Case Report

Propylthiouracil induced leukocytoclastic vasculitis: A rare manifestation

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ABSTRACT

Propylthiouracil (PTU) is a common drug used in patients with hyperthyroidism. It may cause perinuclearantineutrophil cytoplasmic antibodies (p-ANCA) in few patients with Graves' disease. This antibody has been associated with different forms of vasculitis. We report a patient who presented with cutaneous manifestations of leukocytoclasticvasculitis with simultaneous development of p-ANCAs during PTU therapy for Graves' disease.

Key words: Propylthiouracil, perinuclearantineutrophil cytoplasmic antibodies, graves' disease, vasculitis

Introduction

The thionamide group of drug such as propylthiouracil is generally first-line drug in the therapy of hyperthyroidism. This drug may cause mild and severe side effects. The most common mild side effects are transient granulocytopenia, pruritus, urticaria, generalized maculopapular and papularpurpuric rashes, arthralgia, myalgia, and drug-induced fever. Skin eruptions occur in 4-6% of adults treated with PTU. The most common severe side effects are agranulocytosis, thrombocytopenia, aplastic anemia, hepatitis, cholestatic jaundice, splenomegaly, lupus-like syndrome, polyarteritisnodosa, vasculitis, pancreatitis, nephrotic syndrome and disseminated intravascular coagulation.[1,2] We report a rare case of leukocytoclasticvasculitis as a manifestation of PTU hypersensitivity.

Case Report

48 years old female patient was admitted to our endocrinology clinic with the complaints of palpitations, sweating, heat intolerance andskin lesions. We learned that hyperthyroidism was detected eightyears ago, she used antithyroid drug (patient cannot remember the name of drug) for twoyears, thyroidectomy was recommended and the patient did not continue her follow-ups because of fear of the surgery, she did not receive any antithyroid treatment for sixyears. Finally she referred to the internal medicine clinic andpropylthiouracil 50 mg (3 × 1) therapy started. Skin lesions were occurred in the 15thday of the treatment. Large numbers of necrotic-looking vasculitic skin lesions were revealed on her right ear, chest, bilateral lower extremity and abdomen [Figure 1]. WBC: 3.7 K/uL, Neu: 1.3 K/uL, Hgb: 12.1 g/dl, Plt: 251 K/uL,

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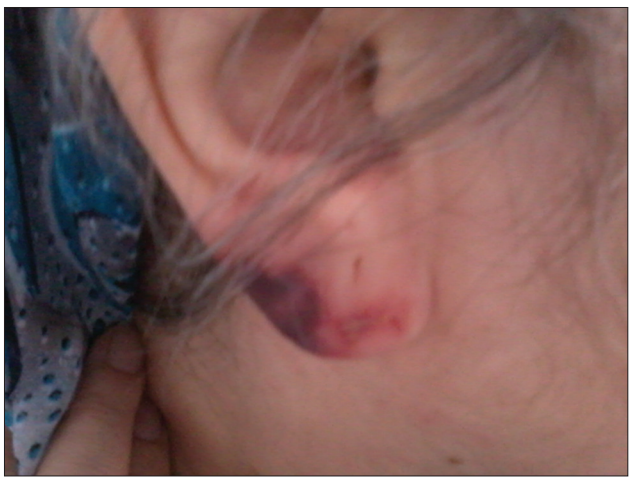

Figure 1: Vasculitic lesion on the ear skin

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TSH: 0.0059 mIU/ml, T4: 13.97 pmol/L, T3: 5.79 pmol/L, Sedimentation: 45 mm/h, CRP: 109.5 mg/L was detected on his blood analysis. The patient's other routine blood chemistry andcomplete urinalyses were normal. Hepatitis markers were negative. ANA (-), p-ANCA (+), c-ANCA (-) were detected. We suspected PTU-induced vasculitis and PTU treatment was stopped. Skin biopsy was performed because of skin lesions. It was reported as leukocytoclastic vasculitis. Thyroid gland size and its blood supply were increased and no nodule formation was observed in the Doppler ultrasound. Thyroid uptake was calculated as 8.7%. Thyroid scintigraphy was accordance with Graves' Disease. Vasculitic lesions began to improve after stopping PTU treatment. In the light of clinical and laboratory findings she was diagnosed leukocytoclasticvasculitis caused by PTU, with positive p-ANCA. Radioactive iodine treatment was performed as permanent antithyroid treatment. Skin lesions completely disappeared in her follow up.

Conclusion

We report a case of leukocytoclasticvasculitis caused by PTU, with positive p-ANCA. PTU is well known to cause vasculitisassociated with positive ANCA titres, and this typically occurs late in the treatment.

Two specific types of ANCA are c-ANCA and p-ANCA. PTU induced vasculitis has been associated with p-ANCA and laboratory findings of our case was also compatible with this diagnosis. The pathogenesis of PTU induced vasculitis is not clearly understood. The cause of PTU-induced vasculitis is unknown origin, although immune complex deposition is considered to be the pathogenetic mechanism of hypersensitive vasculitis. However, PTU has been shown to accumulate p-ANCA, which subsequently promotes antibody formation by polyclonal activation of B lymphocytes in susceptible individuals.[1,3-5]

The most common skin findings during the administration of antithyroid drugs are generalized maculopapular and papularpurpuric rashes, with an incidence of 4-6%.[1] 748 people reported to have side effects when taking Propylthiouracil. Among them, 10 people (1.34%) have Leukocytoclasticvasculitis.[6]

In our case, vasculitis appeared during the 15thday of treatment. We assumed that the vasculitis was due to PTU because the lesions rapidly regressed when the drug was discontinued.

When biopsies are obtained in the acute phase of active disease, the typical pattern of neutrophil infiltration is readily observed.[3,4] In our patient, skin biopsy showed leukocytoclasticvasculitis.

Although most patients recover completely simply by withdrawal of PTU,[7,8] some patients who have severe renal involvement or impairment of multiple organ systems may require high dosages of prednisone for several months.[1,9] In our case hepatic and renal functions were normal.

In conclusion, we report a patient who presented with cutaneous manifestations of leukocytoclasticvasculitis with simultaneous development of p-ANCAs during PTU therapy for Graves' disease. The importance of this study is to call attention to the occurrence of serious cutaneous manifestationassociated with a systemic drug frequently used in internal medicine. Early diagnosis and withdrawal of the suspected medication is mandatory.

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