Case Report

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Pathology

ULCERATIVE COLITIS WITH POSITIVE PROTEINASE-3 ANTINEUTROPHIL CYTOPLASMIC ANTIBODY

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ABSTRACT Proteinase-3 (PR-3) antineutrophil cytoplasmic antibody (ANCA) is a diagnostic marker for Wegner's granulomatosis. Presence of PR-3 ANCA is extremely rare in ulcerative colitis (UC). Herein we are reporting 2 cases of Ulcerative Colitis which were positive for PR-3 ANCA. Two male patients aged 35 and 57 years presented with features with features of ulcerative colitis with blood and mucus in stool. There was no involvement of respiratory tract, nasal mucosa, skin or kidney in either patient. The laboratory examination of one patient was negative for rheumatoid factor and anti dsDNA antibody, but positive for antinuclear antibody (ANA) and PR-3 ANCA. In the second patient, only PR3 ANCA was positive while tests for ANA, anti ds DNA antibody and rheumatoid factor were negative. Histopathologically both cases were diagnosed as Ulcerative Colitis. Hence we conclude that PR3-ANCA may cause ulcerative colitis

KEYWORDS : ANA, anti ds DNA antibody, PR3 ANCA, ulcerative colitis

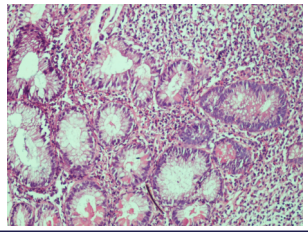
INTRODUCTION

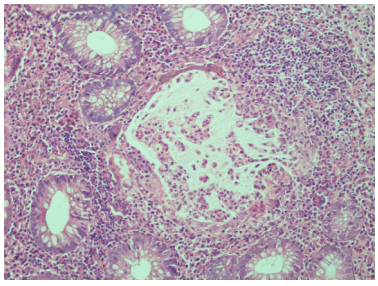
Ulcerative colitis (UC) is a chronic relapsing disorder characterized by attacks of bloody diarrhoea mixed with stringy mucoid material, lower abdominal pain and cramps that is temporarily relieved by defecation. The disease may persist for days, weeks or months. Mostly patients have mild disease but have at least one relapse in ten years.[1] Pathogenesis of UC is not clear. Radiological tests and mucosal biopsy are required to confirm the diagnosis. Drugs like 5-amino salicylic acid, steroid and cyclosporine are used in the treatment.[2] Colectomy is performed in refractory cases of UC which do not respond to above drugs. Recently some workers have found proteinase3 antineutrophilic cytoplasmic antibody (PR3 ANCA) in serum of refractory ulcerative colitis patients.[3] Herein we are reporting two cases of UC who were positive for PR3 ANCA; the cases are being documented because of rarity.

CASE HISTORY.

Two male patients aged 35 and 57 years referred from Gastroenterology OPD of SS Hospital BHU, Varanasi, presented with features of ulcerative colitis with blood and mucus in stool. Diagnosis was done by endoscopy along with Histopathological examination. The formalin fixed paraffin embedded sections were stained with haematoxylin & eosin stain. The section showed bits of colonic mucosa displaying cryptitis, crypt abscess and crypt distortion. Lamina propria showed dense mixed inflammatory infiltrate comprising of neutrophils, lymphocytes, plasma cells and eosinophils. [Fig 1&2]. Histopathologically both cases were diagnosed as Ulcerative Colitis. Both these patients were under treatment with drugs like 5-amino salicylic acid, steroid and cyclosporine. Clinically there was no involvement of respiratory tract, nasal mucosa, skin or kidney in either patient. The laboratory examination of one patient was negative for rheumatoid factor and anti dsDNA antibody, but positive for antinuclear antibody (ANA) and PR-3 ANCA. In the second patient, only PR3 ANCA was positive while tests for ANA, anti ds DNA antibody and rheumatoid factor were negative.

Antinuclear antibodies(ANA), Anti dsDNA, Myeloperoxidase and PR3-ANCA was done by indirect ELISA kit of phadia Co supplied by MS OSB Agencies, Geeta colony, New Delhi. IgM Rheumatoid factor was done by ELISA Kit. supplied for ANA ratio of more than 1:4, for dsDNA Ab value above 55 1U/ml , for PR3 value above 6 Units/ml was taken as positive.





DISCUSSION

ANCA is a group of antibodies directed against certain proteins in the cytoplasm of neutrophils. There are 2 major categories of ANCA that can be determined by immunofluorescence staining. Perinuclear ANCA (pANCA) refers to the more localized perinuclear or nuclear staining pattern; cytoplasmic ANCA (cANCA) refers to the diffuse, granular staining pattern. It has been shown that ANCA is associated with small-vessel vasculitis. MPO-ANCA is related to polyangitis or allergic granulomatous angiitis, and PR3-ANCA is a specific and sensitive marker of Wegener's granulomatosis[4-6]

The detection of ANCA is an important test for diagnosis of vasculitis specially Wegner's granulomatosis (WG) and microscopic polyarteritis nodosa. This is also used in classification of crescentic glomerulonephritis.[7] In WG, usually systemic necrotising granulomatous vasculitis are seen. Lung and kidney are the common sites of involvement. If disease involves intestine, patient may present with bloody diarrhoea.

PR3 is a serine protease specific for IL-32 binding protein. Limited cleavage of IL-32 by Pr3 enhances activity of cytokines.[8] PR3 degrades extracellular matrix protein. A linkage of p-ANCA with UC has been well described in the literature.[9-12] This may be directed against myeloperoxidase, lactoferrin , elastase , cathepsin G. Reports of PR3 ANCA (C-ANCA) in UC are sparse in the literature. Earlier reported studies have found PR3 ANCA positivity in refractory UC cases, in which no respiratory or lung lesion was present. , however, they could not find any correlation between PR3 ANCA with clinical features [3] It can't be solved whether PR3 ANCA was cause or effect of UC. In our study, both the cases were under treatment and not refractory cases out of two cases, case 1 was positive for ANA, although no symptoms related to any collagen vascular disease were present.

Thus, we conclude from our study that PR3 ANCA leads to gastro-intestinal specific vasculitis which produces necrosis of mucosa and blood vessels causing UC- like picture. Presence of ANA along with

ANCA in one of our case suggests autoimmune nature of UC.

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REFERENCES

1. Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotrans Pathologic basis of diseases, 8th ed, 2010 p811-2.
2. Timmer A, McDonald JWD, MacDonald JK. Azathioprine and 6-mercaptopurine for maintenance of remission in ulcerative colitis. Cochrane Database of Syst Rev 2007;24:CD000478.
3. Xu J, Yang CH, Chen XY, Li XH, Dai M, Xiao SD. A subset of ulcerative colitis with positive proteinase-3 antineutrophil cytoplasmic antibody.World J Gastroenterol 2008;14:7012-5.
4. Ozaki S. ANCA-associated vasculitis: diagnostic and therapeutic strategy. Allergol Int 2007; 56: 87-96
5. de Groot K, Jayne D. What is new in the therapy of ANCA associated vasculitides? Take home messages from the 12th workshop on ANCA and systemic vasculitides. Clin Nephrol 2005; 64: 480-484
6. Nolle B, Specks V, Ludemann J, Rohrbach MS, De Remee DA, Gross WL. Anticytoplasmic autoantibodies: their immunodiagnostic value in Wegener's Granulomatosis. Ann Intern Med 1989; III: 28-40
7. Cohen Tervaert JW, Goldschmeding R, Elema JD, et al. Autoantibodies against myelolysosomal enzymes in crescentic glomerulonephritis. Kidney Int 1990;37:799-806.
8. Kallenberg CGM, Brawer E, Weening JJ, Cohen Tervaert JW. Antineutrophil cytoplasmic antibodies: current diagnostic and pathophisiological potential. Kidney Int 1994;46:1-15.
9. Novick D, Rubinstein M, Azam T, Rabinkov A, Dinarello CA, Kim SH. Proteinase 3 is an IL-32 binding protein. Proc Natl Acad Sci 2006;103:3316-21.
10. Cambridge G, Rampton DS, Stevens TR, et al. Anti-nuclear antibodies in inflammatory bowel disease: prevalence and diagnostic role. Gut 1992; 33:668-74
11. Bansi DS, Chapman RW, Fleming KA. Prevalence and diagnostic role of antineutrophil cytoplasmic antibodies in inflammatory bowel disease. Eur J Gastroenterol Hepatol 1996;8:881-5.
12. Freeman HJ. Atypical perinuclear antineutrophil cytoplasmic antibodies in patients with Crohn's disease. Can J Gastroenterol 1997;11:689-93.