www.nephropathol.com DOI: 10.15171/jnp.2019.40 J Nephropathol. 2019;8(4):e40

Journal of Nephropathology

Renal thrombotic microangiopathy in an ANCA-associated vasculitis

Ana Teresa Domingos[1*], Sara Barreto[2], Eduarda Carias[1], Ana Cabrita[1], Helena Viana[3,4], Mário Góis[3,4]

[1]Department of Nephrology, Centro Hospitalar e Universitário do Algarve, Faro, Portugal
[2]Department of Nephrology, Hospital Garcia de Orta, Almada, Portugal
[3]Department of Nephrology, Hospital de Curry Cabral, Centro Hospitalar e Universitário de Lisboa Central, Portugal
[4]Laboratory of Renal Morphology, Hospital de Curry Cabral, Centro Hospitalar e Universitário de Lisboa Central, Portugal

ARTICLE INFO

Article type:
Case Report

Article history:
Received: 20 August 2019
Accepted: 3 October 2019
Published online: 19 October 2019

Keywords:
ANCA-associated vasculitis
Renal thrombotic microangiopathy
Kidney biopsy
Prognosis

ABSTRACT

Anti-neutrophil cytoplasmic antibody (ANCA) disease remains a diagnostic challenge due to the heterogeneity of possible clinical presentations. We present the case of a 63-year-old white male with a known history of ANCA-associated vasculitis (AAV) with anti-myeloperoxidase antibodies (MPO) – mainly with respiratory manifestations – treated with corticosteroids and cyclophosphamide, resulting in partial improvement. Six months later he was referred to the nephrology department for rapidly progressive renal failure and a kidney biopsy was performed, which showed several glomeruli globally sclerosed and others presenting fibrous crescents. Vascular involvement was also noted with several small arteries revealing endothelial swelling and entrapped erythrocytes within a fibrin thrombus. Immunofluorescence was negative. A high percentage of parenchymal fibrosis and no evidence of active extra-renal manifestations dictated no specific treatment. The patient is currently monitored in a low clearance nephrology consultation. Evidence of thrombotic microangiopathy (TMA) is an uncommon histological finding in kidney biopsies of patients with AAV, being associated with worst prognosis.

Case Report

Implication for health policy/practice/research/medical education:
Evidence of thrombotic microangiopathy is an uncommon histological finding in kidney biopsies of patients with ANCA-associated vasculitis, being associated with worst prognosis.

Please cite this paper as: Domingos AT, Barreto S, Carias E, Cabrita A, Viana E, Góis M. Renal thrombotic microangiopathy in an ANCA-associated vasculitis. J Nephropathol. 2019;8(4):e40. DOI: 10.15171/jnp.2019.40.

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA) disease remains a diagnostic challenge due to the heterogeneity of possible clinical presentations. Marked differences in signs, symptoms, degree of activity and disease severity may difficult a timely diagnosis and treatment. When renal involvement ensues, evidence of thrombotic microangiopathy (TMA) is an uncommon histological finding in kidney biopsies of patients with ANCA-associated vasculitis (AAV), being associated with worst prognosis (1,2).

2. Case Presentation

We present a case of a 63-year-old white male with a known history of ANCA-associated vasculitis (AAV) with anti-myeloperoxidase antibodies (MPO), initially diagnosed in the context of severe respiratory manifestations. He was treated with corticosteroids and cyclophosphamide, with partial respiratory improvement. However, several subsequent infectious complications occurred, as well as acute kidney injury with transient need for hemodialysis. One of these sessions was complicated by gallbladder perforation (from ischemia and consequent necrosis), with subsequent generalized peritonitis, having required cholecystectomy. After achieving control of the underlying pathologies and proper fluid management, renal function improved considerably, and dialytic therapy was no longer needed. A multifactorial etiology was assumed, with a probable component of acute tubular necrosis that recovered favorably. He was discharged with

*Corresponding author: Ana Teresa Domingos,
Email: atdomingos@chalgarve.min-saude.pt, ana_t_d@sapo.pt

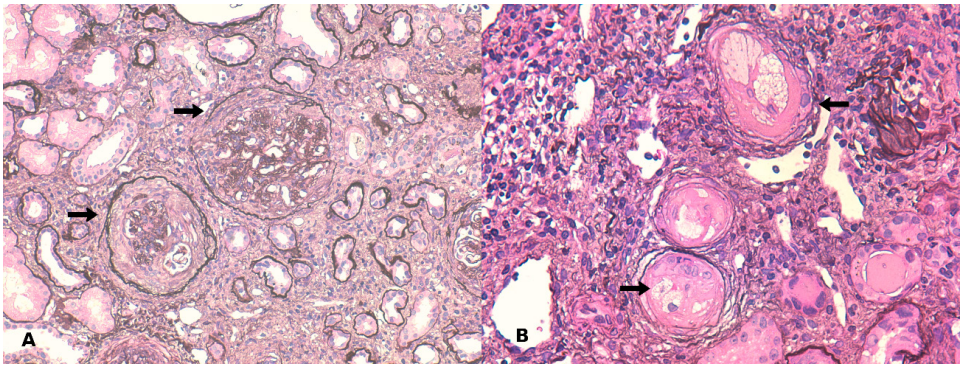

Figure 1. Panel A: PAS ×400. Panel B: Methenamine Silver Stain (×400).

multidisciplinary follow-up.

Six months later, he was once more referred to the nephrology department for rapid deterioration of renal function, generalized edema and hypertension. No additional manifestations were recognized, including unspecific systemic features. The etiological evaluation was remarkable for the presence of positive ANCA-MPO (>860 UA/mL, reference range 0-7 UA/mL), slight hematuria and proteinuria (urine protein to creatinine ratio of 11 000 mg/g). Given the presence of rapidly progressive renal failure, a kidney biopsy was performed to clarify diagnosis and probable prognosis. The sample obtained showed a total of 13 glomeruli, five of them being globally sclerosed and four presenting fibrous crescents (Figure 1, panel A). Vascular involvement was also noted, with several small arteries revealing endothelial swelling and entrapped erythrocytes within the fibrin thrombi (Figure 1, panel B). Immunofluorescence was negative. Considering the high percentage of parenchymal fibrosis and no current evidence of active extra-renal manifestations, no specific treatment was initiated. The patient is currently monitored in a low clearance nephrology consultation, with an estimated glomerular filtration rate of 11 mL/min/1.73 m^2 (CKD-EPI equation).

Discussion

There are few reports concerning histologic signs of TMA in patients with AAV (1-4). The association between TMA and AAV may lie primarily in the fact that vasculitis is an injury and infiltration of vascular endothelial cells, facilitating TMA phenomena (3). However, clinical association seems much rarer when compared with the frequency of histological signs of TMA (in a subclinical set) (1,2,4).

Some studies have linked these findings to a worse renal prognosis (1,2,4). The existence of TMA seems to correlate with more severe kidney injury, almost always requiring dialysis (2). In a recent Chinese research (1), TMA was independently associated with all-cause mortality in patients with AAV. In addition, they describe a higher than expected incidence of these concomitant findings – TMA and AAV.

In this particular case, clinical signs of TMA were absent; however, evidence of severe renal impairment/lesion was noticeable, both clinically and morphologically. Accordingly, functional prognosis was poor. Given the high percentage of parenchymal fibrosis and no evidence of active extra-renal manifestations by the time of biopsy, no specific treatment was initiated. Otherwise, several authors suggest that plasma exchange, treatment with corticosteroids (IV pulses followed by oral therapy), cyclophosphamide or rituximab may be indicated (3, 5-7).

Conclusion

Evidence of TMA is an uncommon histological finding in kidney biopsies of patients with AAV, being associated with worst prognosis. Clinicians must be alert to the existence of these unusual manifestations, especially considering its crucial prognosis impact.

Authors' contribution

Equal authorship of ATD and SB. MG and HV helped in the selection of the most representative images. They also provided surpassing assistance concerning morphopathological matters and tireless constructive feedback. A special thanks to AC and EC for their support and clinical guidance. All authors approved the final manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient, gave his consent to be publish as a case report.

Funding/Support
None.

References
1. Chen SF, Wang H, Huang YM, Li ZY, Wang SX, Yu F, et al. Clinic pathologic characteristics and outcomes of renal thrombotic microangiopathy in anti-neutrophil cytoplasmic autoantibody-associated Glomerulonephritis. Clin J Am Soc Nephrol. 2015;10:750-8. doi: 10.2215/CJN.07910814.
2. Dellal A, Bige N, Hilliquin P, Boffa JJ, Rondeau E, Hatron PY, et al. Thrombotic microangiopathy associated with anti-neutrophil cytoplasmic antibody-associated vasculitis: a French nationwide retrospective case control study and literature review. Rheumatology (Oxford). 2019;58:1873-5. doi: 10.1093/rheumatology/kez167.
3. Zhang R, Zhou JF, Liang MJ, Huang YJ, Li AH, Su N, et al. Thrombotic microangiopathy with ANCA-associated vasculitis in a child: a case report and review of literature. Int J Clin Exp Pathol. 2017;10:2255-8.
4. Manenti L, Vaglio A, Gnappi E, Maggiore U, Allegri L, Allinovi M, et al.Association of Serum C3 concentration and histologic signs of thrombotic microangiopathy with outcomes among patients with ANCA-associated renal vasculitis. Clin J Am Soc Nephrol. 2015;10:2143-51. doi: 10.2215/CJN.00120115.
5. Irifuku T, Naito T, Ogawa T, Masaki T. Successful treatment with plasma exchange for ANCA-negative pauci-immune crescentic glomerulonephritis with D-negative hemolytic uremic syndrome. Clin Nephrol. 2014;82:268-72. doi: 10.5414/CN107847.
6. Agrawal V, Vaidya CK, Ye J, Freeman J, McKiernan C, Blier PR, et al. Concomitant thrombotic thrombocytopenic purpura and ANCA-associated vasculitis in an adolescent. Pediatr Nephrol. 2011;26:1317-20. doi: 10.1007/s00467-011-1862-5.
7. Asamiya Y, Moriyama T, Takano M, Iwasaki C, Kimura K, Ando Y, et al. Successful treatment with rituximab in a patient with TTP secondary to severe ANCA-associated vasculitis. Intern Med. 2010;49:1587-91. doi: 10.2169/internalmedicine.49.3135.