Immune changes are observed after radioiodine treatment for hyperthyroidism in Graves’ disease patients

Sarah Côté-Bigras¹, Jean Verreault², Diane Rottembourg³

¹Department of Pediatrics, Department of Nuclear Medicine and Radiobiology, Faculty of Medicine, University of Sherbrooke, Canada

Introduction
Graves’ disease (GD) involves autoimmunity against thyrotropin receptor (TSHR) bearing cells, leading to hyperthyroidism and often orbitopathy. When hyperthyroidism is treated with radioactive iodine (RAI), exacerbation of the orbital disease can occur.

Hypothesis
We hypothesized that RAI has immune effects affecting the balance between auto-reactive T cells and T cells with regulatory properties.

Methods
• Identifying TSHR peptide sequences targeted by auto-reactive T cells
  Circulating T cell interferon gamma (IFN-γ) production in the presence of TSHR peptides was measured by ELISPOT assay.
• Monitoring lymphocyte populations
  o Regulatory CD4+CD25highFOXP3+ (Treg) and Natural Killer Vα24-Vβ11·CD3+ (NKT) T cells were counted by flow cytometry.
  o Treg immunosuppressive property in inhibiting non-specific proliferation of dye-labeled responder T cells was assessed by in vitro co-culture assay.

Data analysis
All data were expressed as the mean ± SEM. Statistical comparisons were performed using One-way ANOVA (Figure 1, 2A et 4), Kruskall-Wallis ANOVA (Figure 2B) and F Test (Figure 3). P values < 0.05 were considered to be statistically significant; **P < 0.01; *** P < 0.001; NS, Not significant.

Results

Figure 1. RAI therapy has a mild effect on auto-reactive T cells specific to thyroid peptides. T cell IFN-γ production in the presence of TSHR peptides was measured in 10 GD patients and in 10 HS. Significant response to at least one peptide was measured in 2/10 (○ and □) and 3/10 (○, □ and ⊱) GD patients before and after RAI therapy, respectively, and in none of the controls.

Figure 2. There is a decrease in frequency of Treg but not NKT cells before RAI treatment in GD patients. Treg (A) and NKT (B) cells were counted in 24 GD patients and in 5 NG patients before RAI treatment, as well as in 19 untreated HS over the same time period.

Figure 3. Numerical variation of Treg and NKT cells after thyroid radiation appears to be greater in GD patients. Proportion variation of Treg (A) and NKT (B) cells were analysed in 13 GD patients and in 3 NG patients before and one month post-RAI treatment, as well as in 15 untreated HS over the same time period.

Figure 4. RAI therapy induces a decrease in the suppressive function mediated by Treg in GD patients. Suppressive capacity of Treg was assessed in 9 GD patients and in 3 NG patients before and one month post-RAI treatment, and in 9 HS over the same time period. Responder T cells from the pre-treatment sample were co-cultured with Treg.

Conclusion
RAI therapy in GD patients induces:
• Changes in frequency of peripheral T cells with regulatory properties
• A decreased suppressive function mediated by Treg.

These effects may be involved in the exacerbation of autoimmune processes observed following radiation damage to the thyroid gland.

Targeting Treg could be a promising approach in controlling autoimmune processes following this treatment.