Propylthiouracil induced Anti-neutrophil cytoplasmic antibody-associated vasculitis with skin lesions and granulocytopenia


Istanbul University, Istanbul Medical Faculty, department of Internal Medicine division of Endocrinology and Metabolism

Introduction:
Thionamide group drugs such as propylthiouracil (PTU) and methimazole (MMI) are generally first choice therapy for hyperthyroidism. In Turkey and Asia, PTU is a widely used drug, and can cause severe side effects in %0,3 of patients such as agranulocytosis, hepatitis, disseminated intravascular coagulation, vasculitis. Drug-induced vasculitis which is characterized by inflammation and cellular infiltration of small vessels and presence of anti-neutrophil cytoplasmic antibodies (ANCA). ANCA is found in two forms-cytoplasmic (cANCA) and perinuclear (pANCA). Both of the forms can be detected in anti-thyroid drug induced vasculitis. We report a case of perinuclear antineutrophil cytoplasmic antibody-associated vasculitis developed during treatment with PTU for Graves disease.

Case:
A 58-year old woman admitted to the emergency department with painful gangrenous, ecchymotic lesion at her right ear and left arm for 15 days. Ear lesions were considered as erythema gangrenosum in an ENT clinic 10 days ago and anti-pseudomonal treatment had begun but no amelioration observed. Her medical history was significant for Type 2 Diabetes for twelve years and Graves Disease for four years. There had been a similar lesion at her left ear 6 months ago resulted with auto-amputation of the left auricle. She had been using PTU 100 mg/day and pre-mixed insulin injection twice a day. We found non-tender, mobile cervical lymphadenopathies, enlarged liver and spleen together with ear lesions in physical examination.

Leukocyte: 12/10³ µl
HGB: 8.5 g/dL
Hct: 25.2
MCV: 86.5 µl
Plt: 200.000/10³ µl
Glucose: 254 mg/dl(70-100)
Urea: 17 mg/dl(0-30)
Creatinin: 0.6 mg/dl(0.7-1.4)
Potassium: 3.9 mmol/L (3.5-5.1)
AST: 14 IU/L (0-42)
Calcium: 5.1 mg/dl (8.5-10.5)
ALP: 18 IU/L (0-45)
Phosphorous: 3.7 mg/dl (2.7-4.3)
LDH: 179 mg/dl (240-480)
CRP: 17.6 mg/L (0-5.0)

Biopsy of the affected skin revealed leukocytoclastic vasculitis. As additional tests excluded systemic vasculitis, propylthiouracil-induced vasculitis was diagnosed. Propylthiouracil was discontinued and the skin lesions disappeared, granulocytopenia has revealed over time without the need of any specific therapy.

Conclusions:
Regular follow-up of patients on anti thyroid drug is mandatory because it is not well defend at what dose and at which state of PTU administration leads to vasculitis. Physicians and also the patients should be aware of the major adverse reactions of antithyroid drugs.

References: