A Case of Weber-Christian Disease With Collapsing Glomerulopathy

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• **We report a case of Weber-Christian disease confirmed by skin biopsy in a patient who presented with collapsing glomerulopathy and lipophagic interstitial nephritis. On renal biopsy, glomerular visceral epithelial cells, tubular cells, and interstitial macrophages were loaded with inclusions that were morphologically consistent with oxidized lipoproteins, suggesting that lipids derived from the panniculitis may have an etiopathogenic role.** ***Am J Kidney Dis*** **48:484-488.**

INDEX WORDS: Weber-Christian disease; collapsing glomerulopathy; panniculitis; proteinuria.

WEBER-CHRISTIAN DISEASE is an inflammatory disease characterized by relapsing nodular panniculitis first described by Pfeifer[1] in 1892. In 1925, Weber[2] characterized the disease as a relapsing nonsuppurative nodular panniculitis. In 1928, Christian[3] noted fever as a part of the entity. The term Weber-Christian disease came into use in 1935. Here, we report a case of an African-American man with Weber-Christian disease associated with collapsing glomerulopathy.

CASE REPORT

A 33-year-old African-American man was admitted to the hospital with recurrence of febrile panniculitis. Weber-Christian disease was diagnosed 4 years before when he presented with painful subcutaneous nodules on his arms and legs (Fig 1). Since then, he experienced 1 flare of the disease every year. He denied drug abuse, recent travel, or use of nonsteroidal anti-inflammatory drugs or over-the-counter medications.

At the time of admission, he reported fever, chills, nausea, generalized body aches, and anorexia. His medications included prednisone, hydroxychloroquine, pantoprazole, and alendronate (1 dose 3 days before admission). Physical examination on admission showed a temperature of 102°F, blood pressure of 133/64 mm Hg, and heart rate of 88 beats/min. No subcutaneous nodules were noted. Physical examination was otherwise unremarkable.

Initial laboratory results showed the following values: hemoglobin, 13.5 g/dL (135 g/L); white blood cells, 3,100/μL; serum creatinine, 1.9 mg/dL (168 μmol/L); serum albumin, 3.7 g/dL (37 g/L); erythrocyte sedimentation rate, 34 mm/h; urinalysis with protein greater than 300 mg/dL (>3 g/L); red blood cells, 20 to 30/high-power field with no casts and total 24-hour urinary protein excretion of 3.4 g; C3, 102 mg/dL (1.02 g/L); and C4, 36 mg/dL (0.36 g/L). Antinuclear antibodies, rheumatoid factor, hepatitis B surface antigen, hepatitis C antibody, venereal disease research laboratory, and human immunodeficiency virus test results were negative. Blood and urine culture results were negative.

A renal ultrasound showed enlarged kidneys (right, 13.8 cm; left, 15.7 cm) with markedly increased echogenicity. Chest radiograph was unremarkable.

Renal Biopsy

Light microscopy showed severe capillary collapse with segmental and global sclerosis (Fig 2), accompanied by severe tubulointerstitial nephritis with predominance of mononuclear cells and focal increase of foam cells, as well as fat-laden histiocytic and epithelioid cells (oil red O and $CD68^+$) with granulomatous appearance (Fig 3). There also was a granulocytic component in the latter with frequent apoptotic cells and tubulitis with occasional cell necrosis (Fig 3).

In the interstitium there were cells with the appearance of macrophages containing lipid droplets similar to those observed in the glomerular visceral epithelial cells (Fig 3). Apoptosis of inflammatory cells was frequent. Occasional cells of epithelioid appearance showing prominent rough endoplasmic reticulum and large multilobed nuclei were observed (Fig 4). Immunofluorescence showed only traces of immunoglobulin M and C3.

Ultrastructurally, the glomeruli had collapse of capillary loops with sclerosis and hyperplastic swollen visceral epithelial cells containing numerous variegated lipid inclusions and large vacuoles that replaced the uriniferous space (Fig 5). The interstitium showed macrophages containing numerous lysosomes and phagolysosomes that layered along the tubular basement membranes (Fig 6). In addition, some capillaries contained macrophages adherent to capillary walls (Fig 7).

After the renal biopsy report, the patient was treated with intravenous methylprednisolone (50 mg twice daily) and discharged on treatment with prednisone, 50 mg twice daily, and lisinopril, 10 mg/d. Serum creatinine level on discharge

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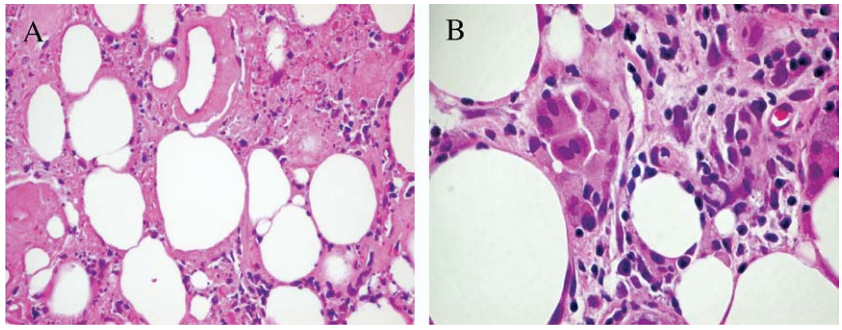

Fig 1. Biopsy specimen of a subcutaneous nodule shows (A) fat necrosis with destruction of adipocytes and necrotic inflammatory cells and (B) fat cells surrounded by numerous mononuclear and giant cells, as well as foam cells.

was 2.2 mg/dL (195 μmol/L). Four weeks later, serum creatinine level had decreased to 1.6 mg/dL (141 μmol/L), and 24-hour urinary protein excretion had decreased to 700 mg.

DISCUSSION

Weber-Christian disease, also known as relapsing febrile nodular panniculitis, is an infiltrative inflammatory disease of the adipose tissue[3,4] that usually occurs in young white females. It is characterized by tender subcutaneous nodules often associated with constitutional and other symptoms, such as fever, arthralgias, and myalgias. The nodules are tender and erythematous, may develop serous or serosanguinous drainage, and often heal leaving an atrophic area.[5,6] They typically are located over the extremities, but also can occur over the posterior thorax, abdominal area, breasts, face, or buttocks. Occasionally, nodules may involve the cranium, scrotum, or mesentery of the small or large bowel, leading to bowel obstruction.[4,6] The disease can present as a severe systemic illness involving the heart, lungs, liver, or kidneys, eventually leading to death.[4,5] The cause of this disease is unknown, but some suggested that the inflammatory process may be immune mediated.[7,8] The diagnosis usually is made by excisional biopsy of a nodule. The panniculitis typically is lobular, although it may be both lobular and septal.[4,5] Other features include a mononuclear or pleomorphic cellular infiltrate with fat-laden macrophages.[4,5] Panniculitis also can occur associated with a variety of systemic diseases and clinical syndromes, including thermal injury,[9] trauma,[10] systemic lupus erythematosus,[11,12] rheumatoid arthritis,[13] Hodgkin disease,[14] erythema nodosum,[15] sarcoidosis,[16] and α_1-antitrypsin deficiency.[17]

There is no specific treatment for patients with Weber-Christian disease. Numerous medications have been tried, including corticosteroids, antimalarials,[8,18] and immunosuppressive agents.[19-22] Immunosuppressive therapy usually is reserved for patients with progres-

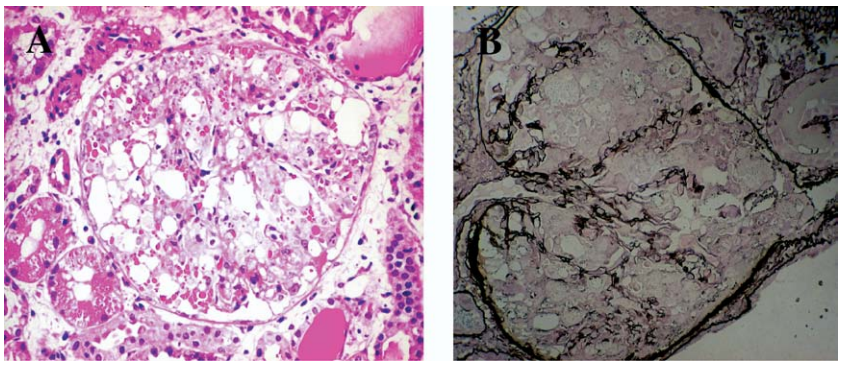

Fig 2. Light microscopic picture of a glomerulus shows severe capillary collapse. (A) Most of the glomerular volume consists of swollen vacuolated hyperplastic visceral epithelial cells containing protein reabsorption droplets. Capillaries are collapsed and frequently imperceptible. (Hematoxylin and eosin; original magnification ×350.) (B) Glomerulus with collapsed capillary loops in several lobules. (Jones silver methenamine; original magnification ×300.)