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Case Report

Rapid Progression of Papillary Thyroid Carcinoma Following Initiation of Semaglutide (Wegovy) for Weight Loss: A Case Report

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Abstract: Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide, have demonstrated promising efficacy in the management of obesity and type 2 diabetes mellitus. While their association with medullary thyroid carcinoma (MTC) has been documented in preclinical studies, the relationship between GLP-1 RAs and differentiated thyroid carcinomas, particularly papillary thyroid carcinoma (PTC), remains unclear. We present a case of rapidly progressive PTC in a patient shortly after initiating semaglutide for weight loss. Case Presentation: A 35-year-old woman with a history of obesity and prior bariatric surgery presented with a rapidly enlarging anterior neck mass five weeks after initiating semaglutide (0.25 mg weekly). No previous thyroid abnormalities had been documented. Ultrasonography revealed a 6.8 cm solid, hypoechoic nodule in the right thyroid lobe, and fine-needle aspiration (FNA) confirmed features consistent with aggressive PTC. Despite recommendations for urgent surgical intervention, the patient deferred thyroidectomy for six months in favor of dietary management. Discussion: Although GLP-1 RAs can activate GLP-1 receptors on thyroid C-cells and have been associated with MTC in rodent models, their role in the pathogenesis or progression of PTC is poorly understood. The temporal association and atypically rapid tumor growth in this case raise concerns regarding a potential link between GLP-1 RA therapy and accelerated PTC progression. Conclusion: This case highlights the need for further investigation into the potential impact of GLP-1 receptor agonists on differentiated thyroid cancers, particularly in patients with no preexisting thyroid disease.

Keywords: papillary thyroid cancer; GLP-1 RA; semaglutide

1. Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), including semaglutide, represent a significant advancement in the pharmacologic management of obesity and type 2 diabetes mellitus, offering substantial benefits in glycemic control and weight reduction. Semaglutide, marketed as Wegovy for weight loss, has gained widespread use due to its clinical efficacy and safety profile.

Preclinical studies have demonstrated an association between GLP-1 receptor activation and C-cell hyperplasia or medullary thyroid carcinoma (MTC), leading to a class-wide black box warning and contraindication in patients with a personal or family history of MTC or multiple endocrine neoplasia type 2 (MEN2). However, the relevance of these findings to differentiated thyroid cancers such as papillary thyroid carcinoma (PTC) is uncertain.

We present a case of rapidly progressive PTC in a patient shortly after receiving low-dose semaglutide therapy, raising important questions about the potential GLP-1 receptor–mediated effects on differentiated thyroid tissue.

2. Case Presentation

A 35-year-old woman with a medical history of obesity and prior bariatric surgery presented with a rapidly enlarging anterior neck mass in June 2024. The mass was incidentally detected during an urgent care visit for abdominal discomfort, approximately five weeks after administration of semaglutide (0.25 mg subcutaneously weekly) to achieve weight loss. She had completed five doses before discontinuing the medication upon discovery of the mass. Physical examination and her medical history did not find any thyroid abnormalities.

Ultrasound evaluation revealed a dominant 6.8 cm hypoechoic, solid nodule in the right thyroid lobe with punctate echogenic foci and increased vascularity. Thyroid function tests, including thyroid-stimulating hormone (TSH) with reflex-free thyroxine (T4), were within normal limits (Table 1). Fine-needle aspiration (FNA) cytology demonstrated tumor cells with nuclear grooves, pseudoinclusions, powdery chromatin, and papillary architecture, consistent with papillary thyroid carcinoma, with features suggestive of an aggressive variant.

Surgical consultation recommended prompt total thyroidectomy with anterior neck dissection. The patient, however, declined surgery due to concerns about lifelong thyroid hormone therapy and opted to delay surgical intervention, instead pursuing dietary modifications with a planned reevaluation in six months.

3. Discussion

The oncogenic effects of GLP-1 receptor agonists, particularly on MTC, have been well-documented in animal studies. Rodent models exposed to GLP-1 RAs such as liraglutide and exenatide demonstrated a dose-dependent increase in C-cell proliferation and MTC incidence, attributed to GLP-1 receptor activation on thyroid C-cells [1,2].

Despite these findings, the relevance to human thyroid physiology—particularly differentiated thyroid neoplasms such as PTC—is not well-established. Human C-cells express GLP-1 receptors at significantly lower levels, and large-scale human studies have not consistently shown an increased risk of thyroid malignancy in patients using GLP-1 RAs [3].

Some studies have suggested variable expression of GLP-1 receptors in PTC tissues [4], while genetic analyses have proposed potential associations between GLP-1 pathway variants and susceptibility to differentiated thyroid cancers. Contrasting these hypotheses, recent in vitro studies reported no proliferative effects of semaglutide on PTC cell lines and suggested that GLP-1 RAs may enhance antitumor immune responses [5].

In this case, the rapid growth of a papillary thyroid tumor within five weeks of semaglutide initiation is unusual, given the typically indolent nature of PTC. While causality cannot be established from a single observation, the strong temporal correlation and absence of prior thyroid pathology raise the possibility of a potential relationship between GLP-1 RA therapy and accelerated tumor progression.

To date, no published cases have described a similar pattern of rapid PTC growth following GLP-1 RA exposure. This case contributes to a growing body of anecdotal evidence that may signal a rare but clinically relevant phenomenon warranting further study.

4. Conclusions

This case underscores the need for increased vigilance and further research into the potential association between GLP-1 receptor agonists and differentiated thyroid carcinomas. Although current evidence does not support a causal link between GLP-1 RAs and papillary thyroid carcinoma, the atypically rapid tumor growth in this patient following semaglutide initiation suggests that certain PTC subtypes—or patients with specific molecular susceptibilities—may respond differently to GLP-1 RA exposure.

Future research should focus on elucidating the molecular mechanisms of GLP-1 receptor activity in differentiated thyroid tissues, assessing GLP-1 receptor expression in various PTC subtypes, and evaluating patient-specific risk factors. Until more definitive data is available, clinicians should exercise caution and consider thyroid surveillance in patients who develop neck symptoms while on GLP-1 RA therapy, even in the absence of prior thyroid disease.

Table 1. Results of Thyroid Stimulating Hormone with Reflex T4 assays

Date	Thyroid Stimulating Hormone (0.460 - 4.680 uIU/mL)
March 2020	1.63
April 2024	1.64
July 2025	1.37

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MS.: data curation, writing—original draft preparation, reviewing and editing; HB: writing—reviewing and editing. All authors have read and agreed to the published version of the manuscript.

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Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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