

## Arthritis associated with carbimazole therapy

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### Abstract

#### *Presentation*

A lady in her 40s came to the Medical Assessment Unit with a swollen, painful left wrist for one week and was unable to make a fist. She has no previous rheumatological condition. She was recently diagnosed with hyperthyroidism two months ago and started on carbimazole 30mg once a day. This dose was reduced to 20mg due to intolerance and derangement in her liver function test and low WCC. She stopped carbimazole a week before her presentation.

#### *Diagnosis*

X-ray results showed normal joint alignment and no evidence of chondrocalcinosis. Chest X-ray was unremarkable. Based on the clinical history and examination, a suspicion of Arthritis related to antithyroid drugs was raised, as there was very low suspicion of crystal disease or inflammatory arthritis. Blood tests including ANA, ENA, RF, CCP, and ANCA all came back negative, essentially ruling out autoimmune arthritis, vasculitis/ connective tissues and further solidifying the diagnosis of drug-related arthritis.

#### *Treatment*

An attempt to aspirate the joint was made however it was a dry tap on 2 attempts and the joint was injected with 40mg of Depomedron and 0.5ml 1% lidocaine. The patient had immediate relief in terms of pain. Telephonic follow-up after 1 week showed completed resolution of swelling and regain of normal function. On discharge, the patient's treatment was already changed to propylthiouracil 100mg once a day.

The patient did not have any further arthralgia and arthritis on new treatment and is currently being followed up in the Endocrine clinic.

#### *Discussion*

Antithyroid medications used for hyperthyroidism treatment can cause various side effects, including severe ones like Antithyroid Arthritis Syndrome (AAS), presenting as joint pain, fever, and rash. AAS is

an autoimmune drug reaction, often misdiagnosed as connective tissue disease or ANCA-positive vasculitis. Its exact mechanism is unclear, but it may involve copper complex formation causing synovial inflammation or autoantibody production. Arthralgia, a milder side effect, doesn't require treatment cessation but can be an early sign of arthritis. This case highlights the important information about antithyroid medications and their potential side effects, with a specific focus on Antithyroid Arthritis Syndrome (AAS) which is a rare side effect of antithyroid medications.

## Presentation

A 49-year-old lady of African origin, presented to the Medical Assessment Unit with a swollen left wrist for one week and an inability to make a full fist after she woke up in the morning. She denied any trauma, fall, or twist recently. She has no previous history of any rheumatological conditions. She also complained of shoulder pain that lasted for a week along with tiredness, sickness, and lack of energy. She tried Ibuprofen (NSAID) for pain relief, which helped with the pain but made her nausea worse.

At this point, no other joints were involved, and there was no rash, fever, or any other systemic symptoms. No red flags of inflammatory arthritis were found. No triggering factors (red meat, alcohol excess, diuretics, dehydration) for gout were identified. There was no history of any recent infectious (viral) triggers.

She was a mother of three children, and she was attributing her agony to holding her newborn baby, even though she had previously experienced no such problems.

She was diagnosed with autoimmune hyperthyroidism (Hashimoto's with positive TRAB and TPO antibodies) 2 months before this presentation and was commenced on Neomercazole 30mg. The patient was intolerant to this dose and developed shoulder griddle pain and generalized arthralgia along with elevated liver enzymes and low WCC. Hence dose was reduced to 20mg and stopped a week before the presentation.

She had no additional co-morbidities, was a non-smoker, drank no alcohol, and worked as a homemaker. She had no allergies documented.

On examination patient was vitally stable and afebrile, cardiovascular, respiratory, and GI exams were unremarkable.

The musculoskeletal exam showed a good range of movement in both shoulders. The left wrist was tender and swollen, more prominent on the dorsal aspect along with restricted movement and a loose grip. Neurovascular exam was normal.

## Diagnosis

All baseline tests were requested including an x-ray of the wrist joint to evaluate further. The blood panel is below

<b>Hemoglobin</b>	<b>9.4</b>	<b>g/dl</b>	<b>12.0 to 15.0</b>
<b>MCV</b>	<b>84.0</b>	<b>fl</b>	<b>83 to 101</b>
<b>WCC</b>	<b>5.8</b>	<b>x10<sup>9</sup>/l</b>	<b>4.0 to 10.0</b>
<b>Platelets</b>	<b>367</b>	<b>10<sup>9</sup>/L</b>	<b>150 to 410</b>
<b>Prothrombin Time(Plasma)</b>	<b>14.0</b>	<b>secs</b>	<b>9.4 to 12.5</b>
<b>Urea</b>	<b>4.7</b>	<b>mmol/L</b>	<b>2.5 to 6.7</b>
<b>Creatinine</b>	<b>49</b>	<b>umol/L</b>	<b>49 to 90</b>
<b>Estimated GFR</b>	<b>123</b>		<b>61 to 249</b>
<b>Sodium</b>	<b>140</b>	<b>mmol/L</b>	<b>136 to 145</b>
<b>Potassium</b>	<b>3.5</b>	<b>mmol/L</b>	<b>3.5 to 5.1</b>
<b>Total Bilirubin(Adult)</b>	<b>4</b>	<b>umol/L</b>	<b>3.4 to 20.5</b>
<b>ALT (SGPT)</b>	<b>16</b>	<b>U/L</b>	<b>1 to 55</b>
<b>Gamma G.T</b>	<b>134</b>	<b>U/L</b>	<b>9 to 36</b>
<b>Alk.Phosphatase</b>	<b>125</b>	<b>U/L</b>	<b>40 to 150</b>
<b>Albumin</b>	<b>39</b>	<b>g/L</b>	<b>40 to 150</b>
<b>Total Protein</b>	<b>71</b>	<b>g/L</b>	<b>64 to 83</b>
<b>Corrected Calcium</b>	<b>2.40</b>	<b>mmol/l</b>	<b>2.10 to 2.60</b>
<b>Phosphate</b>	<b>0.94</b>	<b>mmol/L</b>	<b>0.74 to 1.52</b>
<b>C- Reactive Protein</b>	<b>52.0</b>	<b>mg/L</b>	<b>0.2 to 5.0</b>
<b>Rheumatoid Factor</b>	<b>13</b>	<b>IU/mL</b>	<b>0 to 30</b>
<b>Uric Acid</b>	<b>336</b>	<b>umol/L</b>	<b>150 to 350</b>
<b>Iron</b>	<b>3.9</b>	<b>umol/L</b>	<b>9 to 30.4</b>
<b>Transferrin</b>	<b>1.18</b>	<b>g/L</b>	<b>1.8 to 3.82</b>
<b>Transferrin Saturation</b>	<b>13.2</b>	<b>%</b>	<b>20 to 50</b>
<b>B12</b>	<b>1869</b>	<b>pg/mL</b>	<b>187 to 883</b>
<b>Folate</b>	<b>8.0</b>	<b>ng/mL</b>	<b>3.1 to 20.5</b>

<b>Ferritin</b>	<b>581</b>	<b>ng/mL</b>	<b>5 to 204</b>
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Chest X-ray was unremarkable.

Based on the clinical history and examination, a suspicion of Arthritis related to antithyroid drugs was raised, as there was very low suspicion of crystal disease or inflammatory arthritis.

Blood tests including ANA, ENA, RF, CCP, and ANCA all came back negative, essentially ruling out autoimmune arthritis, vasculitis/ connective tissues and further solidifying the diagnosis of drug-related arthritis.

### **Treatment**

An attempt to aspirate the joint was made however it was a dry tap on 2 attempts and the joint was injected with 40mg of Depomedron and 0.5ml 1% lidocaine. The patient had immediate relief in terms of pain.

Telephonic follow-up after 1 week showed completed resolution of swelling and regain of normal function.

On discharge, the patient's treatment was already changed to propylthiouracil 100mg once a day.

The patient did not have any further arthralgia and arthritis on new treatment and is currently being followed up in the Endocrine clinic.

### **Discussion**

Antithyroid medications are widely used for the treatment of hyperthyroidism along with radioactive iodine and surgery. These medications include thiouracil derivate (propylthiouracil) or thioimidazol derivate (carbimazole, methimazole, and thiamazole). These medications come with a variety of side effects ranging from mild cutaneous reactions and arthralgias to life-threatening ones like agranulocytosis, hepatitis, and polyarthritis. The side effects are also dose-dependent<sup>1</sup>.

Antithyroid arthritis syndrome (AAS) is an underappreciated medical condition that occurs within eight weeks of starting antithyroid medications. The patient usually presents with arthralgia, myalgia, arthritis, fever, and rash. It is an autoimmune idiosyncratic drug reaction that usually settles once the

offending medication is stopped. However, the symptoms may persist for years. NSAIDs can be used for pain relief. However, corticosteroids are not recommended due to reduced efficacy. The symptoms are usually similar to connective tissue disease and ANCA vasculitides and therefore this condition can be easily misdiagnosed<sup>2</sup>. The exact mechanism is not known but many of the researchers believe that the antithyroid agents make a complex with copper which affects the glutathione metabolism resulting in the release of interleukins to cause synovial inflammation. Alternatively, some of the researchers claim that the antithyroid agents bind to the macromolecules resulting in autoantibody production leading to inflammation. However, there is no evidence of antibody production in this syndrome. The onset of symptoms and the presence or absence of autoantibodies (ANCA) helps in the diagnosis of this condition<sup>3</sup>.

In contrast to antithyroid arthritis syndrome, arthralgia is a mild side effect of antithyroid medications. It does not necessitate cessation of the treatment and doesn't raise inflammatory markers like ESR and CRP. However, this could be the earliest symptom of arthritis<sup>4</sup>.

#### **Declarations of Conflicts of Interest:**

None declared.

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