



HYPERTHYROIDISM

ANCA–positive small-vessel vasculitis is a rare but severe disorder associated with antithyroid drug therapy

BACKGROUND

Antithyroid drugs (ATDs), including propylthiouracil (PTU) and methimazole (MMI), represent an important treatment option for hyperthyroidism, and especially Graves' disease. Although ATDs are usually well tolerated, various side effects have been reported since their initial administration in 1946. Most side effects are minor; however, there are two severe side effects from these medications, agranulocytosis and acute liver failure. In addition, cases of blood vessel inflammation (vasculitis) associated with antineutrophil cytoplasmic antibodies (ANCA) have been described, more often related to PTU than MMI use. ANCA-associated vasculitis affects the small vessels in different organs, frequently the kidneys, lungs and skin, thus resulting in various clinical manifestations. The aim of this study is to summarize the published data regarding the frequency and factors that contribute to the development of ANCA and ANCA-associated vasculitis in hyperthyroid patients treated with ATDs.

THE FULL ARTICLE TITLE

Balavoine AS et al. Antineutrophil cytoplasmic antibody-positive small-vessel vasculitis associated with antithyroid drug therapy: how significant is the clinical problem? *Thyroid* 2015;25:1273-81. Epub October 19 2015.

SUMMARY OF THE STUDY

A search of the English medical literature between September 1993 and February 2015 found a total of 261 reports of hyperthyroid patients who developed ANCA-associated vasculitis while taking ATDs. ANCA antibodies were present in the blood in a higher percentage of patients taking PTU (4% to 64%, average 30%) compared to those taking MMI (0% to 16%, average 6%). A high percentage (64%) of children with Graves' disease had ANCA antibodies in a Japanese study. Importantly, only a low proportion of patients with Graves' disease (0% and 13%) had ANCA antibodies before starting ATD treatment. These findings indicate that the initiation of ATD treatment can result in development of ANCA antibodies.

An average of 15% of patients with ANCA corresponding to 3% of all patients taking ATDs developed vasculitis related to ANCA, 75% of these patients being on PTU, while 25% were on MMI. Patients with high blood ANCA levels and those taking ADT treatment for a long period of time had a higher risk to develop vasculitis. Based on the cases reported to the FDA, the risk of vasculitis related to PTU use in children was 50 times higher compared to the risk expected for adults.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

ANCA-associated vasculitis is a very rare but severe side effect from ATD treatment. Risk factors for this disorder including the type of medication used (PTU vs. MMI), longer treatment duration and young age. Consistent with the guidelines published by the American Thyroid Association, MMI should be the ATD treatment of choice, since more cases have been associated with PTU than MMI use. ANCA-associated vasculitis develops usually after months to years of treatment. However, there are no current recommendations to screen for the presence of ANCA in the blood the patients who are on ATD treatment for a long period of time. The ATD treatment should be discontinued immediately in patients who develop vasculitis, and this usually results in a rapid clinical improvement. Blood ANCA levels usually decrease; however, they can remain detectable for years after the ATD discontinuation. Children with Graves' disease on ATD treatment should be monitored closely, since they have a higher risk of developing ANCA and ANCA-associated vasculitis.

— Alina Gavrilă, MD, MMSC

ATA THYROID BROCHURE LINKS

Hyperthyroidism: <http://www.thyroid.org/hyperthyroidism/>

Graves' Disease: <http://www.thyroid.org/graves-disease/>

**HYPERTHYROIDISM**, continued**ABBREVIATIONS & DEFINITIONS**

Antineutrophil Cytoplasmic Antibody (ANCA)—autoantibodies directed against antigens from polynuclear neutrophils and monocytes, which represent different types of white blood cells, the infection-fighting cells of the blood.

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

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease (autoantibodies).

Methimazole: 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.

Agranulocytosis: a marked decrease in the white blood cell count that causes a patient to be more likely to develop an infection. This is commonly associated with a fever and/or a sore throat.

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

Graves' disease: the most common cause of hyperthyroidism in the United States. It is an autoimmune disease caused by antibodies that attack the thyroid and turn it on.