American Journal of Medical Case Reports, 2022, Vol. 10, No. 3, 45-47
Available online at http://pubs.sciepub.com/ajmcr/10/3/1
Published by Science and Education Publishing
DOI:10.12691/ajmcr-10-3-1

Pauci-immune Crescentic Glomerulonephritis: Case Report

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Received January 20, 2022; Revised February 23, 2022; Accepted March 01, 2022

Abstract Pauci-immune glomerulonephritis (PIGN) is a potentially life-threatening condition that progresses rapidly to renal failure within days or weeks. Here we present a 62 -year-old African American female who was found to have acute kidney injury at the time of presentation. Further workup including renal biopsy showed anti-neutrophilic cytoplasmic antibodies (ANCA) associated pauci-immune crescentic glomerulonephritis. The patient was started on steroids and cyclophosphamide however, the patient's kidney function continued to get worse and required hemodialysis. Unfortunately, our patient passed away after two months of diagnosis secondary to cardiac arrest.

Keywords: *Pauci immune glomerulonephritis, crescentic glomerulonephritis, survival*

Cite This Article: Wisam Mnkana, Nikita Wong, Eman EL-Sawalhy, Ahmed Abdelrahim, Hussein Gaith, Zhang Ping, and Rabih Bazzi, "Pauci-immune Crescentic Glomerulonephritis: Case Report." *American Journal of Medical Case Reports*, vol. 10, no. 3 (2022): 45-47. doi: 10.12691/ajmcr-10-3-1.

1. Introduction

PIGN accounts for 80% of rapidly progressive GN. It is more commonly seen in whites than in black, with around equal distribution between males and females [1]. It is often associated with anti-neutrophilic cytoplasmic antibodies (ANCA), but 10% of the cases are ANCA negative [1]. Treatment with corticosteroids with or without immunosuppressive therapy (either cyclophosphamide or azathioprine) is recommended [10,11]. The 1- year mortality rate can be up to 80% if left untreated however, with aggressive treatment the 5-year mortality rate is 25% [2]. There is a limited number of cases reported in the literature.

2. Case Presentation

A 62 year-old-African American woman with a past medical history of hypertension, chiari malformation, and complex regional pain syndrome presented to the hospital complaining of facial swelling and sinus congestion. On admission, physical examination revealed frontal and maxillary sinuses tenderness along with facial swelling and bilateral lower extremity edema. It also revealed a high-grade temperature of 101.8°F, heart rate of 85 beats/minute, respiratory rate of 16/minute, blood pressure of 155/87 mmHg, and body mass index of 45.35kg/m^2. Laboratory findings showed acute kidney injury (AKI), with a creatinine of 5.32 mg/dL (baseline of 1.1-1.2 mg/dL), low glomerular filtration rate (GFR) of 9 mL/min/1.73m^2, and hemoglobin level of 10 g/dl. The patient was started on antibiotics secondary to her sinus infection and the nephrologist was consulted due to her acute kidney injury.

The patient denied any history of arthritis, recent infection, non-steroidal anti-inflammatory medications use, or history of connective tissue disease. The urine analysis showed 2+ protein, 3+ blood, and red blood cells whereas the random urinary protein/creatinine ratio was elevated at 4.45 (normal <0.20). Renal ultrasound was done and revealed normal sized kidneys without hydronephrosis. Further workup revealed elevated ANA of 1:1280 (normal <1:160), elevated rheumatoid factor of 39 IU/mL (normal < 15 IU/mL), elevated P-ANCA of > 1:640 (normal < 1:20) and negative anti-dsDNA, glomerular basement membrane (GBM) antibody and complement levels. Renal biopsy revealed cellular crescent formation, mild to moderate tubular atrophy, and interstitial inflammation (Figure 1). Immunofluorescence microscopy (IF) revealed no linear positive staining for IgG, C3, kappa, and lambda, therefore consistent with ANCA associated crescentic glomerulonephritis, pauci-immune type. Electron microscopy (EM) showed segmental fusion of foot processes but no thickening of glomerular basement membranes ANCA associated pauci-immune crescentic glomerulonephritis. The patient was started on IV methylprednisolone 125 mg every 12 hours however, her

renal function got worse for which she was started on cyclophosphamide. The patient's admission was complicated by left lower extremity deep venous thrombosis and pulmonary embolism so she was started on oral anticoagulation. Following that, the patient became clinically stable and her creatinine was improved to reach 3.57 mg/dL and GFR of 15 mL/min/1.73m2. Patient was then discharged home on cyclophosphamide to be taken every 28 days for a total of 4 cycles and 50 mg of prednisone to be taken once daily. As an outpatient follow-up, patient had blood work done that showed worsening of her renal function, for which decision was made to initiate hemodialysis. After seven days of starting the dialysis, patient had witnessed cardiac arrest at home for which emergency medical service was called and cardiopulmonary resuscitation (CPR) was initiated but she passed away secondary to cardiopulmonary arrest in less than two months of being diagnosed with crescentic glomerulonephritis pauci-immune type.

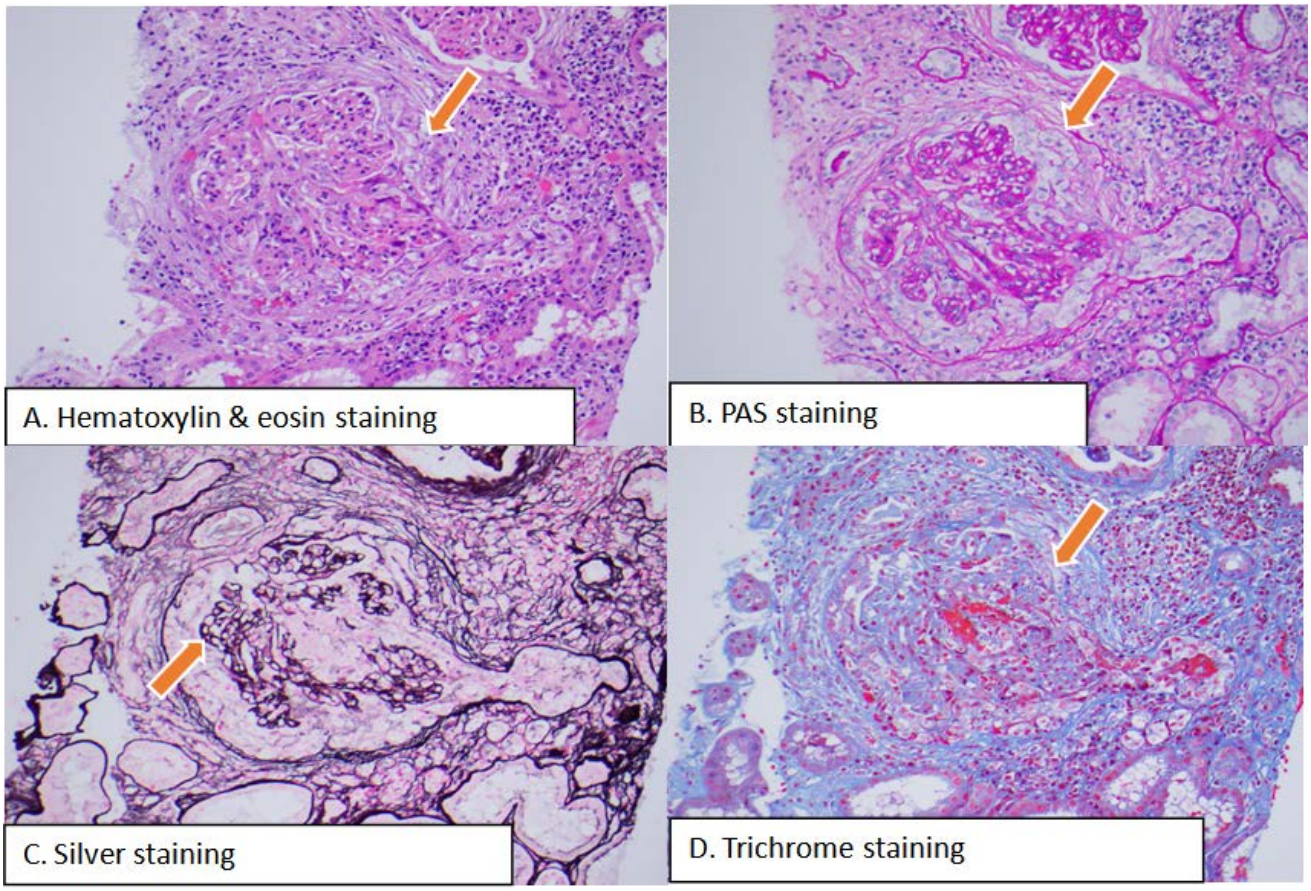

Figure 1. Electron microscopy x200: showing crescentic glomerulonephritis by different stains (arrows indicate cellular crescent)

3. Discussion

Rapidly progressive glomerulonephritis (RPGN) is divided into 3 categories: PIGN, anti-GBM GN, and immune complex GN. PIGN is the most common of the three, and 90% of cases are associated with ANCA [1]. It is called pauci immune because there are few or nonimmune deposits seen by IF or EM [4]. The 1-year mortality is high of 80% however, with immunosuppressive therapy can result in 5-year survival of 75% [2]. Factors that decrease the chance of survival include old age, pulmonary hemorrhage, and dialysis dependency. Our patient ended being dialysis dependent.

Kidney biopsy is important even in lung predominant disease because of high diagnostic yield and safer procedure [3]. It appears that the first step in the pathogenesis of PIGN is the rupture of the glomerular basement membrane, leading to the entry of fibrin and other plasma proteins from the capillary lumen. This will lead to the arrival of T cells, macrophages, and fibroblasts to the site of injury inducing inflammatory response. This extra capillary proliferation within the glomerulus is referred to as "crescent formation". There are target antigens that are generally associated with glomerulonephritis and vasculitis called myeloperoxidase (MPO) and proteinase 3 (PR3). ANCA which is anti-neutrophile cytoplasmic autoantibodies will bind with MP and PR3 resulting in activation of neutrophils and monocytes and this will result in reactive oxygen production and release of enzymes that damage endothelial cells and glomeruli. ANCA will also result in the release of neutrophil extracellular traps (NETs) which are made of chromatin fibers and autoantigens including MPO and PR3 [5,6] and result in damage to endothelial cells and entire glomeruli. Infection with staph aureus can enhance the ability of neutrophils to build NET in vasculitis [5]. Patient who has granulomatosis with polyangiitis is usually chronic nasal carriers of staph aureus [7,8]. Of note our patient initially presented with sinus pain and congestion and this may have aided in activation of NET.

Generalized nonspecific manifestations of systemic inflammatory disease, such as fever, malaise, anorexia,

weight loss, myalgia, and arthralgia, can be seen as clinical manifestations. GFR at the time of diagnosis is the best clinical predictor of renal outcome [1] as seen in our patient. Respiratory tract disease and PR3-ANCA are predictors of higher relapse rates [9] which was relevant in our patient through subsequent admission with AKI requiring dialysis.

The crucial aspect in treating pauci-immune glomerulonephritis is the quick diagnosis and early administration of immunosuppressive therapy given the rapid deterioration course the disease can propose. ANCA levels are important as they can raise suspicion and aid in early detection with renal biopsy. ANCA positive PIGN is treated with a combination of corticosteroid and cyclophosphamide [10], then switching to azathioprine after remission [11]. Our patient received corticosteroid along with cyclophosphamide monthly. She was progressed to end-stage renal disease requiring dialysis due to worsening renal function about one month after diagnosis. The major cause of death is severe infections however, cardiac arrest is a rare cause of death as in our patient [12].

Conflict of Interest

None of the authors have any conflicts of interest to declare.

Disclosure of Funding

None of the authors have any source of funding to declare.

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