Neutropenic Fever: A Rare Life-threatening Complication of Methimazole induced Agranulocytosis.

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INTRODUCTION

Agranulocytosis is an infrequent but potentially life-threatening complication of antithyroid medications such as methimazole. Patients recently started on antithyroid medicines should be closely monitored for flu-like symptoms such as fever and sore throat, followed by timely discontinuation of medications to prevent fatal outcomes. Clinicians may be faced with diagnostic uncertainty when patients on methimazole present with symptoms of hyperthyroidism such as fever, diarrhea, and laboratory derangements like neutropenia.¹ ²

CASE DESCRIPTION

A 21 year old female with a past medical history of Grave’s disease presented with fever, vomiting and watery diarrhea for 5 days.

She was started on methimazole 3 weeks prior due to thyrotoxicosis.

Physiological Exam

- Patient appeared diaphoretic and tremulous.
- Mucous membranes were dry with posterior oropharyngeal erythema and palpable anterior cervical lymph nodes.
- Thyroid gland was warm and enlarged.

Initial Labs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total WBC Count</td>
<td>1800/mL</td>
</tr>
<tr>
<td>Absolute Neutrophil Count</td>
<td>580</td>
</tr>
<tr>
<td>TSH</td>
<td>&lt;0.05 uIU/mL</td>
</tr>
<tr>
<td>Free T4</td>
<td>4.69 ng/dL</td>
</tr>
<tr>
<td>Free T3</td>
<td>23.56 ng/dL</td>
</tr>
<tr>
<td>Thyroid Stimulating Antibody</td>
<td>457%</td>
</tr>
</tbody>
</table>

Vitals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>102.6°F</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>112/min</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>117/68 mm Hg</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>22/min</td>
</tr>
<tr>
<td>SpO₂</td>
<td>98% on room air</td>
</tr>
</tbody>
</table>

Clinical Course

1 Year Ago
- COVID-19 infection followed by ongoing unrecognized hair loss, palpitations, insomnia, unintentional weight loss.

3 Months Ago
- Incidental finding of significantly enlarged thyroid gland on CT head and C-spine.

2 Months Ago
- Blood work consistent with hyperthyroidism.

1 Month Ago
- Thyroid Ultrasound: Thyromegaly. Diffusely heterogeneous thyroid parenchyma without discrete nodule. Diffusely increased thyroid parenchymal vascularity.
- Thyroid uptake scan: Markedly enlarged thyroid gland with homogenous glandular activity, compatible with Graves’ disease.
- Initiated on metoprolol.

15 Days Ago
- Presented to the emergency room in thyroid storm. Initiated on methimazole 1.5 mg three times daily, propranolol, cholestyramine. Patient had resolution of symptoms outside of mild tremor and intermittent palpitations.
- Methimazole increased to 30 mg three times daily along with propranolol.

Day 1
- Presented to the emergency room again with worsening fever, diarrhea, nausea, vomiting.
- Total white blood cell (WBC) count of 1800/mL with an absolute neutrophil count (ANC) of 580. Methimazole was held.

Day 2
- Started on cefepime due to concern of neutropenic fever. A gastrointestinal source was considered given her presenting symptoms, and meningitis was feared on day 2 when she endorsed a new headache and had neck stiffness prompting a lumbar puncture.

Day 5
- Despite extensive workup, could not find a source of infection and antibiotics were discontinued. Subsequently, started on filgrastim. ANC improved to 3007/mL after 2 days following a nadir of 380/mL.

Day 7
- The patient underwent a total thyroidectomy on day 7 and was discharged home with a plan for outpatient follow-up with endocrinology.

DISCUSSION

- Antithyroid drugs should be held as early as possible in patients presenting with infectious symptoms and should be checked for neutropenia to prevent fatal complications such as neutropenic sepsis.¹ ²
- Moreover, patient education is critical and should not be undervalued during the prescription of antithyroid drugs.¹

REFERENCES


CT Brain & Cervical Spine without contrast – Marked thyromegaly with tracheal narrowing.

Thyroid uptake scan - markedly enlarged thyroid gland with homogenous activity consistent with Grave's disease.