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Case Report

Acute Tubulo-interstitial Nephritis with Positive Anti-Neutrophil Cytoplasmic Antibodies

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Abstract

Introduction: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis involving the kidney usually comprises pauci-immune, necrotizing glomerulonephritis with crescents. Mononuclear tubulo-interstitial infiltrates are common in ANCA associated vasculitis, but these have usually been described in conjunction with glomerulitis. Acute tubulo-interstitial nephritis (ATIN) is a common cause of acute kidney injury that is most frequently induced by drugs or infections. Idiopathic ATIN has rarely been reported in association with the presence of a positive ANCA. These two entities seem to share a common immunological basis.

Case report: We report a 75 years-old male patient who presented with acute kidney injury and his serum tested positive for p-ANCA by indirect immunofluoresence with a titer of 1/320. Testing by ELISA demonstrated anti-myeloperoxidase (MPO) specificity with a level of 28.8 IU/mL. His kidney biopsy showed features of ATIN with no glomerular involvement. Treatment with corticosteroids led to improvement of his kidney function and serology for ANCA became negative. In this case report ATIN seems to be associated with ANCA positivity, in the absence of other obvious causes for the acute tubulo-interstitial insult.

Conclusion: ATIN can be associated with positive ANCA without features of renal-limited vasculitis or systemic vasculitis. This can occur in the absence of drug exposure. The outcome in our case was favorable with corticosteroid therapy.

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Introduction

Tubulo-interstitial nephritis (TIN) is a kidney disease restricted to the tubules and interstitium. It can cause acute or chronic renal insufficiency. Acute tubulo-interstitial nephritis (ATIN) has a variety of causes, including drugs, systemic infections and autoimmune diseases. In systemic disorders, glomerular alterations are consistent findings [1].

Renal involvement in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis is characterized by focal segmental, crescentic and/or necrotizing glomerulonephritis. Rare cases of ATIN associated with the presence of ANCA have been reported. These cases were mostly drug-related [2-6] or occurred as part of confirmed or supposed vasculitis [7-12]. To date, only few cases of ATIN had been reported to be associated with ANCA positivity, without evidence of renal or systemic vasculitis, drugs or other presumed causes of ATIN [13, 17]. The pathogenesis of this association is not clearly defined.

Case report

We hereby describe a 75 years-old white male patient, with no significant past medical history, who was admitted with acute renal failure. He reported three months history of asthenia, anorexia and weight loss. There was no significant drug history of note. On admission his weight was 41 kg (body mass index at 16 kg/m²), his blood pressure was 120/60 mmHg, and he was afebrile. Further systemic clinical examination was unremarkable. His urinalysis showed hematuria and proteinuria, but was negative for nitrite and leukocytes,

and sterile at bacteriological examination. His 24 hour urine collection showed 1.4 gm of protein.

Further laboratory tests showed an elevated serum creatinine of 6.5 mg/dL, blood urea of 126 mg/dL and low serum potassium of 3.1 mmol/L. His C-reactive protein was elevated at 51 mg/L and fibrinogen level was 6 g/L with a moderate polyclonal hypergammaglobulinemia at 17 g/L. His blood count showed normochromic normocytic anemia with hemoglobin level of 7.2 g/dL. Sternal marrow aspiration revealed slight myelodysplasia consistent with the patient's age. His liver enzymes were normal. Serum complement levels were also normal. Anti DNA, anti-nuclear antibodies (ANA), anti-SSA and anti-SSB were negative. His serum tested positive for p-ANCA by indirect immunofluoresence with a titer of 1/320. Testing by ELISA demonstrated anti-myeloperoxidase (MPO) specificity with a level of 28.8 IU/mL.

Renal biopsy was done and showed separation of the interstitium by fibro-edema, together with a diffuse and intense inflammatory infiltrate of lymphocytes, plasma cells and neutrophils. The tubules showed diffuse epithelial necrosis, atrophy, with significant tubulitis and lesions rich in neutrophils. The glomeruli showed slight mesangial expansion with no cellular proliferation or any other recognized abnormality. Immunofluoresence techniques revealed no significant deposits.

Corticosteroid therapy was started in the form of oral prednisolone 40 mg per day, with gradual tapering. Improvement in kidney function was evident, with serum creatinine dropping down to 1.5 mg/dL and ANCA seroconversion from positive to negative after three months of therapy.

Discussion

ANCA associated vasculitis involving the kidney usually comprises a pauci-immune, necrotizing glomerulonephritis with crescents. Mononuclear tubulo-interstitial infiltrates are common in ANCA associated vasculitis, but these have usually been described in conjunction with glomerulitis [18]. Acute TIN is a common cause of acute kidney injury. Drugs and infections are the most frequent etiological agents. Idiopathic ATIN is a rare entity and has rarely been reported in association with the presence of a positive ANCA. These seem to share an immunological basis.

In our patient, the presence of p-ANCA at the time of the diagnosis of ATIN was surprising. This antibody is a hallmark of microscopic polyarteritis, granulomatosis with polyangiitis and idiopathic necrotizing glomerulonephritis. TIN can be a predominant finding in these diseases alongside the glomerular involvement, although the latter may be only focal and segmental. Our case originality lies in the type of renal injury observed, manifesting as interstitial disease without evident glomerular injury and without an identifiable cause. In our case, renal biopsy findings and clinical follow-up made the diagnosis of classical vasculitis unlikely. Indeed, no specific histological lesions and no infection or drug intake had been found. ANCA in this case represent the most likely cause of tubulo-interstitial damage. However, we cannot reject the hypothesis of an unusual and more benign presentation of vasculitis.

As pure ATIN is a relatively rare pathologic finding among ANCA-related acute kidney injury we can only speculate on the possible pathogenetic mechanisms. It has been suggested that following an upper respiratory tract infection an increase in cytokines such as interleukin-1 might lead to the expression of MPO and proteinase 3 on the surface of leukocytes. Endothelial tubular cell injury may be induced by the adhesion of these leukocytes (ANCA-cytokine sequence theory) [19]. These processes might lead to ATIN.

Conclusion

We reported a case of ATIN associated with positive ANCA which had neither features of renal-limited vasculitis nor systemic vasculitis and in the absence of drug exposure. The outcome in our case was favorable with corticosteroid therapy.

References

1. Greenfield JP, Kleinknecht D, Droz D. Acute interstitial nephritis. In: Schreier RW, Gottschalk CW, editors. Diseases of the Kidney. 4th ed. Boston (MA): Little and Brown; 1988. Volum 2; p. 1461-1487.

2. Kitahara T, Hiromura K, Sugawara M, Hirato J, Sato S, Ueki K, Maezawa A, Yano S, Nojima Y, Naruse T. A case of cimetidine-induced acute tubulointerstitial nephritis associated with antineutrophil cytoplasmic antibody. Am J Kidney Dis. 1999 Feb;33(2):E7.

3. Feriozzi S, Muda AO, Gomes V, Montanaro M, Faraggiana T, Ancarani E. Cephotaxime-associated allergic interstitial nephritis and MPO-ANCA positive vasculitis. Ren Fail. 2000 Mar;22(2):245-51.

4. Singer S, Parry RG, Deodhar HA, Barnes JN. Acute interstitial nephritis, omeprazole and antineutrophil cytoplasmic antibodies. Clin Nephrol. 1994 Oct;42(4):280.

5. Sakai N, Wada T, Shimizu M, Segawa C, Furuichi K, Kobayashi Ki, Yokoyama H. Tubulointerstitial nephritis

with anti-neutrophil cytoplasmic antibody following indomethacin treatment. Nephrol Dial Transplant. 1999 Nov;14(11):2774.

6. Rocha JL, Fernández-Alonso J. Acute tubulointerstitial nephritis associated with the selective COX-2 enzyme inhibitor, rofecoxib. Lancet. 2001 Jun 16;357(9272):1946-7.

7. Ernam D, Atikcan S, Yilmaz A, Atalay F, Demirağ F, Memiş L. An unusual renal presentation of Wegener's granulomatosis. Tuberk Toraks. 2003;51(2):193-6.

8. Banerjee A, McKane W, Thiru S, Farrington K. Wegener's granulomatosis presenting as acute suppurative interstitial nephritis. J Clin Pathol. 2001 Oct;54(10):787-9.

9. Lee L, Saunders J, Zhou XJ, Maalouf NM. Acute interstitial nephritis complicating a new diagnosis of Wegener's granulomatosis. Hawaii Med J. 2008 Jan;67(1):12-4.

10. Wen YK, Chen ML. Microscopic polyangiitis atypically presenting with tubulointerstitial nephritis. Clin Nephrol. 2006 May;65(5):356-60.

11. Son D, Kanda H, Yamaguchi A, Kawabata K, Kawakami T, Kubo K, Higashihara M, Shimizu J, Uozaki H, Kuramochi S, Misaki Y, Takeuchi F, Yamamoto K. Myeloperoxidase antineutrophil cytoplasmic antibody-associated vasculitis with diffuse tubulointerstitial nephritis. J Nephrol. 2009 May-Jun;22(3):417-20.

12. Wańkowicz Z, Obroniecka I, Morzycka-Michalik M. [Nephropathy after use of Chinese herbs: rapidly progressive interstitial renal fibrosis or renal vasculitis?]. Pol Arch Med Wewn. 1996 Nov;96(5):474-8.

13. Arimura Y. [Tubulointerstitial nephritis associated with ANCA-associated vasculitis]. Nihon Jinzo Gakkai Shi. 2011;53(4):604-9.

14. Nakamura N, Yaegaki M, Sugawara T, Shirato K, Kumasaka R, Nakamura M, Shimada M, Fujita T, Murakami R, Osawa H, Yamabe H, Okumura K. Acute tubulointerstitial nephritis with antineutrophil cytoplasmic antibody. Hong Kong J Nephrol. 2006; 8(1):33–5.

15. Lockwood CM. Antineutrophil cytoplasmic autoantibodies: The nephrologist's perspective. Am J Kidney Dis. 1991 Aug;18(2):171-4.

16. Schönermarck U, Schirren CA, Mistry-Burchardi N, Weiss M, Eichhorn P, Samtleben W. Interstitial nephritis and high titers of PR3-ANCA: an unusual manifestation of ANCA-associated disease. Clin Nephrol. 2005 Nov;64(5):383-6.

17. Nakabayashi K, Sumiishi A, Sano K, Fujioka Y, Yamada A, Karube M, Koji H, Arimura Y, Nagasawa T. Tubulointerstitial nephritis without glomerular lesions in three patients with myeloperoxidase-ANCA-associated vasculitis. Clin Exp Nephrol. 2009 Dec;13(6):605-13.

18. Jennete JC. Renal involvement in systemic vasculitis. In: Jenette JC, Olson JL, Schwartz MM, Silva FG, editors. Heptinstall's pathology of the kidney. Philadelphia: Lippincott-Raven; 1998. p. 1059–95.

19. Falk RJ, Terrell RS, Charles LA, Jennette JC. Anti-neutrophil cytoplasmic autoantibodies induce neutrophils to degranulate and produce oxygen radicals in vitro. Proc Natl Acad Sci U S A. 1990 Jun;87(11):4115-9.