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RESEARCH ARTICLE

HYPOTHYROIDISM DURING ONCOLOGY PROTOCOLS: A REPORT ON THREE CASES

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Abstract

Introduction: Hypothyroidism is commonly associated with different types of chemotherapy and immunotherapy. However, it remains largely unexplored, untreated, and is often neglected. We have reported 3 cases in order to highlight this endocrine consequence

Cases Report: The first two cases we reported were carriers of autoimmune thyroiditis with radio-biological confimation responsible for hypothyroidism. The first of them was followed up for colorectal carcinoma under chemotherapy with 5Fluorouracil based molecules and platinum drugs, the second case for metastatic pulmonary adenocarcinoma under immuno-chemotherapy: bevacizumab, paclitaxel and carboplatin. However, the last patient presented with hypothyroidism due to thyroid atrophy with negative immunological work-up, and was being treated for cavitary neoplasia with cisplatin and doxorubicin.

Discussion and Conclusion: Cytotoxic effects of chemotherapy due to ribonucleic/desocyrubonucleic alteration, followed by cell apoptosis concerns tumour tissue, but also rapidly metabolising tissues such as the endocrine glands, and particularly thyroid cells, causing thyroid atrophy. In the other hand, immunomodulatory effects are responsible for thyroiditis. While immunotherapies involve cytotoxicity of T lymphocytes, classically resulting in hypothyroidism sometimes preceded by thyrotoxicosis, leading in all cases to induced hypothyroidism.

Introduction:-

Thyroid disorders are the most common endocrinopathies associated with immunotherapy and chemotherapy, dominated by hypothyroidism, and should be systematically screened before and after any protocol. Management is usually based on substitution, except in rare cases, but this should not contraindicate the resumption of treatment.

For this reason, multidisciplinary consultation is desirable in order to monitor these patients.
We are going to discuss this side effect through 3 cases that we received in endocrinology consultation.

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Cases report :

Case 1:

A 65-year-old patient treated for colorectal carcinoma who had undergone capicetabine and oxaliplatin-based chemotherapy, the last of which had been given 2 months previously. He was referred to us for management of hypothyroidism with TSH greater than 100 uUi/l due to thyroiditis, which was diagnosed on the basis of a heterogeneous stippled appearance on cervical ultrasound and hypermetabolic on FDG PET, in addition to a positive immunological work-up with anti-TPO antibodies: 121.10 ui/ml and anti-TG antibodies: 576 ui/ml. The patient was gradually treated with levothyroxine up to a dose of 75ug/d with a good clinico-biological progression: The control TSH level was 11.5 ui/ml, prompting a therapeutic adjustment to 100 ug/d of levothyroxine.

Case 2:

A 62-year-old patient undergoing treatment for metastatic lung neoplasia who had received immunochemotherapy with bevacizumab, paclitaxel and carboplatin.

Referred to us for hypothyroidism with TSH level at 44.024 uui/ml due to thyroiditis, identified by ultrasound, and confirmed by positive anti thyroperoxidase antibodie. He was placed on progressive-dose levothyroxine with incremental increases of 25 ug.

Case 3 :

Patient aged 58, followed for a neoplasia of the cavum classified T4N3B having benefited from 33 radiotherapy sessions and 6 chemotherapy sessions based on cisplatin and doxorubicin, and who was referred to us for hypothyroidism 31.93uui/ml on ultrasound thyroid hypotrophy. He was started on levothyroxine at a progressive dose with incremental increases of 25 ug/week up to a dose of 75 ug/day, with good progression.

Discussion and Conclusion:-

It seems that cytotoxic effects of most chemotherapies, such as platinum drugs, doxorubicin, 5FU derivates and cabicetabine, are mainly based on the alteration of DNA and RNA synthesis.

In fact, it seems that the metabolism of chemotherapy drugs blocks anabolic pathways, which disrupts the synthesis of DNA (deoxyribonucleic acid), and also leads to inhibition of RNA and protein synthesis. Since DNA and RNA are essential for cell division and growth, it is conceivable that these chemicals may cause imbalances between cell growth and apoptosis, and can also deteriorate mitotic phases, as in the case on pactitaxel. These effects are more intense in cells that proliferate and metabolise more rapidly, as in tumour processes, but also in the endocrine system, particularly thyroid. This induces thyroid atrophy by various mechanisms, as in the case of our last patient, and autoimmune thyroiditis, as in the case of our first two patients. However, certain similarities between capecitabine in particular and synthetic antithyroid drugs are suspected in the pathophysiology of hypothyroidism during chemotherapy. This effect could be linked to the structural similarity between 5FU and propylthiouracil, that suggests that 5FU based chemotherapies inhibits the thyroperoxidase which is responsible for releases iodine to be added to the tyrosine residues of thyroglobulin in order to produce thyroid hormones, and also inhibits the enzyme 5′ deiodinase, which converts T4 into T3.

Relying on this effect, capicetabine is increasingly being tested in thyroid carcinoma chemotherapy, especially CMT, but its effectiveness is still limited.

On the other hand, immunotherapies involve cytotoxicity of T lymphocytes, classically resulting in hypothyroidism sometimes preceded by thyrotoxicosis.

Several cases have been reported in the literature attesting to a decrease in thyroid function associated or not with underlying autoimmune thyroiditis

Disclosure:

The authors have no conflicts of interest to disclose.

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