Propylthiouracil-induced autoimmune disease

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Hyperthyroidism is a condition characterized by excessive production of thyroid hormones. Propylthiouracil (PTU) is commonly used as first line drug in the management of hyperthyroidism. This is a case report of 24-year-old female, a known case of hyperthyroidism since 4 years, who came with a history of fever and myalgia since 3 days and dyspnea with coughing out of blood since 1 day. Patient was taking PTU (100 mg per day) since 4 years for hyperthyroidism. Patient was immediately intubated for type-II respiratory failure. Diagnosed to be having PTU-induced autoimmune disease. PTU was stopped and treated with methylprednisolone and cyclophosphamide. Clinical features improved over a period of 8 days and discharged home successfully. Having a high suspicion for the onset of autoimmune disease in hyperthyroidism patients who are on PTU therapy and timely treatment with immunosuppressants and supportive care along with the withdrawal of the drug can make a difference in morbidity and mortality.

Keywords: Drug-induced lupus, hemoptysis, hyperthyroidism, propylthiouracil, vasculitis

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Abstract

Hyptothyroidism is a condition characterized by excessive production of thyroid hormones. Propylthiouracil (PTU) is commonly used as first line drug in the management of hyperthyroidism. This is a case report of 24-year-old female, known case of hyperthyroidism since 4 years, who came with a history of fever and myalgia since 3 days and dyspnea with coughing out of blood since 1 day. Patient was taking PTU (100 mg per day) since 4 years for hyperthyroidism. Patient was immediately intubated for type-II respiratory failure. Diagnosed to be having PTU-induced autoimmune disease. PTU was stopped and treated with methylprednisolone and cyclophosphamide. Clinical features improved over a period of 8 days and discharged home successfully. Having a high suspicion for the onset of autoimmune disease in hyperthyroidism patients who are on PTU therapy and timely treatment with immunosuppressants and supportive care along with the withdrawal of the drug can make a difference in morbidity and mortality.

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In the emergency department patient was conscious, febrile, tachypnoic, pulse rate - 120 beats/min, blood pressure - 100/60 mmHg, SpO₂ - 91% with face mask 10 L of oxygen, GRBS - 112 mg/dl, and on auscultation bilateral coarse crepitation were heard. Arterial blood gas analysis showed pH - 7.125, PO₂ - 52.2, PCO₂ - 63, and HCO₃ - 20.2. Patient was immediately intubated and given positive pressure ventilation in view tachypnea, hypotension, and type-II respiratory failure. Complete blood picture showed hemoglobin - 6.9 g/dl, white blood cell of 3200 cells/cumm (neutrophils - 73%), platelets - 1.65 lakhs/cumm, erythrocyte sedimentation rate - 53 mm/h. Prothrombin time 13.5 s (control 11–14 s), INR - 1.51, and activated partial thromboplastin time - 25.4 s (control 30–40 s). Serum electrolytes, liver function test, and kidney function test were normal. Routine urine analysis showed plenty of red blood cells. Electrocardiogram showing sinus tachycardia and two-dimensional-echo showed no regional wall motion abnormality with good left ventricular function.

Chest X-ray showed [Figure 1] bilateral homogenous opacities. Thyroid function tests were normal. Chest computed tomography showed [Figure 2] diffuse
multifocal patchy areas of consolidation and ground glassing in both lungs (alveolar hemorrhage). Venous Doppler of both legs was normal. Bronchoalveolar lavage (BAL) showed hemosiderin-laden macrophages. Culture of BAL fluid and blood was negative for bacteria, tuberculosis, and fungus. Serum antinuclear antibodies (ANA) +ve, anti-dsDNA −ve, anti-histone antibody +ve, p-ANCA +ve, c-ANCA −ve, and anti-GBM −ve with low C3 and C4.

In view of above features, we suspected PTU-induced autoimmune disease (drug-induced lupus [DIL] and/vasculitis) and hence PTU was stopped. Treated with methylprednisolone (1 g) pulse therapy for 3 days followed by one dose of cyclophosphamide (750 mg). Image-3 showing chest X-ray during the recovery phase (after cyclophosphamide therapy) with a bilateral clearance of haziness. Received one unit of packed red blood cell’s during the stay. Clinical features and laboratory parameters improved over a period of 8 days and patient could be extubated on 8th day and gradually weaned from BIPAP support to nasal prongs, later shifted to room and discharged home successfully on day 12. Figure 3 showing chest X-ray of the same patient before discharge.

Discussion

Hyperthyroidism is a condition characterize by excessive production of thyroid hormones. It is common in women than men (5:1 ratio) with an overall prevalence of approximately 1.3%.[5] PTU is commonly used as first line drug in the management of hyperthyroidism. PTU inhibits the synthesis of thyroid hormones by blocking the oxidation of iodine in the thyroid gland. PTU can induce adverse autoimmune responses such as DIL or vasculitis.[6] The risk of developing DIL with using PTU is <1% of the treated patients.[7] Patients with PTU-induced DIL have more serositis, musculoskeletal, and gastrointestinal involvement with positive ANA, anti-DNA, and anti-histone antibodies, whereas the ANCA-associated vasculitis will present with upper airway, pulmonary, and renal involvement with c-ANCA positive.[8] Our patient had positive for anti-histone antibodies which suggest DIL and positive p-ANCA with lung (alveolar hemorrhage) and renal involvement (hematuria) show features of vasculitis.

PTU-induced vasculitis often occurs in a few weeks to years after starting the treatment. Our patient was on PTU treatment since 4 years. The disorder is not dose-dependent and usually improves after discontinuation of the drug,[9] while about 50% of PTU-induced vasculitis need steroids or immunosuppressive drugs.[10]
The proposed mechanism for PTU-induced vasculitis is due to the interaction between PTU and neutrophil myeloperoxidase (MPO). MPO and hydrogen peroxide produced by neutrophils can metabolize the drug leading to the reactive intermediates that are immunogenic for T-cells and stimulate the immune system.[11]

This case report mainly emphasizes to have a high suspicion for the occurrence of the drug-induced autoimmune disorder in patients with hyperthyroidism treated with PTU. Early diagnosis and treatment with immunosuppressants agents along with supportive care and withdrawal of the drug can make a difference in morbidity and mortality.

References