GOSERELIN INHIBITING UPTAKE ON SODIUM PERTECHNETATE TC-99M THYROID SCAN: A CASE REPORT

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ABSTRACT

Introduction: **Thyroiditis may be induced by goserelin (a long acting analogue of gonadotropin - releasing hormone) prescribed for the treatment of pain and bleeding of endometriosis. Goserelin induced thyroiditis has a possibility of affecting thyroid function and hence may cause poor uptake on sodium pertechnetate Tc-99^{m} thyroid scan.**

Case presentation: **This case report highlights a rare instance of a middle-aged woman with symptomatic toxic goitre whose sodium pertechnetate Tc-99^{m} thyroid scan uptake was inhibited by goserelin therapy.**

Conclusion: **Medical personnel caring for patients on goserelin need to be aware of the possibility of it affecting thyroid function.**

Keywords: Goserelin, GnRH agonist, Thyroid gland, Sodium pertechnetate Tc99m, Endometriosis, Case report

INTRODUCTION

Goserelin is a long-acting analogue of gonadotropin-releasing hormone (GnRH) which inhibits secretion of gonadotropin from the pituitary gland.[1] It does this by reversible suppression of the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary gland.[2] The GnRH analogue has a greater affinity for its receptor, as high as 10-20 times.[3,4] As a treatment for endometriosis, it thins out the endometrial lining prior to ablative therapy, and relieves pain and bleeding.[5] Few cases of goserelin-induced thyroiditis have been published in medical literature. We present a report of a sodium pertechnetate Tc-99^{m} thyroid scan with uptake inhibited by goserelin.

CASE PRESENTATION

A 42-year old woman presented to our department with a two-year history of symptomatic toxic goitre. She had bilateral proptosis, hyperhidrosis, heat intolerance, menstrual irregularity, weight loss despite hyperphagia and increased appetite, and more recently, hoarseness. She had no history of excessive consumption of goitrogens. She had however grown up in a mountainous region of the country.

Her main clinical findings were bilateral proptosis, goitre, with no tracheal deviation, retrosternal extension nor palpably enlarged regional cervical lymph nodes. There were no scalp swellings. She also had tachycardia of 96/min although her blood pressure was normal at 120/70 mmHg. An assessment of Graves' disease with thyroid-associated ophthalmopathy was made. Prior to her presentation, she had been commenced on oral carbimazole 20 mg twice daily and atenolol 25 mg daily.

Her thyroid function test result, which had been done two weeks prior to her presentation, was consistent with primary hyperthyroidism (see Table 1). Neck ultrasound showed diffusely enlarged thyroid lobes, with heterogeneous echotexture and minimal flow on colour Doppler interrogation. A solitary sub-centimetre hypoechoic nodule was seen in the left lobe which showed moderate flow on colour interrogation. The left lobe was larger than the right (15.0 cm^3 and 11.9 cm^3, respectively) resulting in a combined volume of 26.9 cm^3. The overall impression was diffuse goitre with a solitary left thyroid nodule.

Table 1: Patient's thyroid function test at presentation depicting primary hyperthyroidism

	Result	Reference range	Unit
TSH	0.05	0.3-4.5	μIU/ml
FT4	56.67	8.9-17.2	pg/ml
FT3	30.34	1.2-4.2	pg/ml

TSH = thyroid stimulating hormone; FT4 = free thyroxine; FT3 = free triiodothyronine

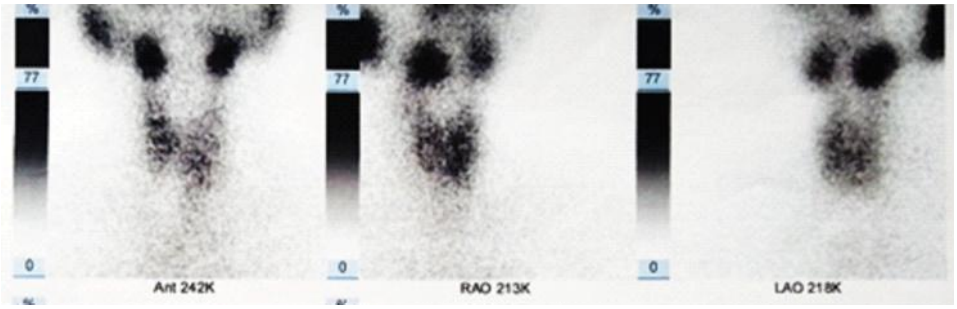

Figure 1: Initial Tc-99m pertechnetate thyroid scan; thyroid uptake markedly reduced compared to salivary gland uptake on anterior (ANT), right anterior oblique (RAO) and left anterior oblique (LAO) views

Ultrasound-guided fine needle aspiration biopsy was considered for the nodule seen in the left lobe. However, its small size made successful biopsy unlikely. Moreover, repeat ultrasound three days showed no evidence of the nodule.

She had a technetium-99^{m} pertechnetate ($^{99m}TcO_4^-$) thyroid scan after stopping carbimazole for five days. The thyroid scan revealed generalised diminished uptake in the thyroid gland; which was relatively less than salivary gland uptake. (See Figure 1.) At this resolution, neither "hot" nor "cold" nodules could be discerned. However, there was an impression of extension of the thyroid gland inferiorly to the level of the sternal notch marker. Scan findings were deemed suggestive of ongoing thyroiditis possibly secondary to carbimazole use.

She was planned for an additional $^{99m}TcO_4^-$ thyroid scan, after repeated counselling about foods to avoid. She re-presented four days later for the thyroid scan; she also had a repeat thyroid function test (Table 2). However, the repeat nuclear thyroid scan showed no improvement, with persistent suboptimal uptake (see Figure 2). She then eventually disclosed a history of being on Zoladex® (goserelin) regimen for treatment

Table 2: Repeat thyroid function test showing biochemical picture of subclinical hyperthyroidism despite reduced thyroid uptake on pertechnetate thyroid scan

	Result	Reference Range	Units
FT4	18.91	6.5-22	pmol/L
TSH	0.010	0.35-4.94	mIU/L

of endometriosis. The treatment had commenced about a year prior to her first thyroid scan, and almost three years after the onset of hyperthyroid symptoms. The image of the repeat technetium-99^{m} pertechnetate thyroid scan is shown in Figure 2.

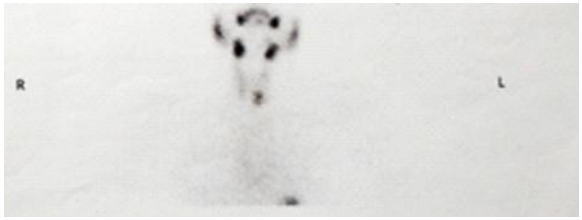

Figure 2: Repeat thyroid scan with tc-99m Pertechnetate showing persistent reduced uptake on the anterior view. Focal uptake is seen in a nodule in the inferomedial aspect of the left lobe.

She was thus found to be unsuitable for radioactive iodine therapy at the time. Her management plan was future review with another $^{99m}TcO_4^-$ thyroid scan once she has finished her course of Zoladex® injections. Thereafter, radioiactive iodine therapy would be booked once thyroid scan uptake is satisfactory. However, she is yet to present for a follow-up $^{99m}TcO_4^-$ thyroid scan.

DISCUSSION

As a therapeutic measure, goserelin has been associated with quite a few adverse reactions and drug interactions.[6] The World Health Organization VigiAccess database of adverse reactions reported 8,805 reported side effects from goserelin at the time of writing this article. The highest occurrence of these reports was from Europe (52%) while a sparse 1% originated from Africa. The modal age groups of those affected were 18-44 and 45-64 years with a frequency of 18%. Overall, the highest frequency was in those aged 18-75 years and above 75%. Endocrinologic side effects were 62 in number (0.007%). Of all endocrine reactions, 23 (0.003%) were thyroid-related. Specifically, hypothyroidism was reported in eight instances, and hyperthyroidism in seven.[7] Asides this, the literature is lacking about goserelin effect on $^{99m}TcO_4^-$ thyroid scan.

The subject of goserelin causing thyroid dysfunction has been investigated. Quite a few studies have shown

evidence of its negative effect on thyroid function.[7–9] For instance, GnRH has been shown to significantly elevate thyroid-stimulating hormone (TSH) in women recipients.[10] On the other hand, it has also been linked to the development of Graves' disease (GD).[9]

Oestrogen affects thyroid function by causing an increase in serum thyroxine-binding globulin (TBG) concentrations due to increased sialylation of TBG. In this state, TBG has a slower hepatic clearance, which prolongs its half-life.[11,12] TBG bears more than 70% of bound thyroxine and triiodothyronine.[13] Furthermore, oestrogen receptors have been demonstrated in the developing foetal thyroid as well as in adult thyroid tissue.[14] The oestrogen component of contraceptive pills has been linked to the development of subclinical hypothyroidism.[15]

Given the premise that thyroid function is affected by oestrogen, it is plausible that oestrogen-deprived states may result in poorer thyroid function. That appears to have happened in this patient. The uptake of Tc-99^{m} TcO_4 on the thyroid scan has been shown to vary with increasing levels of TSH, free thyroxine, free triiodothyronine, thyroid-stimulating antibodies, TSH-binding inhibitory immunoglobulin, and patient age.[16] The mechanism of goserelin inhibition of uptake of Tc-99^{m} TcO_4 has been deliberated. Onset of thyroid dysfunction following goserelin use is not immediate; reported instances start from one to four months after onset of treatment.[17] Thus, the cause of its side effects has been attributed to induced states of low oestrogen, rather than spikes of gonadotropin, in these patients. In addition, it was observed that goserelin did not seem to affect thyroid function in women without pre-existing thyroid disease. However, it aggravated pre-existing disease.[18] The spectrum of goserelin-induced thyroid disorders included hyperthyroidism, hypothyroidism and a mixture of both in affected individuals.[17–19]

In an attempt to allay the side effects experienced by patients, 'add-back' therapy has been described. This involves administering goserelin along with hormone replacement therapy for endometriosis.[20,21] It has served to provide symptomatic relief without reducing therapeutic outcome for such patients.

We recommend that patient preparation for nuclear thyroid scans and radioiodine treatment include enquiries about ongoing or prior GnRH therapy. Dysthyroid women receiving goserelin thrapy will benefit from thyroid function monitoring. Randomised clinical trials are required to determine outcomes of thyroid function and thyroid scans in patients on GnRH analogues and those without.

CONCLUSION

Goserelin-induced thyroiditis is a rare phenomenon; the medical personnel caring for such patients need to be aware of the possibility of its affecting thyroid function, leading to poor uptake on the pertechnetate thyroid scan.

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