The curious case of thyroid dysfunction and the monoclonal antibody

NHS
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INTRODUCTION

- Alemtuzumab was the first humanised monoclonal antibody. It is used in haematological malignancies and multiple sclerosis.
- It is associated with secondary autoimmune adverse effects including Graves' disease, hypothyroidism, Goodpasture's disease and ITP.

THE CASE

A 46-year old male

Background: Relapsing remitting multiple sclerosis July 2011.

2 relapses on β-IFN-1a.

Rx: Alemtuzumab infusion 12 mg for 5 days (12/08/12)

12 months later 12 mg for 3 days (12/08/13)

No family history of autoimmune disease

No dysthyroid symptoms

Deranged thyroid tests on regular monitoring 25 months after last infusion

Examination: Pulse 68/min, regular

No goitre or neck nodules

No peripheral or eye signs of Graves' disease

Date & Drug Treatment	TSH (mu/l, 0.34-5.6)	FT3 (pmol/l, 3.8-6.0)	FT4 (pmol/l, 7.9-20.0)
26/03/15	2.69		
28/07/15	0.93		
28/07/15 Carbimazole 20 mg/d	**0.18**	**28.9**	**54.0**
25/09/15 Carbimazole 5 mg/d	0.15	4.2	10
03/11/2015 Levothyroxine 50 mcg/d	**75.8**	**3.6**	**4.6**
24/12/2015	7.5	5.0	12.5

Other Investigations:

- Anti TPO antibodies- positive at 65 IU/ml (0-8)
- Anti TSH Receptor antibodies positive at > 40 U/l (<1.8)

Levothyroxine was increased to 100 mcg/d, patient now doing well.

Adverse effects	Care MS I & II Trials [1] Alemtuzumab 12mg			
	Year 1 (n=811)	Year 2 (n=810)	Year 3 (n=772)	Year 4 (n=731)
Hyperthyroidism	1.2%	4.1%	11.9%	6.0%
Hypothyroidism	1.7%	2.7%	4.9%	2.7%
Thyroiditis	0.7%	1.5%	1.9%	1.4%

DISCUSSION

1. The incidence of thyroid dysfunction associated with Alemztuzumab can be up to 36%[2].
2. Mechanism of autoimmunity: profound lymphopenia and raised IL-21 levels increase cell cycling, leading to self reactive T-cells.
3. A range of thyroid disorders can be associated with Alemtuzumab - Graves' disease, thyroiditis, subclinical thyrotoxicosis and hypothyroidism[3].
4. Patients can have no symptoms, as in our case, so regular monitoring is essential.
5. Anti-thyroid drugs, radioiodine treatment and surgery have all been used successfully in this condition[4].

Take Home Messages

- Alemtuzumab causes autoimmune thyroid dysfunction in about 30% cases
- Regular monitoring of thyroid tests following Alemtuzumab are required for at least 4 years after the last infusion

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