A Case Report Of Acute Tubulo-Interstitial Nephritis (ATIN): Offending Agent C-ANCA

Dr. Neel K. Jalawala*, Dr. Pankaj J. Akholkar*, Dr. Parth Jani**, Dr. Devarshi Shukla***

*3rd Year Resident Doctor, **Senior Resident, ***Associate Professor, Department Of General Medicine, Government Medical College, Bhavnagar 34001

Abstract: Antineutrophilic cytoplasmic antibody (ANCA) has been reported to be associated with systemic vasculitis. However, there are few reports regarding ATIN and ANCA without drug involvement. In this article, we present a case of ATIN with a high titre of ANCA, without systemic disease or any responsible drug. Here we present a case of A 41 year female, p/w breathlessness at rest, decreased urine output, fever and anorexia for 10 days. She had no other significant medical illness. Laboratory investigations were done where creatinine, urea, potassium levels and ESR were significantly raised and urine analysis showed proteinuria. RA Factor, ANA titre and C- ANCA were positive. Kidneys on USG s/o B/L increase in echogenicity with normal size and preserved CMD. Percutaneous Renal biopsy performed showed tubular atrophy with few foci of lymphocytic tubulitis and focal intratubular neutrophilic casts. Interstitium shows patchy moderate mixed inflammatory infiltrates. Emergency HD was done on admission followed by pulse therapy of Methyl prednisone after which her renal function improved and patient got better and was subsequently discharged on oral prednisone. ATIN is a relatively rare pathologic finding among ANCA-related renal injury. ATIN can be associated with positive ANCA without features of renal limited vasculitis or systemic vasculitis and can also occur in absence of drug exposure. [Jalawala N Natl J Integr Res Med, 2023; 14(2):40-42, Published on Dated: 15/03/2023]

Key Words: Acute Tubulointerstitial Nephritis, C- ANCA, Renal Biopsy, Vasculitis

Author for correspondence: Dr. Pankaj J. Akholkar, Associate Professor, Department of General Medicine, Government Medical College, Bhavnagar 364001, E-Mail: drpankaj_md@yahoo.com Mobile: 9825312175

Introduction: Antineutrophilic cytoplasmic antibody (ANCA) has been reported to be associated with systemic vasculitis, such as microscopic polyangiitis, Wegener's granulomatosis, Chung-Strauss syndrome and crescentic necrotizing glomerulonephritis.[1]

Two major ANCA antigens have been identified: proteinase 3 (PR3), which produces a cytoplasmic staining pattern termed C-ANCA, and myeloperoxidase (MPO), which produces a perinuclear pattern termed P-ANCA on ethanol-fixed neutrophils by indirect

Immune fluorescence.[2] There have been several reports regarding ATIN and ANCA; most were associated with drugs, e.g. cimetidine, cefotaxime, omeprazole, indomethacin and rofecoxib.[3]

However, there are few reports regarding ATIN and ANCA without drug involvement. In this article, we present a case of ATIN with a high titer of ANCA, without systemic disease or any responsible drug.

Case Study: A 41 year female, p/w breathlessness at rest, decreased urine output, fever and anorexia for 10 days. Patient had history of similar episodes before 1 month without any other significant medical illness.

Vitals: Temp: Normal, Pulse: 110 bpm, Blood Pressure- 180/120 mmHg, RS - BAE +nt with B/L fine crepitation in middle and lower zone; while Rest of the system WNL.

Laboratory Investigations: Hb: 7.4 g/dl, haematocrit: 25%, TLC: 10680/cumm with Neutrophils 95%, Lymphocytes 3% and Eosinophils 2%, platelets count: 2.1 lac/cumm.

Creatinine: 3.7 mg/dl, Urea: 154 mg/dl, Na+: 133 mEq/L, K+: 6.8 mEq/L, Total Protien: 5.7 g/dl and albumin: 2.6 g/dl, CRP: 10 mg/dl, ESR: 138mm/hr. Urine Analysis: protienuria+2, WBC casts, RBC3-5/hpf.

RA Factor: Positive

ANA Titre: Positive with titre of 1:80 with homogenous, speckled and C- ANCA positive, Kidneys on USG s/o B/L increase in echogenicity with normal size and preserved CMD. Doppler

study showed no significant abnormalities among medium or small vessels.

Percutaneous Renal biopsy performed showed tubular atrophy with thyroidization some with simplified lining and few foci of lymphocytic tubulitis and focal inratubular neutrophilic casts.

Interstitium shows patchy moderate mixed inflammatory infiltrates rich in lymphocytes with foci of fibrosis, periglomerular fibrosis and patchy mild edema. A focus of epitheloid histiocytic collection seen around glomerulus. Vessels having myointimal hyperplasia.

Emergency HD was done on admission followed by pulse therapy of Methyl prednisone as 1 mg/kg/day for 5 days. Her renal function improved & CRP decreased gradually. Patient got better and was discharged with oral prednisone.

Discussion: In this case, there was neither systemic vasculitis nor drug that might have affected the present episode of ATIN. However, there are several reports regarding ATIN with ANCA, most of them associated with drugs; while there are few reports about ATIN with ANCA without any responsible drug; pure ATIN is a relatively rare pathologic finding among ANCA-related renal injury, our case is very interesting to speculate on the mechanism of ATIN[4].

The exact pathogenesis are not clear. It has been suggested that an increase in cytokines, such as interleukin-1, after upper respiratory tract infection might lead to the expression of MPO and PR3 on the surface of leukocytes, and endothelial tubular cell injury may be induced by the adhesion of these leukocytes (ANCA-cytokine sequence theory)[5].

Further, some genetic expression of mRNAs for MCP-1, MCP-3, and TCA3, results in multiple CC chemokines liberation which plays a role in the recruitment of leukocytes causing infiltration in interstitium and in glomeruli[6].

These processes might cause ATIN. Unexplained kidney injury with or without oliguria and exposure to a potentially offending agent usually points to the diagnosis.

Peripheral blood eosinophilia adds supporting evidence but is present in only a minority of patients. Urinalysis reveals pyuria with white blood cell casts and haematuria. Urinary eosinophils are neither sensitive nor specific for AIN; therefore, testing is not recommended.

Kidney biopsy is generally not required for diagnosis but reveals extensive interstitial and tubular infiltration of leukocytes, including eosinophils[7].

Depending on the duration of exposure and degree of tubular atrophy and interstitial fibrosis that has occurred, the kidney damage may not be completely reversible.

Steroid pulse therapy may accelerate kidney recovery but does not appear to impact long-term kidney survival.

It is best reserved for those cases with severe kidney injury in which dialysis is imminent or if kidney functions continues to deteriorate despite stopping the offending drug.

The rationale for using plasma exchange rests heavily on the assumptions that ANCAs are pathogenetic and can be efficiently removed by plasma exchange where pulse steroid therapy fails to improve renal function.

Plasma exchange could also exert a beneficial effect by eliminating mediators of inflammation and tissue injury[8].

Thus, awareness, early detection and treating patients at risk may prevent them from developing end-stage renal disease (ESRD).

Conclusion: A case of young female without any significant past medical illness or drug history presented with ATIN with ANCA positive status without systemic manifestation that showed significant response to steroid pulse therapy which is a preferred treatment in such cases.

Early diagnosis and early intervention in this case resulted in improvement in the renal function and prevention of further progress of renal injury. It is interesting to speculate on the mechanism of ATIN.

References:

1. Fienberg R, Mark EJ, Goodman M, McCluskey RT, Niles JL. Correlation of antineutrophil cytoplasmic antibodies with the extrarenal histopathology of Wegener's (pathergic)

granulomatosis and related forms of vasculitis. Human pathology. 1993 Feb 1; 24(2):160-8.
2. Radice A, Sinico RA. Antineutrophil cytoplasmic antibodies (ANCA). Autoimmunity. 2005 Feb 1; 38(1):93-103.
3. Raghavan R, Eknoyan G. Acute interstitial nephritis–a reappraisal and update. Clinical nephrology. 2014 Sep; 82(3):149.
4. Nakamura N, Yaegaki M, Sugawara T, Shirato KI, Kumasaka R, Nakamura M, Shimada M, Fujita T, Murakami R, Osawa H, Yamabe H. Acute tubulointerstitial nephritis with antineutrophil cytoplasmic antibody. Hong Kong Journal of Nephrology. 2006 Apr 1; 8(1):33-5.
5. Gross WL, Schmitt WH, Csernok E. ANCA and associated diseases: immunodiagnostic and pathogenetic aspects. Clinical & Experimental Immunology. 1993 Jan; 91(1):1-2.
6. Ou ZL, Natori Y, Natori Y. Gene expression of CC chemokines in experimental acute tubulointerstitial nephritis. Journal of Laboratory and Clinical Medicine. 1999 Jan 1; 133(1):41-7.
7. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. Harrison's principles of internal medicine, 21e. New York, NY, USA:: Mcgraw-hill; 2015. pg. no: 2357
8. De Vriese AS, Fervenza FC. PEXIVAS: the end of plasmapheresis for ANCA-associated vasculitis?. Clinical Journal of the American Society of Nephrology. 2021 Feb 8; 16(2):3079.

Conflict of interest: None
Funding: None
Cite this Article as: Jalawala N, Akholkar P, Jani P, Shukla D. A Case Report Of Acute Tubulo-Interstitial Nephritis (ATIN): Offending Agent C-ANCA. Natl J Integr Res Med 2023; Vol.14(2): 40-42