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RESEARCH ARTICLE

DILATED CARDIOMYOPATHY: COMPLICATION OF POST-RADIATION HYPOTHYROIDISM: ABOUT A CASE AND REVIEW OF THE LITERATURE

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Abstract

Introduction: Dilated cardiomyopathy (dcm) can result from a prolonged thyroid hormone deficiency. If pericardial effusion is the most frequent cardiac involvement; found in 30% of cases; myxedematous dcm is rare and therefore its frequency is difficult to determine.

Clinical Case: We report the case of a 53-year-old patient admitted to the emergency room for management of an attack of global heart failure related to a dilated cardiomyopathy with severe left ventricular dysfunction secondary to a hypothyroidism discovered in the aftermath radiation therapy for breast cancer. The evolution was favorable after the administration of hormone replacement therapy with total disappearance of clinical signs, normalization of the thyroid balance and recovery of left ventricular function.

Discussion: The clinical signs of post-radiation hypothyroidism are frequently blunt and unspecific. They can be confused with clinical signs and treatment of the disease as well as with its nutritional, physical and psychological consequences. The average time to onset of post-radiation hypothyroidism is estimated by the majority of authors between 2 and 5 years. The prolonged deficit in thyroid hormones leads to cardiovascular disturbances. This suggests that this deficiency changes the geometry, relaxation and contraction of the heart muscle. Dcm is therefore considered a rare presentation of hypothyroidism.

Conclusion: DCM is a progressive dilation of one or both ventricular cavities with impaired contraction of the heart muscle. When it is idiopathic, it is usually an irreversible condition. If the cause is reversible like the case of our patient, the cardiac functions can be restored after treatment of the etiology. This is how we recommend the adequate and diligent treatment of any form of hypothyroidism in order to avoid the passage to the myxoedematous heart stage.

Introduction:-

The reversible form of dilated cardiomyopathy (DCM) can be secondary to alcohol consumption, pregnancy, uncontrolled chronic tachycardia, hypothyroidism, hyperthyroidism, drug use and other endocrine dysfunctions. [1,2]

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The cardiovascular manifestations of hypothyroidism were first described by Zondek in 1918 under the term myxedematous heart. The link between DCM and hypothyroidism has been reported in four patients with heart failure refractory to digitalis and diuretics successfully treated with hormone therapy [3]. Indeed, DCM results from a prolonged deficiency in thyroid hormones of primitive origin or by Hashimoto's thyroiditis. If pericardial effusion is the most frequent cardiac involvement; found in 30% of cases [4,5]; myxedematous DCM is rare and therefore its frequency is difficult to determine [6].

Thyroid dysfunction has been reported to cause accelerated atherosclerotic changes and cardiovascular disease [7]. Currently, it is well established that thyroid hormones have effects on heart function. Hypothyoidia can then cause hemodynamic changes such as bradycardia, decrease in cardiac output from 30% to 50%, mild diastolic hypertension, slightly increased average blood pressure [8] and an increase in serum cholesterol and homocysteine [9,10].

Cardiovascular harm is reversible if hypothyroidism is diagnosed and treated early.

Several etiologies can be at the origin of this thyroid dysfunction including radiotherapy, a technique used as a curative treatment in certain patients with breast and especially cavum cancers. Post-radiation hypothyroidism is a little-known entity because the symptomatology is not very specific and the diagnosis is most often made late.

We illustrate through this work a clinical case of a patient with DCM secondary to post-radiation hypothyroidism in the aftermath of breast cancer; rare but possible outcome; and whose prognosis depends on the earliness of the diagnosis and the therapeutic management.

Clinical Case:
She is a 53-year-old woman, hospitalized in cardiology for an attack of inaugural global heart failure, progressive installation evolving for 5 months. In her history we find breast cancer treated surgically by a mastectomy followed by adjuvant treatment made of chemotherapy and radiotherapy. The patient was put on Herceptin for 5 years and then declared cured. We also note in these antecedents a hospitalization for pericarditis. Two years after the radiotherapy cures, the diagnosis of hypothyroidism was raised and the post-radiation origin was retained. The patient was put on hormone therapy with poor therapeutic compliance.

The patient has no modifiable cardiovascular risk factors.

The clinical examination finds:
1. Blood pressure at 96/65 mmHg
2. Heart rate at 105 cycles per min and 02 saturation at 97% in ambient air.
3. Cardiac auscultation: slight deafening of the heart sounds with a breath of aortic regurgitation and a breath of mitral regurgitation.
4. Signs of right heart failure: Hepatomegaly, edema of the lower limbs reaching the knees.
5. Pulmonary auscultation: rattles crackling at the bases
6. No nodule on palpation of the thyroid gland

The initial electrocardiogram records a regular sinus rhythm at 100 cycles per min, a PR interval at 200 ms.

The chest x-ray shows cardiomegaly with a cardio-thoracic ratio at 0.60 and bilateral hilar overload.

Echocardiography shows dilation of the left ventricle with a telediastolic diameter at 67 mm and a telesystolic diameter at 57 mm. Presence of spontaneous contrast in intra left ventricular (LV). The study of segmental kinetics is in favor of akinesia of the apex, adjacent segments, and middle segments of the anterior and antero-septal walls with hypokinesia of the inferoseptal wall. The systolic function of LV is severely impaired: shortening fraction at 12% and ejection fraction at 22%. Analysis of the pericardium shows minimal circumferential pericardial effusion. The color doppler shows a moderate functional mitral regurgitation by dilation of the mitral ring with a slight aortic regurgitation.

Biological assays show microcytic hypochromic anemia (hemoglobin at 9.1 g/dl), total cholesterol at 2.59 g/l and triglycerides at 2 g/l. The thyroid hormone assay confirms hypothyroidism with an FT4 level of 1.1 ng/l and an

increase in thyroid-stimulating hormone (TSH)> 100 µU / l. Cervical ultrasound shows an atrophy of the thyroid gland. The search for antithyroid antibodies came back negative.

Hormone therapy based on L-thyroxine was restarted at a dose of 25 µg/ day with a progressive dose escalation of 25 µg every 4 to 8 weeks up to a dose of 100 µg/ day. On the cardiac side, the patient was put on an injectable diuretic to control the flare-up of heart failure and then a treatment for chronic heart failure was started based on captopril, bisoprolol and spironolactone combined with an anticoagulant treatment.

Eight weeks after a well-maintained medical treatment, an ultrasound and biological clinical check was carried out and showed a favorable evolution with a disappearance of peripheral signs of hypothyroidism, an improvement in LV function and a normalization of thyroid hormones (FT4 = 12,3 ng/l and TSH = 2.3 µU / l.)

Discussion:-

Most of the publications concerning hypothyroidism after external radiotherapy relate to patients treated for Hodgkin's disease or malignant lymphoma [11], more rarely for cancer of the head and neck (especially of the larynx) [12,13] and exceptionally for breast [14] or nasopharyngeal cancer [12]. The clinical signs of post-radiation hypothyroidism are frequently blunt and unspecific. They can be confused with clinical signs and treatment of the disease as well as with its nutritional, physical and psychological consequences.

Hypothyroidism may be due to a deficiency in TSH or TRH, secondary to hypothalamic-pituitary lesions induced by the treatment of certain cancers [15]. TSH deficiency may be the only manifestation of pituitary damage or be accompanied by a fall in gonadotropins, ACTH or, most commonly, growth hormone [15]. The average time to onset of post-radiation hypothyroidism is estimated by the majority of authors between 2 and 5 years [13]

Regarding breast cancer, publications are rare. Joensuu and Viikari [16] measured TSH and T4 in 80 patients irradiated after mastectomy with an average follow-up of 7.2 years. A dose of 45 Gy was delivered in three or four weeks to the parasternal, subclavicular and axillary ganglion areas. The incidence of hypothyroidism was 21%. Similarly, Bruning et al. [17] reported a clinical hypothyroidism rate of 2 to 3% and an isolated elevation of TSH in 10 and 25% of patients treated for breast cancer, depending on the radiation beam used.

The risk of postradical hypothyroidism is greater in subjects over the age of 60. Colevas et al. [12] reported in their study a higher risk in this age group.

Hypothyroidism has deleterious effects on the heart. In the normal state, the thyroid exerts a chronotropic, inotropic dromotropic and lusitrope positive action. This therefore results respectively in an acceleration of the heart rate, an improvement in the conductivity, contractility and diastolic relaxation of the myocardium. In addition, they decrease peripheral vascular resistance [18]. These interactions can be direct on the cardiomyocyte by fixation of the hormones on their specific nuclear receptor or indirect: either through a circulatory effect (effect on the total blood volume and on peripheral vascular resistance), or through the sympathetic cardiac innervation [19]. These actions are possible thanks to the possible genomic effect of thyroid hormones on the regulation of transcription into mRNA of genes associated with the contractile system [1] and to their non-genomic effect on the ion channels of the cardiomyocyte membrane. [20.21]

The prolonged deficit in thyroid hormones leads to cardiovascular disturbances characterized by:

1. A normal or lowered heart rate. Bradycardia between 40 and 60 beats / minute is found in only 1/3 of hypothyroid patients while the remaining 2/3 keep a normal heart rate. A 40% decrease in cardiac output compared to normal with a proportional reduction in oxygen consumption. This decrease in cardiac output is the direct consequence of bradycardia and the decrease in total blood volume, but also the decrease in myocardial contractility itself directly linked to the deficiency in thyroid hormones [22];
2. an increase in peripheral vascular resistance with a slight increase in mean arterial pressure and diastolic arterial pressure in 20% of cases [23];
3. capillary hyperpermeability responsible for diffuse serous effusions, especially pericardial;
4. In addition, hypothyroidism causes hypercholesterolemia secondary to the decrease in the clearance of total cholesterol and LDL-cholesterol [23].

A study on the correlation of hypothyroidism and secondary dyslipidemia was carried out in Mayo clinics on 268 patients and showed that 91.4% of them were hypothyroid with secondary dyslipidemia [24]. The cardiovascular risk in hypothyroidism is not only due to dyslipidemia, but to other metabolic factors such as increased homocysteine levels, decreased fibrinolytic activity, endothelial dysfunction and hemodynamic changes. All of these factors carry a thrombotic risk and high-risk cardiovascular disease.

Thyroid hormones are also believed to have an anti-atherogenesis effect by promoting the expression of vasodilating substances such as nitric dioxide (NO) and by inhibiting the expression of the angiotensin II receptor which plays a role in vasoconstriction [25].

Thyroid hormones are also involved in the synthesis and transcription of the protein responsible for myocardial relaxation, and the regulation of electromechanical properties by activating the ion channels of the heart. This suggests that deficiency of thyroid hormones changes the geometry, relaxation and contraction of the heart muscle. Kumar considers DCM as a rare presentation of hypothyroidism [26]. On the other hand, Marovic found that 18% to 49% of patients with dilated cardiomyopathy had an associated disorder in their thyroid gland [27].

The mechanism of this DCM is still under discussion: myxedematous infiltration of myocardial fibers, edema and vacuolation of myocardial cells with alteration in the expression of cardiomyocytic genes [28]. Heart failure, which remains a rare complication, often results from the decompensation of a preexisting heart disease following a prolonged deficit in thyroid hormones which concomitantly leads to a decrease in cardiac output and an increase in peripheral vascular resistance [22]. The occurrence of angina or myocardial infarction remains a rare complication which can however be precipitated by hormone therapy following the acceleration of the heart rate and the increase in myocardial contractility which will increase consumption previously reduced myocardial oxygen.

However, the introduction of prudent and progressive hormone therapy [29] is often more favorable than harmful for coronaropathy. Indeed, the joint reductions in pre- and post-charge compensate for this increase in oxygen consumption. Coronary angiography is not systematic before the initiation of hormone therapy, but it can be considered if appearance of angina and this for the purpose of possible myocardial revascularization [22].

Pericarditis is a common cardiac manifestation of hypothyroidism. Our patient had presented in this history a pericarditis and whose etiological research was not established early due to the unspecific character of the clinical symptomology of hypothyroidism.

Bhardwaj reported in 2010 the case of a 36-year-old woman who presented with DCM following severe hypothyroidism discovered during progressive dyspnea. The evolution was favorable after the administration of hormone therapy with complete disappearance of clinical signs and recovery of LV function [30].

This remarkable development was also observed in our patient admitted for an attack of global heart failure in connection with a DCM in severe LV dysfunction attributed to the thyroid hormone deficiency following radiation therapy. Note that before the diagnosis was retained, the other etiologies of DCM were discarded.

Hypothyroidism seems more common in women, however Seol reported a 36-year-old man who had classic symptoms of congestive heart failure with 16% in ejection fraction. His thyroid check-up showed TSH> 100mU / I. The diagnosis of Hashimoto's thyroiditis was made and the patient was treated with hormone therapy. The evolution was marked by a normalization of the biological balance [31].

The reported DCM cases would vary by age, Kumar reported a 14-year-old woman who had a similar heart presentation; she was diagnosed with Hashimoto's thyroiditis [26]

Hormone therapy has proven its ability to eradicate cardiovascular abnormalities. Indeed, a study by Fazio mentioned that treatment with levothyroxine, especially in people with elevated serum TSH levels, could correct dyslipidemia and overall heart function [32].

This study also has the merit of having demonstrated the role of thyroid hormones in the expression of cardiomyocytic genes with increased synthesis of the fraction of isoenzymes of myosin with 2 heavy chains.

So therefore, hypothyroidism is a real cause of DCM. Recognizing the thyroid origin of this cardiomyopathy is essential, indeed no criteria distinguishes it from other causes of cardiomyopathy apart from the clinical and biological signs of hypothyroidism and its reversibility under hormon therapy. This treatment with L-thyroxine is likely to improve myocardial performance in a very short time which can be further shortened by the prescription of tri-iodothyronine.

Conclusion:-

DCM is a progressive dilation of one or both ventricular chambers with impaired contraction of the heart muscle. When it is idiopathic, it is usually an irreversible condition. If the cause is reversible like the case of our patient, the cardiac functions can be restored after treatment of the etiology. This is how we recommend the adequate and diligent treatment of all forms of hypothyroidism in order to avoid the passage to the myxedematous heart stage.

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