# A case of propylthiouracil-induced antineutrophilic cytoplasmic antibody-positive vasculitis successfully treated with radioactive iodine

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**SUMMARY**

Antineutrophilic cytoplasmic antibody (ANCA) associated vasculitis is one of the rare complications of propylthiouracil treatment. Having a variable clinical spectrum, it may be presented with both skin limited vasculitis and life-threatening systemic vasculitis. In this study, we present a case that developed ANCA-positive vasculitis with skin and kidney involvement (hematuria and proteinuria) six months after propylthiouracil treatment was initiated for toxic nodular goiter. Proteinuria recovered dramatically subsequent to radioactive iodine treatment following ceasing the drug.

**Key words:** *Propylthiouracil, Antineutrophilic cytoplasmic antibody (ANCA), Radioactive iodine.*

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## INTRODUCTION

Propylthiouracil (PTU) is one of the most frequently used drugs in treatment of hyperthyroidism. It has been recently reported that complications such as antineutrophilic cytoplasmic antibody (ANCA) positive vasculitis and glomerulonephritis may develop related with PTU treatment (1). Although the pathogenesis of PTU-induced ANCA positive vasculitis has not been clarified yet, oxidative and proteolytic damage of small vessels is considered to play a role (2). In mild cases, recuperation is achieved through discontinuation of PTU whereas immunosuppressive treatment should be required in the presence of systemic involvement (renal involvement, pulmonary involvement, etc.). PTU-induced ANCA positive vasculitis may display a fatal course despite intense immunosuppresive therapy (3). Herein, we present a case of PTU-related ANCA positive vasculitis with renal involvement in a patient who did not respond completely with immunosuppressive therapy but she did respond dramatically to radioactive iodine treatment.

## CASE REPORT

A 56-year old female patient referred to our hospital with complaints of rash on both legs and bloody urine. She reported to have been diagnosed with toxic nodular goitre six months ago and given PTU 100 mg, daily. Her family history was unremarkable. Her physical examination revealed petechial and purpuric lesions spreading from both hips to ankles. Laboratory findings were: thyroid stimulating hormone: 0.11 (N: 0.35-4.95 uIU/mL), free T4: 1.01 (N: 0.78-1.48 ng/dL); complete urine examination revealed + 4 proteinuria with hematuria. The amount of protein in 24-h urine was 1.9 gr/dL. A biopsy was taken from purpuric lesions of the right leg. The

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biopsy showed leukocytoclastic vasculitis. Perinuclear-ANCA (p-ANCA) [studied by immune fluoresceine method (IFA)] was found to be positive whereas cytoplasmic-ANCA was negative. Antinuclear antibodies immunofluorescence assay (ANA-IFA) test was + 3 with a homogeneous pattern, extractable nuclear antigens profile and anti-dsDNA were both negative. The patient was questioned and investigated in terms of other causes that ANA positivity. But there wasn't detect any disease for ANA positivity. Then, renal biopsy was planned but the patient refused the biopsy procedure. Therefore we didn't do renal biopsy. The patient was diagnosed with PTU-induced p-ANCA positive vasculitis and metilprednisolon 32 mg/day, azathioprine 150 mg/day, ACE inhibitor (for proteinuria) were initiated after discontinuation of PTU. In spite of one-month treatment, no significant decrease occurred in proteinuria. Because of the low side effect profile and our past experience, we preferred azatioprine and not methotrexate, or cyclophosphamide. Thyroid scintigraphy was performed for the etiology of hyperthyroidism and a solitary toxic nodul was detected. Radioactive iodine was administered to achieve a permanent response for hyperthyroidism. One month after the radioactive iodine therapy, proteinuria of the patient reduced to normal range. The patient has undergone regular follow-up with azathioprine 150 mg qd and metilprednisolon 4 mg qd.

## DISCUSSION

It is known that PTU may cause ANCA positive vasculitis. The cases of PTU-induced ANCA positive vasculitis were first reported by Dolman et al. (4) and the mechanism of this condition has not been elucidated yet. Binding of PTU that stored in neutrophils to myeloperoxidase (MPO) in cytoplasmic granules has been assumed as the possible mechanism. PTU has been reported to turn into PTU-sulphonate which stimulates immune system to produce immunogenic autoantibodies with cytotoxic activity for T-cells in the presence of MPO and hydrogen peroxide that released from neutrophils (5).

In the course of PTU-induced vasculitis flu-like symptoms, artralgia, myalgia, skin lesions (*i.e.*, purpura), interstitial pneumonia, alveolar hemorrhage, acute respiratory distress syndrome, anemia, nephritis, acute renal failure may develop.

In a series of 27 cases by Gunton et al. in 1999, renal failure was reported to be the most frequent finding (66.7%), which was followed by arthralgia (48%), high fever (37%), skin involvement (29.6%) and respiratory tract involvement (25.9%) (6). Renal involvement may present with proteinuria, microhaematuria or progressive renal failure (7, 8). Although PTU-induced vasculitis often requires immunosupressive treatment, discontinuation of accused drug may suffice in some cases. Pillinger et al. reported 23 cases with PTU-induced ANCA positive vasculitis. Most of the patients recovered after drug discontinuation. Six of these patients received immunosuppressive treatment (steroid and/or cyclophosphamide), one needed hemodialysis and one died (9).

To date, there is no information about the therapy of PTU-induced ANCA positive vasculitis with radioactive iodine. In our case, we used radioactive iodine because the patient's proteinuria continued in spite of immunsuppressive therapy. After the radioactive iodine, proteinuria decreased to normal range. We consider that radioactive iodine may involve in the treatment by neutralizing the antigenic effect originated from PTU exposure.

## CONCLUSIONS

PTU-induced ANCA positive vasculitis is a rare side effect of PTU but sometimes can cause serious complications. Physicans should be aware of this complication during PTU therapy. PTU should be ceased immediately after diagnosis. The patient should undergo close surveillance and if necessary, immunosuppressive treatment must be initiated unhesitantly. Radioactive iodine treatment may enhance recovery in

case of toxic adenoma and PTU-induced p-ANCA positive vasculitis with renal involvement.

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