded baloon-like lobuli. Through this defect the intraluminal materials including cellular elements were seen to break out into the Bowman's space (Fig. 2). Massive inflammatory cell accumulation with the proliferation of parietal epithelial cells formed granulomatous lesions in the destructed glomerular tufts where glomerular structure could no longer be detected (Fig. 3). Glomerular lesions often accompanied pericapsular interstitial inflammatory cell accumulation followed by a fusion of intra and pericapsular granulomatous inflammation (Fig. 4).

Comments

The development of segmental disorganizing glomerulonephritis in this case is seen to be based on the initial local disintegration of the mesangial area followed by the extracapillary extension of the inflammation. In addition to the local necrotizing lesion described as fibrinoid necrosis or thrombotic tuft necrosis, the simplification of the glomerular tuft due to the lytic process in the mesangium seems to play an important role for the formation of progressive glomerular lesion. Similar blood cavity formation has been reported in habu snake poisoning

Fig. 1. Simplification of glomerular tuft due to mesangiolysis. PAM positive fragment possibly of mesangial origin is detected in the dilated lumen (arrow). PAM. × 280

Fig. 2. Rupture of the GBM (arrow). Intraluminal materials are seen to break out into the urinary space. Note formation of crescent (*Cr*). PAM. × 280

Fig. 3. Segmental glomerular granulomatous lesion. Glomerular structure is destroyed in this lesion. PAM. × 280

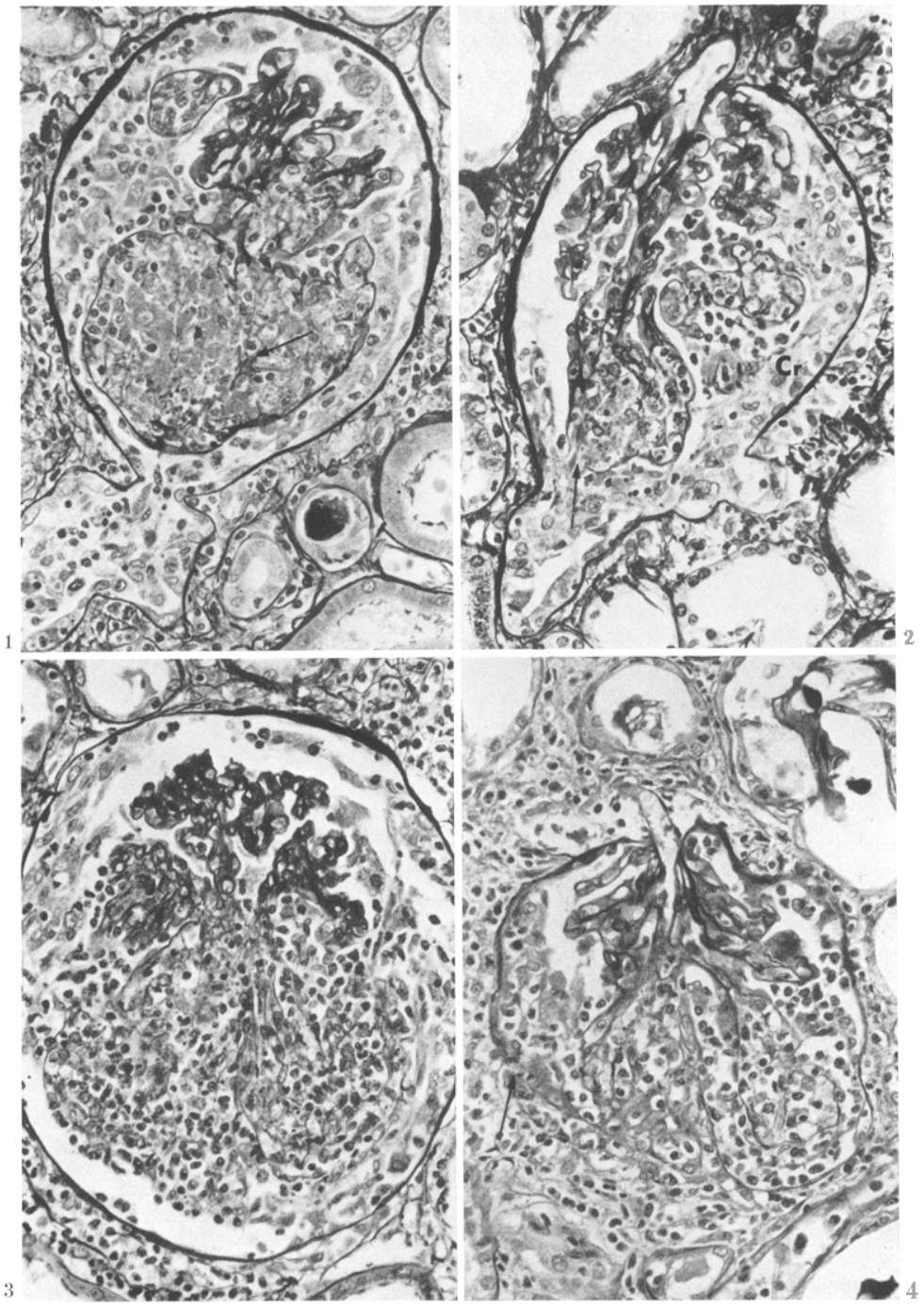

Fig. 4. Pericapsular inflammatory reaction fuses glomerular granulomatous lesion. Note disruption of the capsular basement membrane (arrow). PAS. × 280

and termed as mesangiolysis (Suzuki *et al.*, 1963). Though the initiating factors causing severe segmental injuries to the glomeruli are unclear at present, the process resulting in the granulomatous glomerulitis is quite similar to that formed in some immunologically induced experimental glomerulonephritides in which a large quantity of antigen-antibody complexes is provided to form in the circulation or on the GBM (Kondo *et al.*, 1972; Kobayashi and Shigematsu, 1973; Shigematsu and Kobayashi, 1973). Here again the lytic process proved its importance in the development of disorganizing glomerular lesions (Okabayashi, 1970).

In contrast to the recoverable glomerulonephritis where the transient glomerular hypercellularity is mainly due to phagocytic accumulation and is without any disorganization of glomeruli (Shigematsu *et al.*, 1973), the unhealable glomerulonephritis seems to parallel the breaking down process of glomerular structures. Accordingly, it is suggested that the presence of mesangiolysis or rupture of the GBM implies the progressive and irreversible nature of the glomerular lesions.

The authors wish to acknowledge Mr. T. Yamada for his technical assistance and Mr. Gertz for the preparation of English manuscript.

References

Altmann, H. W., Schicke, H.: Ein Beitrag zur Histologie und zur Einordnung der Wegenerschen Granulomatose. Beitr. path. Anat. **121**, 211–241 (1959)

Anthony, S. F., Wolff, S. M.: Wegener's granulomatosis: Studies in eighteen patients and a review of the literature. Medicine (Baltimore) **52**, 532–561 (1973)

Godman, G. C., Churg, J.: Wegener's granulomatosis. Pathology and review of the literature. Arch. Path. **58**, 533–553 (1954)

Kobayashi, Y., Shigematsu, H.: Rapidly progressive glomerulonephritis in rabbit serum sickness. Excerpta Medica, Internat. congress series **300**, 68 (1973)

Kondo, Y., Shigematsu, H., Kobayashi, Y.: Cellular aspects of rabbit Masugi nephritis. II. Progressive glomerular injuries with crescent formation. Lab. Invest. **27**, 620–631 (1972)

Morita, T., Suzuki, Y., Churg, J.: Structure and development of the glomerular crescent. Amer. J. Path. **72**, 349–368 (1973)

Okabayashi, A.: Nephritides and dysimmunization; with special reference to the significance of lytic process in immunologically induced experimental glomerulonephritis. Jap. J. Nephrol. **12**, 1–17 (1970)

Shigematsu, H., Shishido, H., Kuhara, K., Tsuchida, H., Suzuki, H., Hirose, K., Tojo, S.: Participation of monocytes in transient glomerular hypercellularity in poststreptococcal glomerulonephritis. Virchows Arch. Abt. B **12**, 367–370 (1973)

Shigematsu, H., Kobayashi, Y.: The distortion and disorganization of the glomerulus in progressive Masugi nephritis in the rat. Virchows Arch. Abt. B **14**, 313–328 (1973)

Stejskal, J., Pirani, C. L., Okada, M., Mandelnakis, N., Pollak, V. E.: Discontinuities (gaps) of the glomerular capillary wall and basement membrane in renal diseases. Lab. Invest. **28**, 149–169 (1973)

Suzuki, Y., Churg, J., Grishman, E., Mautner, W., Dach, S.: The mesangium of renal glomerulus. Amer. J. Path. **43**, 555–578 (1963)

Wegener, F.: Über eine eigenartige rhinogene Granulomatose mit besonderer Beteiligung des Arteriensystems und der Nieren. Beitr. path. Anat. **102**, 36–68 (1939)

Dr. Hidekazu Shigematsu, M.D.
Department of Pathology
School of Medicine
Chiba University
Chiba, 280, Japan