# A rare case of a drug-induced vasculitis by hydralazine

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## Learning and objective:

•Recognize clinical presentation of drug-induced vasculitis (DIV) in order to provide the best treatment

• Understand the serology result of DIV

•Recognize the unusual serology presentation on DIV

## Introduction:

Hydralazine-induced vasculitis is a rare disease that can manifest with renal and pulmonary involvement. Drug-induced, anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (DIV) is a very aggressive and severe vasculitis that can lead to renal failure. Seven cases of hydralazine-induced vasculitis in the literature all had renal involvement (pauci-immune glomerulonephritis) (1) Fig.1. Case series have shown that twelve patients who were diagnosed with DIV by hydralazine, nine had C3 abnormalities, five for C4, twelve with ANA, eleven anti-DNA, eleven with anti-histone, and eleven with myeloperoxidase (MPO) (2).

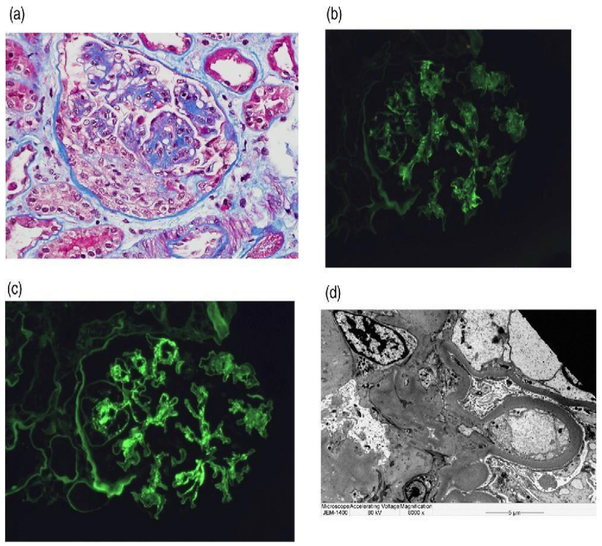



Fig.1. Light microscopy: (a) glomeruli with cellular crescents; (b) IF: glomeruli with trace IgM mensangial deposits; (c) glomeruli with trace IgG mensangial deposits; (d) EM: GBM thickening FPE effacement, and absent deposits on capillary and mensagium (3).

## Clinical case:

34-year-old Caucasian male with a PMH of hypertension (HTN), chronic kidney disease (CKD) stage 3 and mineral-bone disorder (MBD), who was admitted to the hospital in 2017 for dyspnea with a pleural effusion and low-grade fever (37.2 C). On his basic work up, patient presented with an elevated creatinine level.

ROS: no chills and dysuria

Laboratory :

• Creatinine: 3.5 mg/dL, (baseline 2.15 mg/dL).

• Urinalysis: 5 RBC and 1+ proteinuria, and protein creatinine ratio of 0.7

• Coagulation profile: PTT 50.6 (22.5-35.1s), PT 15.1 (11.7-14.5s), INR 1.17 (0.87-1.17)

• Thoracentesis: shows exudative pleural effusion with a negative culture.

Due to the presence of microscopic hematuria and proteinuria (6 g/day) in the setting of acute kidney injury at a relatively young age, subsequent serology was sent for analysis.

Serology on **Fig. 2.(b)**

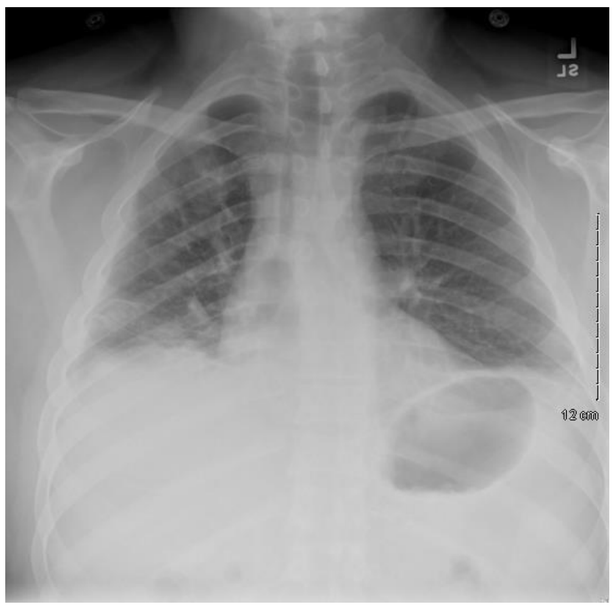
The biopsy was postponed because of an active PTT of 56 with the subsequent mixing test showing prolongation due to serum antiphospholipid antibodies.

Treatment: Discontinued hydralazine and Losartan. Began empiric daily prednisone 60mg and cyclophosphamide 150mg.

Biopsy 1 month after hospitalization: light/electron microscopy and immunofluorescence revealing 1-2+ granular global mesangial positivity for IgM. Glomeruli were negative for IgA, IgG, C1q, albumin, fibrinogen, and kappa. The findings were consistent with diagnosis of **Focal crescentic glomerulonephritis, pauci-immune type (ANCA-associated/clinical).**

After 3 months of prednisone and cyclophosphamide renal function had improved with serum creatinine levels trending back towards 2 mg/dL. Immunosuppressant therapy was subsequently tapered down over the next 3 months. Therapy was discontinued at 6 months with full return of renal function.

(a)




(b)

| Antibodies | Value | Reference |
|---|---|---|
| Myeloperoxidase antibody (Ab) | 126 AU/mL | 0 to 19 AU/mL |
| Proteinase-3 | 42 AU/ Ml | 0 to 19 AU/Ml |
| Anti-Neutrophil Cytoplasmic Ab, IgG | 1:320 | Reference range: <1:20 |
| Antinuclear antibodies | negative | |
| Anti–glomerular basement membrane Ab | <0.2 U | <1.0 U |
| Histone Ab | 2.5 U moderate positive | <5 U |
| C3 complement | 135 mg/dL | 90-180 mg/dL |
| C4 complement | 27 mg/dL | 10-40 mg/dL |

Fig.2. (a) AP X-ray and pleural analysis: Bilateral pleural effusions, right greater than left. Bilateral lung base atelectasis.

## Discussion:

•Hydralazine-induced vasculitis usually presents as ANA positive, with hypocomplementemia. This patient presented with MPO and PR3 antibodies together plus absence of ANA and hypocomplementemia which is very unusual (4). We questioned whether the hydralazine was the only factor that triggered the ANCA vasculitis or was it another non-classical DIV presentation?

•The symptomatic presentation and the response of discontinuing the medication and treatment with immunosuppressive helped confirm the diagnosis.

•The patient had a bleeding risk factor due to the presence of antiphospholipid antibodies and that was very challenging because it delayed to obtain the biopsy. We started with empiric treatment because of progressive symptoms in the patient. Biopsy verified pauci-immune type (ANCA-associated) vasculitis.

## Conclusion:

•There is no definitive serology presentation of DIV. Clinical suspicions and urinalysis is the keystone.

•DIV may present with MPO plus Proteinase-3 antibodies.

•Potential treatment conundrums include discontinuation of hydralazine therapy alone, or discontinuation and treatment with immunosuppressive agents.

•In this case, suppression of hydralazine therapy plus immunosuppressive treatment improved the renal function.

•General internists should be aware of this side effect of hydralazine when managing patients with hypertension. The most effective treatment to stop the progression of renal vasculitis is stop the drug and start immune suppression therapy.

## Reference:

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