Journal of Clinical Nephrology & Kidney Diseases

Case Report
Published: 19 Jul, 2018

Atheroembolic Disease and Antineutrophil Cytoplasmic Autoantibodies

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Abstract

Atheroembolic disease is a systemic disorder associated with diffuse atherosclerosis. The most common triggers are endovascular manipulation like angiography and therapeutic procedures such as cardiovascular surgery or fibrinolytic therapies; also, it may occur spontaneously. Common clinical manifestations include skin lesions and the systemic symptom of the disease can mimic systemic vasculitis. A few anecdotal cases have been reported in which atheroembolic disease was accompanied by a positive perinuclear antineutrophil cytoplasmatic antibody in the absence of clinical or histological evidence of vasculitis.

We report a case of atheroembolic disease diagnosed by renal biopsy in the presence of positive perinuclear antineutrophil cytoplasmatic antibody. The patient was treated whit steroid for 3 months without recovery of renal function. We also review the cases reported in the literature.

Introduction

Atheroembolic Disease (AD) is a systemic disorder associated with diffuse atherosclerosis. The most common triggers are endovascular manipulation like angiography and therapeutic procedures such as cardiovascular surgery or fibrinolytic therapies [1]. Although it may occur spontaneously in more than 20% of cases [2,3]. Common clinical manifestations include skin lesions (livedo, cyanosis or peripheral ischemic lesions) that are present in 50% of cases [4]. The systemic nature of the disease can mimic systemic vasculitis [5-7]. Prognosis is generally poor, with a mortality rate exceeding 70% [1].

No specific management is available for AD, but some authors have recommended corticosteroid treatment [8,9].

A few anecdotal cases have been reported in which AD was accompanied by a positive perinuclear antineutrophil cytoplasmic antibody (p-ANCA) in the absence of clinical or histological evidence of vasculitis, making the diagnosis more challenging [6,10-13].

We report a case of AD diagnosed by renal biopsy in the presence of p-ANCA without accompanying systemic symptoms. We also review the cases previously reported in the literature.

Case Presentation

A 66-year-old white male was referred for a nephrology evaluation due to rapidly progressive impairment of renal function. He had antecedents of longstanding controlled hypertension, dyslipidaemia and type II Diabetes Mellitus with microalbuminuria and mild chronic renal failure (creatinine 1.5 mg/dL; creatinine clearance: 50 mL/min/1.73 m^2). Four months before admission he was evaluated for respiratory symptoms with a pulmonary infiltrate that evolved successfully with antibiotic treatment. A creatinine value of 327 mmol/L (3.7 mg/dL) was detected without further evaluation. In a new test, creatinine was 442 mmol/L (5 mg/dL) and the patient was referred for further evaluation.

On physical examination, the patient appeared in good clinical condition, without complaints and no accompanying symptoms. There was no exposure to nephrotoxic drugs, invasive diagnostic tests or anticoagulant therapy. Proteinuria was 3.69 g/24 hr with microscopic haematuria.

The immunological examination including complement factors, antinuclear antibodies, and serology for Hepatitis B, C and HIV virus was negative. Indirect immunofluorescence was positive for P-ANCA. Enzyme-linked immunosorbent assay confirmed markedly positive anti MPO antibodies with a titre of 116 U/mL. Due to the rapid worsening of renal function and the positive p-ANCA,

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Received Date: *25 Jun 2018*
Accepted Date: *17 Jul 2018*
Published Date: *19 Jul 2018*

Citation:
Betancourt L, Ponz E, Almirall J. Atheroembolic Disease and Antineutrophil Cytoplasmic Autoantibodies. J Clin Nephrol Kidney Dis. 2018; 3(2): 1017.

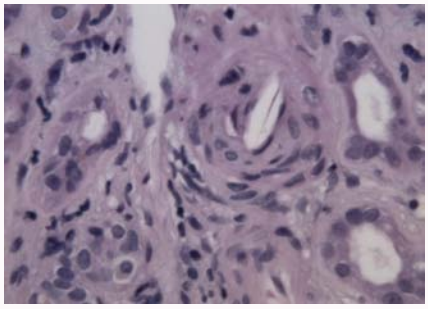

Figure 1: Renal biopsy: The cholesterol crystal.

a Renal Biopsy (RB) was performed. Light microscopy showed 11 glomeruli, 4 of them with global or segmental sclerosis. There was no increase in endo capillary or extracapillary cellularity. Interstitial areas showed moderate fibrosis and mild focal inflammatory infiltrate. Hyperplastic changes were noted in extr aglomerular vessels, suggestive of hypertensive nephroangiosclerosis, highlighting the existence of cholesterol crystals arranged in small vessels (Figure 1). The immunofluorescence examination was negative. Diagnosis of AD was made on the basis of these findings.

Due to the presence of p-ANCA associated with AD, we decided to start treatment with corticosteroids at a dose of 1 mg/kg/day. Replacement therapy with peritoneal dialysis was started simultaneously. Steroids were maintained for 3 months without recovery of renal function. The p-ANCA titre decreased progressively but did not disappear.

Discussion

We report a case of rapidly progressive worsening of renal function secondary to AD in a patient with positive p-ANCA test. This association has exceptionally been reported in the literature [5,6,11-13].

Our patient did not have any known trigger for the disease, as has been described in up to 20% of cases of AD [1]. Two of the seven previously reported cases of AD and positive p-ANCA also had a spontaneous presentation [6,10].

The presence of cholesterol embolism can produce multiple systemic manifestations and inflammatory changes that may simulate a systemic disease [5-7]. In our patient, no systemic manifestations were observed; the only guide sign was the worsening renal function with nephrotic range proteinuria and microhaematuria. Given the positive p-ANCA test and the rapidly progressive renal failure, it was decided to perform RB, which demonstrated AD without any histological evidence of a renal vasculitis.

Due to the progressive worsening of renal function, a trial with corticosteroid treatment was attempted. Steroids have been used in some previous cases of AD [8,9], although the results are inconclusive. The few previous cases of AD with positive p-ANCA were also treated with steroids, although cyclophosphamide was added in two of them [11,12]. In our patient, although corticosteroids decreased the antibody titre, there was no improvement in renal function. After 20 months the patient is still on dialysis.

It is interesting to mention that some series of renal biopsies have found cholesterol emboli coexistent with nephrosclerosis. In the series of Preston et al, from a total of 334 renal biopsies, 14 patients were found to have AD. In 35% of these cases, AD was not the principal diagnosis [14]. Our patient presented histological changes compatible with nephrosclerosis, although the main diagnosis and attributed cause for rapidly worsening of renal function was AD. Both pathologies can coexist more frequently than reported so far as AD is an under diagnosed disease. In fact, it should be pointed out that AD is not so exceptional in autopsy studies, as it has been described in 3.5% of postmortem series, often unrelated to the cause of death [15].

In relation to p-ANCA, in addition to small vessel vasculitis and pauci-immune necrotizing glomerulonephritis, these autoantibodies can also be detected in a variety of other pathologic conditions such as inflammatory bowel disease, rheumatic diseases, autoimmune liver diseases, tumours and infections. In the case we are discussing, the positive p-ANCA in the context of AD further complicates its differentiation from a vasculitic syndrome. In this case, the renal biopsy has been mandatory for proper diagnosis. The pathogenic role of ANCA in such cases is not clear. Although speculative, we believe that the presence of p-ANCA may be caused by the inflammatory status induced by cholesterol crystals inciting an inflammatory foreign body reaction. This association may also be more frequent than reported in the literature due to the under diagnosis of AD disease.

References

1. Scolari F, Ravani P. Atheroembolic renal disease. Lancet. 2010;375(9726):1650-60.
2. Gutiérrez Solís E, Morales E, Rodríguez Jornet A, Andreu FJ, Rivera F, Vozmediano C, et al. Enfermedad renal ateroembólica: un análisis de los factores clínicos y terapéuticos que influyen en su evolución. Nefrologia. 2010;30(3):317-23.
3. Scolari F, Ravani P, Gaggi R, Santostefano M, Rollino C, Stabellini N, et al. The challenge of diagnosing atheroembolic renal disease: clinical features and prognostic factors. Circulation. 2007;116(3):298-304.
4. Thadhani R, Camargo C, Xavier R, Fang L, Bazari H. Atheroembolic renal failure after invasive procedures: Natural history based on 52 histologically proven cases. Medicine (Baltimore). 1995;74:350-58.
5. Sigimoto T, Morita Y, Yokomaku Y, Isshiki K, Kanasaki K, Eguchi Y. Systemic cholesterol embolization syndrome associated with myeloperoxidase-anti-neutrophil cytoplasmic antibody. Intern Med. 2006;45(8):557-61.
6. Peat Ds, Mathieson PW. Cholesterol emboli may mimic systemic vasculitis. BMJ. 1996;313(7056):546-7.
7. Sijpkens Y, Westendorp R, Van Kemenade F, Van Duinen S, Breedveld F. Vasculitis due to Cholesterol embolism. Am J Med. 1997;102(3):302-3.
8. Hasegawa M, Kawashima S, Shikano M, Hasegawa H, Tomita M, Murakami K, et al. The evaluation of corticosteroid therapy in conjunction with plasma exchange in the treatment of renal cholesterol embolic disease. A report of 5 cases. Am J Nephology. 2000;20(4):263-7.
9. Nakahama H, Sakaquchi K. Small dose oral corticosteroid treatment rapidly improved renal function in a patient with an acute aggravation of chronic renal failure due to cholesterol embolism. Nephrol Dial transplant. 2001;16(4):872-3.
10. Kaplan-Pavlovcic S, Vizjak A, Vene N, Ferluga D. Antineutrophil cytoplasmic autoantibodies in atheroembolic disease. Nephrol Dial Transplant. 1998;13(4):985-7.
11. Maesshima E, Yamada Y, Mune M, Yukama S. A case of cholesterol embolism with ANCA treated with corticosteriod and cyclophosphamide. Ann Rheum Dis. 2001;60:726-7.

12. Aviles B, Ubeda I, Blanco J, Barrientos A. Pauci-Immune Extracapillary Glomerulonephritis and Atheromatous Embolization. Am J Kidney Dis. 2002;40(4):847-51.

13. Delen S, Boonen A, Landewé R, Kroon A, Linden SJ, Tervaert J. An unusual case of ANCA positive disease. Ann Rheum Dis. 2003;62:770-81.

14. Preston RA, Stemmer CL, Materson BJ, Perez-Stable E, Pardo V. Renal biopsy in patients 65 years of age or older. An analysis of the results of 334 biopsies. J Am Geriatr Soc. 1990;38(6):669-74.

15. Fries C, Roos M, Gaspert A, Vogt P, Salomon F, Wüthrich RP, et al. Atheroembolic disease--a frequently missed diagnosis: results of a 12-year matched-pair autopsy study. Medicine (Baltimore). 2010;89(2):126-32.