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CASE REPORT

A Case of ANCA-Associated Vasculitis with Positive PR3 and MPO Antibodies

Hongkun Xu [1], Kejie Xie [2]

[1] *Medical College of Shaoxing University, Shaoxing, P.R. China*
[2] *The First Affiliated Hospital of Shaoxing University, Shaoxing, P.R. China*

SUMMARY

Background: **Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune diseases including granulomatous polyvasculitis (GPA), microscopic polyvasculitis (MPA), and eosinophilic granulomatous polyvasculitis (EGPA). The main antigens ANCA targets are protease 3 (PR3) and myeloperoxidase (MPO). PR3-ANCA is mainly related to GPA, while MPO-ANCA is related to MPA. The presence of these antibodies is critical to the diagnosis of AAV.**
Methods: **A case of ANCA-associated vasculitis with PR3 and MPO antibody positive due to PTU was reported.**
Results: **After the patients stopped PTU, PR3 antibody gradually decreased to negative, MPO antibody was relatively stable, and the fluorescent karyotype was p-ANCA. The positive PR3 antibody in this patient was considered to be related to PTU.**
Conclusion: **ANCA, anti-PR3 antibody, and anti-MPO antibody are closely related to systemic vasculitis and are affected by many factors. Abnormal results in clinical work should be reviewed immediately and communicated with clinicians to avoid adverse consequences.**
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Correspondence:
Kejie Xie
Medical Clinical Laboratory
Shaoxing People's Hospital
No. 568, North Zhongxing Road
Shaoxing City 312000, Zhejiang Province
P.R. China
Phone: + 86 13906756226
Email: xiekej@163.com

KEYWORDS

ANCA, PR3, MPO, PTU

CASE PRESENTATION

The female patient, 51 years old, February 2024, felt sore throat and cough after cold, accompanied by a small amount of white sputum, and went to another hospital to check for low white blood cells (no specific report), and there was no significant improvement after anti-infection and white blood cell promotion treatment. April,2024 she was hospitalized in the respiratory department of our hospital due to pulmonary infection. Relevant examinations were completed.

Routine blood testing showed that white blood cells were 4.89 x 10^9/L hemoglobin 89 g/L and platelets were 92 x 10^9/L; C-reactive protein 76.93mg/L; alanine aminotransferase 9.8 U/L, aspartate aminotransferase 13.2 U/L, creatinine 69.2 μmol/L, urea 10.26 mmol/L, uric acid 443.5 μmol/L, estimated glomerular filtration

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Table 1. Results of anti-neutrophil cytoplasmic antibody detection in patient at different times.

	April 18th, 2024	April 24th, 2024	May 16th, 2024	August 6th, 2024	Reference interval
PR3-antibody	**338.0**	**280.0**	**60.5**	**23.0**	**0 - 24.0**
MPO-antibody	**248.0**	**243.0**	**218.0**	**254.0**	**0 - 24.0**
pANCA	+	++	+++		**negative**
cANCA	-	-	-		**negative**

value 88.1 mL/minute; anti-neutrophil cytoplasmic antibodies suggested pANCA+, PR3 338.00 AU/mL, MPO 248.00 AU/mL. We found that PR3 and MPO antibodies were elevated in the anti-neutrophil cytoplasmic antibodies in this patient, but the fluorescent karyotype showed pANCA, which was relatively rare in practice. MPO is a strong cationic protein, which is redistributed around the nuclear membrane after ethanol dissolution, so that the fluorescence karyotype is ANCA (pANCA). Since PR3 is a weak cationic protein and the fluorescent karyotype is the opposite of MPO, is it possible that the positive PR3 antibody in this patient may be caused by other causes?

We analyzed that there may be the following reasons for the positive PR3 antibody in this patient: 1) Instrument failure: The instrument operated normally on that day, no error or alarm was reported, and the test results of other specimens were normal, so this cause can be ruled out; 2) Specimen status: The patient's sample has no hemolysis, fat turbidity and clot, so this reason can also be ruled out; 3) Quality control is out of control: quality control is in control on the day, and the results of Zhejiang Clinical Laboratory Center inter-laboratory quality evaluation are qualified, which can also exclude this reason. However, this patient did have elevated PR3 antibodies. Excluding the reasons of laboratory and specimen, we considered whether it was the patient's own factors.

To confirm the conjecture, we inquired about patient's medical history and found that the patient was a patient with ANCA-associated vasculitis with a history of hyperthyroidism. The patient had been taking propylthiouracil (PTU) for a long time and stopped taking PTU after this admission. Anti-neutrophil cytoplasmic antibodies were rechecked three times during the hospitalization. We found that the PR3 antibody level of the patient was relatively high at the time of admission, and after the withdrawal of the drug for some time, the PR3 antibody level decreased significantly, but the MPO antibody level was relatively stable, and the fluorescent karyotype was pANCA. Subsequently, the patient was discharged from the hospital, and the anti-neutrophilic cytoplasmic antibodies were re-examined on August 6th, 2024. We found that the PR3 antibody level of the patient returned to normal, and the MPO antibody level was still high (Table 1).

DISCUSSION

Antineutrophil cytoplasmic (ANCA)-associated vasculitis (AAV) is an autoimmune disease, mainly involving small and medium vessels, and can be classified into granuloma with polyvasculitis (GPA), microscopic polyvasculitis (MPA), and eosinophilic granuloma with polyvasculitis (EGPA). AAV primarily targets protease 3 (PR3) and myeloperoxidase (MPO) autoantibodies that activate the neutrophil and complement systems, leading to inflammation and damage of blood vessels [1]. ANCA plays an important role in the pathogenesis of ANCA-associated vasculitis, with inflammatory triggering leading to increased membrane expression of MPO and PR3 on neutrophils. The binding of ANCA to PR3 and MPO triggers neutrophil activation, degranulation, and neutrophil extracellular trap (NET) formation, which further releases MPO and PR3 to trigger ANCA, according to immunofluorescence patterns on their ethanol-immobilized neutrophils. ANCA can be divided into cytoplasmic ANCA (cANCA), perinuclear ANCA (pANCA), and atypical ANCA [2]. In ANCA-associated vasculitis, more than 90% of cANCA targets PR3, while approximately 80 - 90% of pANCA recognizes myeloperoxidase (MPO-ANCA) [3]. Cases of PR3 antibody and MPO antibody positive at the same time are rare and may be associated with certain drugs (such as antithyroid drugs, minocycline, methotrexate, etc.), of which anti-thyroid drugs are of note [4,5]. Antithyroid drugs are mainly used for the treatment of hyperthyroidism, mainly including methimazole (MMI) and propylthiouracil (PTU). Complications include granulocytosis, liver failure, birth defects in offspring, skin allergy, and so on [6,7]. At present, relevant studies and reports have found that it is closely related to the development of ANCA, among which the most common induction drug is PTU, and the prevalence of ANCA positive during treatment can reach 4% - 41% [8]. Relevant researchers have found that patients treated with propyl thiouracil (PTU) can have positive MPO and PR3 antibodies, and a high positive rate of IIF-ANCA [9,10].

The patient in this medical record has a history of ANCA-associated vasculitis with hyperthyroidism and has been taking PTU treatment for a long time. The patient stopped taking PTU after admission this time. After stopping PTU for nearly one month, the level of PR3 antibody in the patient decreased significantly, but the

level of MPO antibody was relatively stable, and the fluorescence karyotype was pANCA. Three months later, the patient was re-examined and found to have normal PR3 antibody levels. Based on the above data, we consider that the positive PR3 antibody may be caused by PTU, which suggests that we should take the initiative to analyze the cause when we find abnormal results in the actual work process and communicate with clinicians in time.

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Declaration of Interest:
All authors declare that they have no competing interests.

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