66P: TGF-β1, A CRUCIAL MEDIATOR OF RADIOIODINE THERAPY-INDUCED ANTI-TUMOR IMMUNITY

Adina Elena Stanciu[1], Madalina Bolovan[1], Anca Zamfirescu[2], Marcel Marian Stanciu[3], Marieta Elena Panait[4]

[1]Department of Carcinogenesis and Molecular Biology, Institute of Oncology Bucharest, Romania; [2] Department of Radionuclide Therapy, Institute of Oncology Bucharest, Romania; [3]University Politehnica of Bucharest, Bucharest, Romania; [4]Department of Cancer Biology, Institute of Oncology Bucharest, Romania

Institutul Oncologic Prof.Dr. Alexandru Trestioreanu Bucuresti

Introduction

The success of radioiodine (^{131}I) therapy for papillary thyroid cancer (PTC) is conditioned by the ability of thyroid follicle cells to take up and concentrate iodide [1]. The latest research shows that concurrent Hashimoto's thyroiditis (HT) may impair the ^{131}I uptake in PTC patients [2]. Transforming growth factor-beta 1 (TGF-β1) is involved in various aspects of the immune responses (regulates T-cell homeostasis through multiple mechanisms and modulates the response to exposure to ionizing radiation). Ablative radiotherapy dramatically increases T-cell priming in draining lymphoid tissues, leading to reduction/eradication of the primary tumor or distant metastasis in a CD8+T cell-dependent fashion [3].

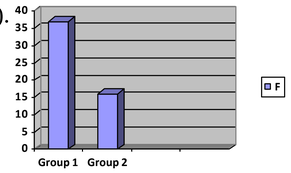
Aim

The study aimed to investigate the differential effect of TGF-β1 on CD8+ T-cells and CD19+ B-lymphocytes in response to ^{131}I therapy in PTC and PTC+HT patients.

Methods and Patients

Patients:
Group 1: 37 female patients with PTC (mean age 42.9±11.8 years)
Group 2: 16 female patients with PTC+HT (mean age 40.1±11.6 years)

All patients received the same dose of ^{131}I (3.7 GBq, first dosage after thyroidectomy).



Methods:
Peripheral blood samples were collected before and 4 days after ^{131}I. The lymphocyte subpopulations were measured by flow cytometry (BD Simultest IMK- Lymphocyte). The serum levels of TGF-β1 and TgAb were measured by ELISA. A dose calibrator was used to measure blood activity with a microcurie accuracy.

Results

Radioactivity of the blood samples was higher in PTC+HT patients than in those without HT (P<0.001). Increased radioactivity of blood collected 4 days after the same dose of ^{131}I/patient intake indicates a low ^{131}I uptake in the PTC+HT group.

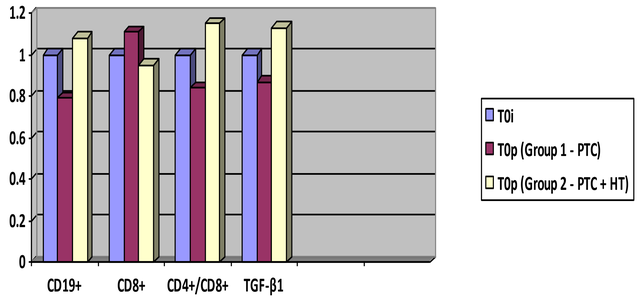
Results

The rate of change was defined as the ratio between the variable measured at time T0p and the baseline value (T0i). These new variables are dimensionless quantities, expressed by number one.

Table 1. Rates of change for each measured biomarkers in the two groups

Biomarkers / Patients	CD19+		CD8+		CD4+/CD8+		TGF-β1	
	T0i	T0p	T0i	T0p	T0i	T0p	T0i	T0p
Group 1 (n=37)	1.00	0.79	1.00	1.11	1.00	0.84	1.00	0.87
Group 2 (n=16)	1.00	1.08	1.00	0.95	1.00	1.15	1.00	1.13

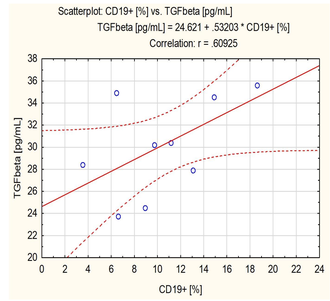
Group 1 – PTC (Papillary Thyroid Cancer)
Group 2 – PTC + HT (Papillary Thyroid Cancer + Hashimoto's thyroiditis)
T0i – baseline (before I-131 therapy)
T0p – 4 days after I-131 therapy

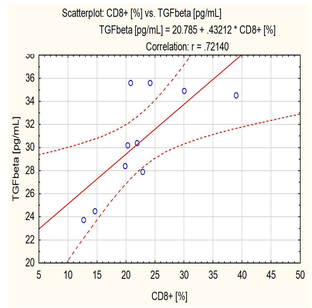


Variation of analyzed biomarkers in the two groups (before and after ^{131}I therapy)

Group 1 (PTC)
TGF-β1 inhibition, after ^{131}I therapy, enhanced anti-tumor immunity mediated by CD8+ T-cells.

Group 2 (PTC+HT)
Increased TgAb titers partially block the therapeutic effect of ^{131}I therapy. CD19+ B lymphocytes titers are associated with increased TGF-β1 concentrations and decreased tumor-specific CD8+ T-cell response. TGF-β1 activation decreased the anti-tumor efficacy of ^{131}I therapy in PTC+HT patients.





Correlations between TGF-β1 and CD19+, CD8+ T cells in PTC+HT group

Conclusions

- The therapeutic efficacy of targeted radionuclide therapy with high-dose depends on the presence of CD8+ T cells both before and after ^{131}I intake.
- Our results identify the inhibition of TGF-β1 as the mechanism through which ^{131}I high-dose supports the function of local, tumor-specific CD8+ effector T cells.
- Our results suggest that TGF-β1 may exert different anti-tumor effects in response to ^{131}I therapy depending on the patients' immune profile.

References

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For more information:
Email: adinaelenastanciu@yahoo.com