



## HYPERTHYROIDISM

# The Onset Of Vasculitis With Antithyroid Drugs Is Both Rare And Unpredictable, But Is More Common With PTU

### WHAT IS THE STUDY ABOUT?

Vasculitis is a generalized disorder of the immune system where antibodies attack blood vessels and cause inflammation. There are many causes of vasculitis and the problems it can cause range from simple lab abnormalities without symptoms to severe reactions that may cause death. Drugs are a major cause of vasculitis, often by causing the development of specific antibodies known as myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA) which then attack blood vessels. The development of MPO-ANCA has been reported by both Methimazole (MMI) and Propylthiouracil (PTU), the two antithyroid drugs that are used in treating patients with hyperthyroidism. The aim of this study was to determine what doses of the drug are involved and what symptoms are the most common in patients with MPO-ANCA-associated vasculitis caused by PTU or MMI.

### THE FULL ARTICLE TITLE:

Noh JY, Yasuda S, Sato S, Matsumoto M, Kunii Y, Noguchi Y, Mukasa K, Ito K, Ito K, Sugiyama O, Kobayashi H, Nihojima S, Okazaki M, Yokoyama S. Clinical characteristics of myeloperoxidase antineutrophil cytoplasmic antibody-associated vasculitis caused by antithyroid drugs. *J Clin Endocrinol Metab* 2009;94:2806-11.

### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to determine what doses of the drug are involved and what symptoms are the most common in patients with MPO-ANCA-associated vasculitis caused by PTU or MMI.

### WHO WAS STUDIED?

The study included 92 patients with Graves' disease who had MPO-ANCA-associated vasculitis as an adverse reaction to antithyroid drugs and thus were reported, as required by law in Japan, to Chugai Pharmaceutical, which makes PTU and MMI.

### HOW WAS THE STUDY DONE?

The adverse drug reports were reviewed on the 92 patients reported to the drug company.

### WHAT WERE THE RESULTS OF THE STUDY?

Of the 92 patients with MPO-ANCA-associated vasculitis, 23 (25%) were taking MMI and 68 were taking PTU (75%); in 1 patient it was not clear which of the two had been taken. There was ~3.5-fold more women than men that developed this complication. Symptoms were severe in 79 patients (86%), moderate in 2 (2%), and mild in 2 (2%). MPO-ANCA-associated vasculitis resolved in 62 patients (67%) and caused death in 2 (2%). The most common systems involved were 1) the kidneys with blood in the urine (38%), 2) the lungs with coughing up blood (19%), 3) the skin with ulcers and bruising (13.8%) and 4) the joints with swelling and pain (13.1%). MPO-ANCA-associated vasculitis affected one system in 41 patients (45%), two systems in 32 patients (35%) and three or four systems in the rest. MPO-ANCA-associated vasculitis occurred with almost any dose of drug, with 50% of patients being on MMI 15 mg/day or less or PTU 200 mg/d or less. Vasculitis occurred after being on the drug anywhere from 1 month to >10 years.

### HOW DOES THIS COMPARE WITH OTHER STUDIES?

MPO-ANCA-associated vasculitis due to PTU has been recognized for some time. Several studies have shown that the vasculitis could spontaneously resolve after cessation of antithyroid drugs and that the long-term outcomes were relatively good. The present study is the largest study of this complication.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Antithyroid drug-induced MPO-ANCA-associated vasculitis is both rare and unpredictable. It occurs more frequently with PTU, but is not correlated with the dose of antithyroid drugs or the duration of therapy. While rare, this complication should be considered in any patient on PTU or MMI who develops blood in the urine, coughs up blood, developed ulcers and bruising or joint pain and swelling.

— Alan Farwell, MD

### ATA THYROID BROCHURE LINKS

Hyperthyroidism: [http://thyroid.org/patients/patient\\_brochures/hyperthyroidism.html](http://thyroid.org/patients/patient_brochures/hyperthyroidism.html)

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## **HYPERTHYROIDISM**, continued

### **ABBREVIATIONS & DEFINITIONS**

**Hyperthyroidism:** a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

**Graves' disease:** the most common cause of hyperthyroidism in the United States.

**Methimazole (MMI):** an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.

**Propylthiouracil (PTU):** an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

**Vasculitis:** a generalized disorder of the immune system where antibodies attack blood vessels and cause inflammation.

**Myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA):** specific antibodies that may be induced by drugs which then attack blood vessels.