

Hypothyroidism related to blocking TSH receptor antibodies (TRAb) after allogenic Hematopoietic Stem Cell Transplantation (allo-HSCT)

Kanza BENOMAR^(a), Catherine MASSART^(b), Leonardo MAGRO^(a), Anne Sophie PARENT^(a),
Michele DHERBOMEZ^(a), Ibrahim YACOUB AGHA^(a), Jean-Louis WEMEAU^(a), Marie Christine VANTYGHM^(a)

(a) Department of, Endocrinology and Metabolism, Biology, Blood diseases, Lille University Hospital

(b) Department of biology and biochemistry, CHU Pontchaillou, Rennes University FRANCE

INTRODUCTION

Allogenic Hematopoietic Stem Cell Transplantation (allo-HSCT) is used as a treatment option in different blood diseases like patients with Acute Myeloid Leukemia (AML). Besides total body irradiation and immunosuppressives drugs (tyrosine kinase inhibitors, bexarotene, alemtuzumab, interferon alpha), massive iodine supply and stress might participate in thyroid dysfunction reported in 50% of allo-HSCT. Primary hypothyroidism occurs in about half of irradiated patients in the year following radiotherapy¹. We report on a rare case of hypothyroidism related to blocking TRAb.

CASE REPORT

A 55-year old man was admitted for myalgia, asthenia, dyspnea, 8kg weight gain, constipation, dry skin, hoarse voice and recent deafness. He had moon face without any goiter. One year before, he had received an unrelated 9/10 human leukocyte antigen matched allo-HSCT for acute myeloid leukemia after chemotherapy including antilymphocyte serum and had achieved full female donor chimerism. He developed an acute graft-versus-host disease (GvHD) grade II one month posttransplantation treated with ciclosporine. Laboratory tests showed high blood cholesterol (3,53g/L; N: 1,5-2,4), triglycerides (2,7g/L; N: 0,3-1,5), CPK (2623U/L; N<195), and TSH (99mUI/mL; N>3,5) levels as well as antithyroperoxidase (179 U/mL; N<4) and TSH receptor antibodies (TBII: 102; N<1) levels with undetectable FT4 and anti-thyroglobulin antibodies. The functional study of TBII confirmed high blocking (TRAbs 92%; N<30) and low stimulating (TSAbs 58%; N<125) activities. The immunophenotyping analysis showed a circulating lymphopenia affecting CD4⁺ (610/mm³; N: 700-1100) and CD8⁺ (351/mm³; N: 500-900). Thyroid ultrasound was normal, Electrocardiogram showed a sinus rhythm with low QRS voltages and widespread T-wave inversions (Figure 1). Levothyroxine treatment was introduced with good clinical and biological evolution and improvement of the electrocardiogram.

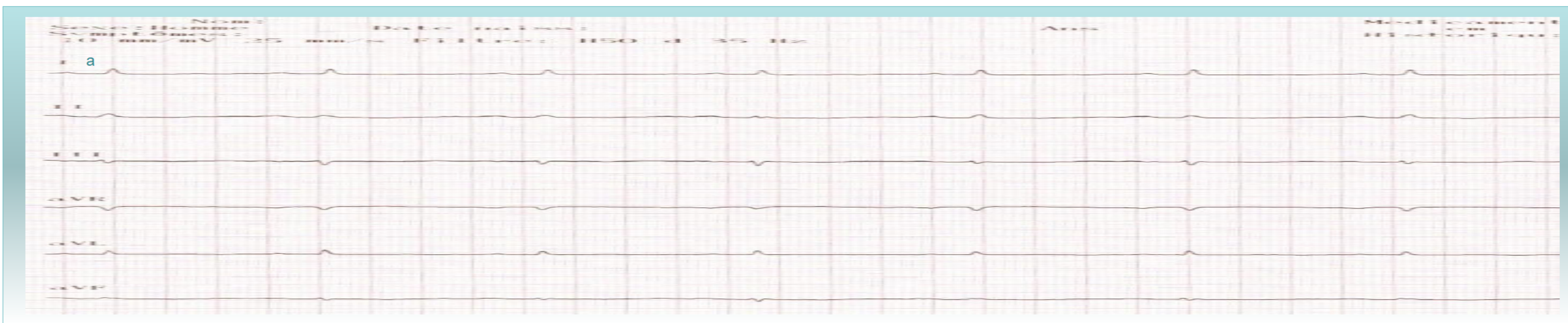


Figure 1 : Electrocardiogram with low QRS voltages and widespread T-wave inversions.

DISCUSSION

The development of autoimmune hypothyroidism is frequent post allo-HSCT and requires regular monitoring of TSH and T4 values, given the difficulty of diagnosis in patients whose complaints can easily be attributed to the causal disease or GvHD.

Immunological dysregulation during T cell engraftment may also favour hyperthyroidism (Graves disease), sometimes preceded by a hypothyroid episode related to blocking TBII, called immune reconstitution syndrome. The presence of blocking TBII has been attributed to donor recipient transfer of B and T lymphocytes (here a female donor) favoring the occurrence of hyperthyroidism. This rare and delayed syndrome has been reported in children post allo-HSCT² or after HIV treatment³ and coincided with a rapid expansion in naive and total CD4. TSAbs and TBAbs have been shown to have similar characteristics (high affinity and similar binding epitopes on the TSH-R). The occurrence of "switching" emphasizes the need for careful patient monitoring and management.

CONCLUSION

Endocrinologists should be aware of this rare but potentially severe adverse event. Thyroid function should be monitored periodically after hematopoietic stem cell transplantation because of its significant incidence especially in the patients who developed a GvHD after alloHSCT.

REFERENCES

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