Acute Glomerulonephritis in an Immunocompetent Elderly Woman after Contact with a Child who Had Been Diagnosed as Erythema Infectiosum

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Abstract

The prevalence of postinfectious glomerulonephritis has decreased in most developed countries. We report the case of a previously healthy, immunocompetent 65-year-old woman who developed acute glomerulonephritis associated with human parvovirus B19 infection. She was referred by her primary care physician for suspected congestive heart failure but she had an elevated creatinine level and an abnormal urinalysis. Renal biopsy showed diffuse endocapillary proliferative glomerulonephritis. After biopsy, we learned that she had been in frequent contact with her grandson who had been diagnosed with erythema infectiosum. Her human parvovirus B19 serum IgM titer was elevated at 3.50, indicating current infection.

Key words: postinfectious glomerulonephritis, human parvovirus B19, immunocompetent elderly woman

Introduction

Postinfectious glomerulonephritis (PIGN) is an immunologic response of the kidney mainly triggered by streptococcal infection, although many other organisms can cause the disease. The prevalence of PIGN has decreased in most developed countries and PIGN is rarely expected clinically. However, in many developed countries, adults now represent the majority age-group at risk for PIGN and those with comorbidities such as diabetes and alcoholism are at increased risk of developing the disease. Although human Parvovirus B19 (HPV B19) is best known for causing the childhood disease erythema infectiosum, better known as Fifth disease, recent case reports have shown a relationship between HPV B19 infection and renal disease. It is difficult to diagnosis HPV B19 in adults due to a lack of typical symptoms and the frequency of PIGN related to HPV B19 in the elderly is unknown.

In this report, we present the case of an elderly immunocompetent host with acute glomerulonephritis following contact with her grandson diagnosed as erythema infectiosum who clinically presented with dyspnea suggestive of congestive heart failure. The present case is the oldest case report to date of HPV B19-associated PIGN listed in PubMed.

Case Report

A 65-year-old woman was referred to our hospital because of orthopnea and pleural effusion. Seventeen days prior to referral, she developed fever without associated symptoms which lasted for five days. Five days prior to referral, she noticed edematous eyelids. One day prior to referral, she had dyspnea and consulted her primary physician. A pleural effusion was noted and the brain natriuretic peptide (BNP) level was elevated. She was referred to our hospital for further evaluation and treatment. She had a no remarkable past medical history or family history. On physical examination her height was 151 cm and weight was 56.8 kg. [her usual weight was about 50 kg]. She was alert and oriented. Her blood pressure was 161/100 mmHg, pulse was 88/min and regular. Her peripheral oxygen saturation was 93% with oxygen flow of 1 L/min. She was puffy and pale, not icteric. Bilateral coarse crackles were audible; no mur-
The following were abnormal laboratory tests on admission: hemoglobin was 9.9 g/dL, hematocrit was 28.3%, MCV was 84.9 fl. Total protein was 5.9 g/dL, serum albumin was 2.9 g/dL, urea nitrogen 66 mg/dL, serum creatinine 1.05 mg/dL, and uric acid 12.8 mg/dL and BNP 519.3 pg/mL. Chest X-ray showed cardiomegaly, mild pulmonary congestion, and bilateral pleural effusions. There were no abnormal findings on ECG. Transthoracic echocardiogram revealed a normal left ventricular (LV) ejection fraction of 63% (Ni>50%) without asynergy of LV wall (LV end-diastolic volume: 84 mL/m² (normal <97 mL/m²). E/A ratio was 0.92 and E/E’ ratio was 11.17 which suggested diastolic LV dysfunction. Mild pulmonary hypertension with 2/4 grade TR and dilated IVC were noted. After admission she was treated as diastolic heart failure (DHF) with furosemide and nitroglycerin. However she developed drug-resistant hypotension and oliguria. Urinalysis showed 3+ hematuria and 3+ protein. Urinary protein was 2-3 g/24h.

Urinary sediment showed 10-20 rbc/HPF and 1-2 granular casts/low power field. Complement C3 and C4 were 99 mg/dL and 23 mg/dL, respectively. CH50 was low at 26 U/mL (normal range 32-54 U/mL); ASO titer was not elevated; MPO-ANCA, PR3-ANCA, anti-GBM, ANA and anti-dsDNA antibody titers were negative. On the ninth day of hospitalization her condition began to improve with spironolactone treatment. Though the dose of diuretic was gradually tapered, her urine volume began to increase and body weight decreased to 47.4 kg. The urinalysis remained abnormal. A kidney biopsy, performed on the twenty-first day of hospitalization, showed diffuse endocapillary proliferative glomerulonephritis with diffuse enlargement of glomeruli with marked hypercellularity and diminution or apparent loss of capillary lumens. Infiltration of neutrophils and monocytes was observed (Fig. 1). The severity of tubular atrophy, interstitial cell infiltration, and fibrosis was mild. Immunofluorescence revealed coarse granular staining of glomerular capillary loops with C3 and IgG (Fig. 2). Electron microscopy showed subendothelial edema, swelling of endothelial cells and infiltration of neutrophils and monocytes in the capillary lumens (Fig. 3). From these pathological findings, PIGN was suspected. It turned out that she had been in frequent contact with her grandson, who had been recently diagnosed with erythema infectiosum (Fifth disease). HPV B19 serum antibody measurement by enzyme immunoassay (EIA) on admission showed an IgM titer of 3.50 (normal range <0.80) consistent with current infection. She was managed without diuretic drugs and antihypertensive drugs.

Her course following the kidney biopsy was characterized by decreasing serum creatinine to a normal range of 0.71 mg/dL with a normalization of urinalysis in two months. Anemia was also resolved. Repeated anti-human parvovirus B19 IgM after three months was normalized to 0.56.

Discussion

PIGN is the classic form of immune-mediated infection-associated glomerulonephritis following a nonrenal infection and is primarily a childhood disease that occurs after an upper respiratory tract or skin infection. Clinical data indicate a global decline in the prevalence of PIGN in developed countries for the past 20 to 30 years due to better and earlier treatment of infection and improvement in living conditions and nutrition. Therefore PIGN is rarely considered clinically in the elderly.

The acute presentation of PIGN ranges from nephritic syndrome which causes volume overload to asymptomatic glomerulonephritis. On the other hand, DHF is a clinical syndrome in which patients have symptoms and signs of heart failure, normal or near normal LV ejection fraction,
and evidence of diastolic dysfunction. The prevalence of DHF increases with age (1-3) and DHF is more common in women than men (4-7). As shown in Table, it is sometimes difficult to distinguish DHF from a severe form of acute glomerulonephritis (volume overload) especially in elderly people because of many similar findings in clinical features and laboratory data. Therefore in order to differentiate the diagnosis, echocardiography is very important. But the high prevalence rate of etiology of DHF such as hypertension and coronary or diabetic heart disease makes the clinical picture confusing. Considering these varied backgrounds there is a possibility of acute glomerulonephritis being overlooked. There was no problem in our initial diagnosis as DHF based on her symptoms, laboratory data and echocardiography. Even in modern times when diagnostic imaging and biomarkers have become developed, evaluation of the urinalysis, including sediment, is an important useful tool to avoid overlooking hidden kidney disease in patients suspected of having heart disease.

Although streptococcus is the most common responsible bacterium for PIGN in both children and adults (8-13), the possibility of a link between kidney disease and HPV B19 infection has been suggested. Several clinical presentations and histologic patterns have been described (14-25). As a clinical picture, female dominance, onset in the second or third decade of life, acute nephritic syndrome with hypocomplementemia often following a prodrome of fever, rash, and arthritis are most common. Nephrotic-range proteinuria is seen as well (14-17, 19, 20, 26-29). Although acute glomerulonephritis is rare in Japan, the present case showed some findings that lead to diagnosis. Therefore it is important whether we can assume as differential diagnosis or not. Representative histologic findings show endocapillary and/or mesangial proliferation often with subendothelial deposits together with granular deposition of C3 and IgG along capillary walls and mesangium, a pattern that is consistent with acute PIGN which was seen in the present case (14-17, 19, 20, 27-29). A variety of renal pathology
findings other than endocapillary and/or mesangial proliferation including FSGS (23, 30), collapsing glomerulopathy (18, 21, 31), membranoproliferative glomerulonephritis with intravascular microthrombi (25), Henoch Schönlein purpura (32), and thrombotic microangiopathy (24), in immunocompetent and immunocompromised hosts has been reported.

HPV B19, a nonenveloped 22-26 single-stranded DNA virus, has been identified as the etiologic agent of *erythema infectiosum.* The only known host is humans and HPV B19 is cytotoxic for erythroid progenitor cells in bone marrow and therefore can lead to mild anemia in otherwise healthy adults (33). Respiratory transmission is the most common mechanism and, as observed in the present case, young children are the main source. It is difficult for physicians to make a correct diagnosis of HPV B19 in older adults because: 1) The high prevalence of antibody HPV B19 IgG in the elderly (up to 80%) (34), and 2) Unlike children, HPV B19 infection in adults is not accompanied by typical rash.

The majority of children and patients with the epidemic form of PIGN have an excellent prognosis, which contrasts with the poor long-term outcome of sporadic cases. Older patients, particularly those aged over 60 years, or those with underlying chronic diseases have a worse prognosis, with 30% to 70% having residual chronic kidney disease. IgA deposition dominant PIGN may be associated with HPV B19 have not yet been fully elucidated. However, the following things are understood. Hump-shaped subepithelial electron dense deposits tend to decrease in PIGN associated with HPV B19. The affinity of HPV B19 to the endothelium results from the presence of globoside a neutral sphingolipid that is also present on red cell membranes, on the endothelium, and is part of the blood group P antigen. The localization of viral nucleic acid to the endothelium suggests a direct role of endothelial cell B19 parasitization in the evolution of the vasculitis and of glomerulonephritis. HPV B19 induces inflammatory processes in human endothelial cells leading to dysregulation of inflammatory signal transducer and activation of transcription and suppressors of cytokine signaling (36), activation of the Ca++ ion channel Ca++ release-activated Ca++ current by parvovirus B19-phospholipase A2 activity, and specific cleavage of the sodium-hydrogen exchanger isoform 1 by HPV B19 induction of caspase 3 (37).

In summary, acute glomerulonephritis which mimics DHF may be difficult to diagnose and HPV B19-associated PIGN should be considered as a possible cause of acute glomerulonephritis in the elderly. To make a prompt diagnosis greater awareness should be paid for the atypical presentation of HPV B19 infection and course of PIGN in the elderly.

The authors state that they have no Conflict of Interest (COI).

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References
