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PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.2392795>Available online at: <http://www.iajps.com>**A Case Study****GENERALIZED LYMPHADENOPATHY, SPLENOMEGALY AND
FEVER DURING PROPYLTHIOURACIL THERAPY:
A CASE REPORT****¹Mohammed Abdulrahman AlShaikh, ²Khaled Saad Alzahrani, ³Marwan A. Albeshri,
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Abstract:

We are reporting a case with rare side effect of propylthiouracil. Thirty-two years old Saudi female diagnosed to have graves disease and treated by propylthiouracil for more than 4 years. She started to complain of fever, joint pain and weight loss for 8 months. Clinically, she was found to be pale, generalized lymphadenopathy and having moderate splenomegaly. Investigation revealed pancytopenia, high ESR, and multiple small cystic nodules in the liver, spleen, and both kidneys. We thought of propylthiouracil as a cause of her problem and advised to discontinue it before doing invasive investigation. Two weeks later she had better appetite, less joint pain, and no more fever. Complete blood count and ESR became improved and normalized in subsequent visits. We are reporting a case of generalized lymphadenopathy, splenomegaly and fever caused by propylthiouracil.

Keywords: *propylthiouracil, vasculitis, Antithyroid drugs, lymphadenopathy.*

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INTRODUCTION:

The use of Antithyroid drugs in the early 1940s revolutionized the management of hyperthyroidism. Since their introduction to control and manage hyperthyroidism, variety of adverse reactions, including, haematological, dermatological, and rheumatological side effects have been linked with the use of antithyroid medications. The incidence of these side-effects is estimated to be between 1-5% which is similar to many other commonly used drugs [1]. The most common side-effects of that have been reported in the literature include skin rash, fever, arthralgias/ arthritis and neutropenia. Other uncommon and very rare side effects are lupus-like reaction, vasculitis, hepatitis, agranulocytosis and thrombocytopenia [2]. Disseminated intravascular coagulation (DIC) is also a rare side effect of propylthiouracil therapy [3]. An antineutrophil cytoplasmic antibody (ANCA) positive vasculitis on propylthiouracil treated patients may be more common than previously considered [4]. Here, we report a case of generalized lymphadenopathy, splenomegaly, and fever following long duration of propylthiouracil therapy in a 32 years old Saudi female.

CASE REPORT:

A 32 years old Saudi woman with Graves's disease, diagnosed 6 years earlier, and received propylthiouracil for the past 3 years. She was advised for radioactive iodine immediately after diagnosis but she refused. She was started on neomercazol for almost 2 years then stopped because she became euthyroid clinically and laboratory. Eight months later she started to have thyrotoxicosis symptoms and her thyroid function tests showed high free T4, and low thyroxin stimulating hormone (TSH). She was commenced again on Antithyroid treatment but propylthiouracil was selected because she planned pregnancy. Few months later she became pregnant, and the dose of the propylthiouracil changed according to thyroid function tests. Pregnancy went without any complication and delivered a healthy baby girl. She continued her treatment with propylthiouracil, with checking the thyroid function test periodically. In the beginning of 2004 she was started to experience joint pain, and night fever. She

was seen by different physician where given antibiotics, and non steroidal anti inflammatory treatment. She was diagnosed as possible rheumatoid arthritis, and steroid was prescribed but she did not take it. She continued to have the joint pain and the fever for almost 10 months, till the time I saw her again on October 2004. I found that the joint pain involving all the joints with no joint swelling or morning stiffness. The fever mainly in the night and associated with night sweats. She lost about 10 kg of her weight during this period with poor appetite. She did not complain of abdominal pain, vomiting, abnormal bowel motion, urinary symptoms, abnormal menstrual cycle, cough, or shortness of breath. Vital signs were normal except temperature was 38.6 in the first day. Deep cervical, axillaries, and inguinal lymph nodes were palpable. It was small scattered, and not tender. She had palpable red skin rashes in the extremities (vasculitis). There were no thyrotoxic signs and no goiter. She was having moderate hepatomegaly and splenomegaly. Cardiac, respiratory and neurological examinations were normal. All joint did not have any deformities or swelling. Fundus examination was normal. The laboratory investigation revealed low white blood cells, normocytic normochromic anemia, low platelets, normal electrolytes, normal creatinine, normal thyroid function tests, negative brucellosis antibodies, negative rheumatoid factor, negative anti nuclear antibody, and ANCA p was positive (Table 1). Chest x-ray revealed normal lung parenchyma, and normal cardiac size with no abnormal radiological finding. Abdominal ultrasound and CT scan showed multiple cystic lesions in the liver, spleen and kidneys with evidence of enlargement of the liver and spleen (figure 1). The possibilities of adult onset polycystic disease or metastasis were raised. In view of long use of propylthiouracil, and reported cases of fever and vasculitis in those cases, i decided to stop the propylthiouracil and followed up after 2 weeks. In follow the fever subsided and the appetite improved. Repeated CBC revealed increasing in WBC and platelets count and reduced ESR level. The multiple lesions in the liver and spleen reduced according to the repeated ultrasound. We considered the radioactive active iodine for treatment of the hyperthyroid once it reoccurs.

Table 1: The Clinical and Investigation Results.

The clinical and investigations.	The results
Fever.	Mainly at night.
Appetite and weight.	Reduced.
Arthralgias.	Present in all joints.
Arthritis.	Not present.
Tremor , tachycardia	Normal.
Goiter.	Not present.
Thyrotoxic eye signs.	Not present.
Chest – heart, examination.	Normal.
Abdomen, examination.	Hepatosplenomegaly.
Lymph nodes.	Generalized enlargement scattered.
skin	Skin rashes in the extremities.
WBC, Platelets, HB, ESR.	2.3000, 123000, 9.5, 86mm/hour.
electrolytes	Normal.
TFT	Normal
Chest x ray.	Normal.
Brucellosis titer.	Negative.
ANA*, RF**, C3 and C4***	All negative, normal complements.
ANCA****.	Present for p only.
Abdominal ultrasound and CT.	Multiple liver, spleen and renal cystic masses.

- *Antinuclear antibodies. ** Rheumatoid factor. *** complements.
- **** Antineutrophil cytoplasmic antibody.



Figure 1: Abdominal CT scan showing multiple cystic lesions in the liver, spleen and kidneys with evidence of enlargement of the liver and spleen.

DISCUSSION:

The most frequent adverse effects related to propylthiouracil and Methimazole, the most commonly used Thionamide, are haematological Transient leucopenia, perhaps the most common side – effect, has been reported in 12% of adult and up to 25% of children, while cutaneous adverse reaction occur in 3-5% of adults and up to 18% of children [5,6]. Generalized maculopapular and popular purpuric eruption are the most common thionamide induced cutaneous reaction, but rarely bullous haemorrhagic generalized vesicular and necrotic ulcerative forms have been described.⁶ Propylthiouracil induce clinically distinctive cutaneous eruption consisting of symmetrical, tender, palpable purpuric lesion, often in a livedoid pattern and involve the ear lobes and malar areas.⁷ Cutaneous vasculitis is usually seen early in the course of propylthiouracil, but also has been observed after long term treatment. Vasculitis involvement of the skin is far more common than other organ. Cases of nephritis, myositis, and cavitory pulmonary infiltrate have been reported [7,8].

The exact pathogenesis of propylthiouracil – induced vasculitis is not known. It has been suggested that circulating immune complexes may play a role as immunoglobulin, and complements have been found in the glomeruli and in the wall of dermal vessels using immunofluorescence [7]. The detection of ANCA in association with vasculitis suggests other possible pathogenic mechanism [9]. No dose dependent or age preference factors has been noted [5,9].

In addition to leucopenia and agranulocytosis, the other reported haematological abnormalities associated with propylthiouracil therapy include anaemia, thrombocytopenia, polyclonal hypergammaglobulinaemia, and DIC [2,3]. Most adverse effects usually reverse with discontinuation of the drug [10]. Steroid, and in some cases, non-steroidal anti-inflammatory drugs have been used successfully to alleviate the symptoms [6, 7, 10]. Our patient responded to discontinuation of the propylthiouracil. She improved clinically where the fever subsided, appetite improved, her weight increased and the enlargement lymph nodes regress. The white blood cell count increased after discontinuation of propylthiouracil and erythrocyte

sedimentation rate decreased. In conclusion I am reporting a case with generalized lymphadenopathy, fever and vasculitis due to propylthiouracil.

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Conflict of Interest: The authors declare no conflict of interest.

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