Hydralazine-induced MPO-ANCA Renal-Limited Vasculitis Masquerading as Lupus Nephritis

Sir,

Hydralazine can rarely induce an antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis and less than 80 such cases have been reported hitherto.[1,2] Here, we report the case of an elderly patient who was diagnosed with hydralazine-induced ANCA vasculitis after taking hydralazine for 5 years.

A 76-year lady presented with complaints of cough and dyspnea for one day and decreased oral intake for three weeks. She had a past history of diabetes mellitus, hypertension (on hydralazine for two years) and chronic kidney disease (baseline creatinine, 1.9 mg/dl 3 months ago with history of microscopic hematuria for 18 months). Physical examination revealed pallor and decreased air entry at both lung bases. Chest radiograph showed bilateral air-space opacities and CT chest revealed consolidation of the lingula. She was started on antibiotics for pneumonia.

Laboratory investigations were notable for anemia (hemoglobin: 7.9 g/dl) and acute kidney injury (creatinine, 4.0 mg/dl). Renal ultrasonography showed bilaterally increased renal parenchymal echogenicity. Urine microscopy showed red cell casts; and urine protein-to-creatinine ratio was consistent with non-nephrotic range proteinuria (300 mg/day). Auto-immune work-up for glomerulonephritis was requested, which was significant for anti-neutrophilantibody (ANA): positive at a dilution of 1:1280 (homogeneous pattern); anti-dsDNA antibody titer: elevated (907 IU/L); ANCA: positive (peri-nuclear pattern); and anti-myeloperoxidase (MPO) antibody titer: elevated (104 AU/mL).

Rest of the auto-immune work-up was within normal limits (Table I). Renal biopsy was performed (Figure 1), which demonstrated a pauci-immune, diffuse necrotizing, crescentic glomerulonephritis.

Based on clinical, serological and pathological findings, a diagnosis of hydralazine-induced MPO-ANCA vasculitis (renal-limited) was made. Hydralazine was stopped immediately and aggressive treatment was initiated with a combination of plasmapheresis and pulse-dose steroids. Plan was to start rituximab therapy as outpatient. Patient's renal function tests had stabilized at the time of discharge and they continued to improve on follow-up.

This patient had evidence of acute kidney injury on top of chronic kidney disease (microscopic hematuria for 18 months) while taking hydralazine for 2 years. Renal biopsy revealed a pauci-immune crescentic glomerulonephritis. Although an idiopathic ANCA vasculitis could cause similar pathologic findings, the combination of exposure to hydralazine (a drug known to cause MPO-ANCA vasculitis), serologic detection of MPO-ANCA, and elevated ANA and anti-dsDNA antibody titers in the absence of clinical manifestations of lupus were all consistent with hydralazine-induced MPO-ANCA vasculitis.[3] Priming of neutrophils, for instance, due to an infection, is known to exacerbate ANCA-mediated vasculitides.[4] In this case, the patient had evidence of pneumonia, which may have exacerbated an ongoing vasculitic process. Elevated anti-dsDNA antibody titers were observed in this case, which are uncommonly seen in hydralazine-induced ANCA vasculitis.[2] This case

Table I: Results of auto-immune panel for the patient.

Investigation	Result
Antinuclear antibody	Positive at a dilution of 1:1280 with a homogeneous pattern
Rheumatoid factor	Negative
Complement protein C3 level	Normal
Complement protein C4 level	Normal
Anti-dsDNA antibody	Titer elevated at 907 IU/L
Anti-Smith antibody	Negative
Anti-RNP antibody	Negative
ANCA screen	Positive with a peri-nuclear staining pattern
Anti-MPO antibody	Titer elevated at 104 AU/mL
Anti-PR3 antibody	Negative
Anti-GBM antibody	Negative
ASO antibody	Negative
Anti-IgA antibody	Negative

ANCA-antineutrophil cytoplasmic antibody; ASO-anti-streptolysin O; dsDNA-double-stranded deoxyribonucleic acid; GBM-glomerular basement membrane; IgA-immunoglobulin class A; MPO-myeloperoxidase; PR3-proteinase 3; RNP-ribonuclear protein.

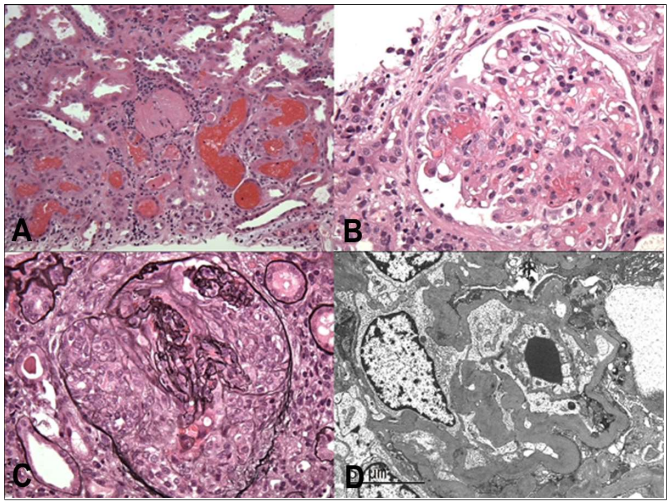

Figure 1: Light microscopic images of renal biopsy specimen demonstrate **(A)** red cell casts, **(B)** hypercellular glomerulus with fibrinoid necrosis and **(C)** crescent formation. **(D)** Electron micrograph shows extra-capillary proliferation, cellular crescents, mildly thickened glomerular basement membrane and extensive foot process effacement.

demonstrates that hydralazine-induced MPO-ANCA vasculitis can present in an indolent manner after a long period of latency and with concomitant elevations of ANA and anti-dsDNA antibody titers. Recognition of this peculiar clinical entity is important to avoid a misdiagnosis of idiopathic lupus nephritis, discontinue hydralazine promptly and institute appropriate treatment of a severe, organ-threatening vasculitis.

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