Different Cause of Thyrotoxicosis - Alemtuzumab Induced Thyrotoxicosis

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Introduction:

One of the causes of Thyrotoxicosis can be medication related. Immunotherapies such as monoclonal antibody treatment is associated with thyroid dysfunction, which includes thyrotoxicosis, hypothyroidism or thyroiditis. This is a case report for a different cause of thyrotoxicosis- Alemtuzumab induced thyrotoxicosis.

Alemtuzumab:

Alemtuzumab (Lemtrada, Genzyme, campath) is a anti CD52 monoclonal antibody that binds to CD52 receptors on lymphocytes leading to complement mediated lysis of the cells leading to profound lymphopenia. It is used to treat hematological malignancies, patients with stem cell transplant, autoimmune disorders such as multiple sclerosis and vasculitis.

NICE has recommended Alemtuzumab as a possible treatment for clinically active relapsing remitting multiple sclerosis defined by clinical features or imaging features. The recommended dose is 12mg/ day by intravenous infusion for 2 treatment courses. The first treatment is for 5 consecutive days followed by 3 consecutive days after one year.

The autoimmune effects are antibody mediated similar to type 2 hypersensitivity reaction, where loss of self tolerance takes place due to severe lymphopenia. The other effects include immune thrombocytopenic purpura, neutropenia and Good pasture syndrome.

Case Report:

30 years old female with history of sinusitis and anxiety states, diagnosed with relapsing multiple sclerosis from May 2005, initially had abnormal sensation and weakness of left side of body with MRI finding of demyelinating lesion in the cervical cord, treated with intravenous methyl prednisolone with good recovery. Unfortunately had multiple relapses, therefore treated with two courses of Alemtuzumab since June 2011. presented with shakiness and a rash in her neck in July 2012. Clinical examination showed a BMI of 24.5, no exophthalmos and no pretibial myxoedema but tremulous sweaty hands. Her investigations as follows:

TSH	**<0.05 mU/l**	**Reference:0.5- 5.5mU/l**
FREE T4	35 pmol/l	Reference: 10.5-20 pmol/l
TPO ANTIBODY	1300	Reference: <50IU/ml
TSH RECEPTOR ANTIBODY	400	Reference: <7U/L

Thyroid function test over the course of three years as follows:

DATE	TSH	FREE T4	FREE T3	Carbimazole
08/11/12	<0.05	21.8	11.3	20 mg
30/11/12	<0.05	14.5	7	10 mg
04/04/13	<0.05	41	18	20mg
11/11/13	27.4	8.8	4.5	10mg
17/01/14	3.32	14.1	-	5mg
22/05/14	<0.05	22.9	-	10mg
08/12/14	9.19	15.1	-	stopped

Discussion:

Her thyroid function test and symptoms were suggestive of thyrotoxicosis, was started on carbimazole 20mg daily by her neurologist and was referred to endocrinology clinic. Her Thyroid receptor antibodies were more than 400 and thyroperoxidase antibodies were more than 1300. After 18 months treatment with carbimazole, was observed with thyroid function tests and had a relapse of thyrotoxicosis in November 2013, she was restarted back on carbimazole. Had a second relapse in September 2015 and received radio iodine due to two relapses, subsequently required thyroxine replacement.

Thyroid dysfunction is diagnosed in up to 30% patients receiving Alemtuzumab with relapsing remitting multiple sclerosis.

Up to 22% had thyrotoxicosis (Graves). This can occur between 6 months to 60 months.

40% required anti thyroid medication, 12% were treated with anti thyroids and radio active iodine and 6% with radio active iodine alone.

15% spontaneously developed hypothyroidism and 23% became euthyroid over 80 months follow up.

Un recognized thyrotoxicosis affects metabolism of other medications that the patients with multiple sclerosis are taking.

The management of Alemtuzumab induced thyrotoxicosis is similar to wild type Graves disease.

Early recognition and treatment is essential for improving the Quality of life.

Its is recommended that TSH should be tested before starting the treatment and every 2-3 months of during Alemtuzumab therapy and 3 monthly upto 4 years after the last treatment.

Conclusion:

Despite the proven efficacy in reducing the relapses and disability in multiple sclerosis, Auto immune disease remains at significant risk. The adverse effect could be due to secondary auto immune disease through suppression of suppressor T lymphocytes. It particularly affects the thyroid gland in up to 20 to 30 percent of patients treated with Alemtuzumab.

This case highlights the need for the physicians using alemtuzumab to be vigilant on the presentation of thyroid dysfunction, thyroid function test at the earliest and prompt treatment.

References:

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Thyroid

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