

## Case Report

# Case of Ovarian Cancer in a Woman with Undiagnosed Graves' Disease: A Case Report and Review of the Literature

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## Keywords

Ovarian cancer · Hyperthyroidism · Graves' disease

## Abstract

Epithelial ovarian cancer (OC) is a leading cause of death among females in the United States, due in part to challenges of diagnosis in the early stages of the disease. While efforts are underway to develop a high-quality screening test, it is equally important to consider whether high-risk populations are appropriate to screen. One such population may be females with hyperthyroidism, as epidemiologic studies have shown an association between this condition and OC. In this report, we present a case of a female with OC and Graves' disease to highlight the potential significance of this association.

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## Introduction

Despite advances in therapy, epithelial ovarian cancer (OC) remains the fifth leading cause of death among females in the United States [1]. The high mortality associated with this diagnosis is attributed to the frequency of presentation at late stages. When diagnosed

at an early stage, the mortality rate decreases from well over 60% to approximately 10% [2–4]. Unfortunately, the disease is generally asymptomatic until late stages, making early diagnosis challenging.

Given the substantial benefit of early diagnosis, many screening strategies have been proposed and explored. A combination of transvaginal ultrasound and single or serial measurements of serum levels of CA-125 is considered the standard screening method, though its positive predictive value is only 24% in the general population given the low overall prevalence of OC [5]. Other methods have been proposed, including a variety of proteomic and microarray-based tests in addition to a new assay that uses high-resolution mass spectrometry to identify a series of diagnostic metabolites [4].

In order to increase the positive predictive value of a screening test for OC, it is important to identify populations at a higher risk for OC than the general population. There are several known risk factors for OC, including advanced age, genetic mutations (i.e., *BRCA1* and *BRCA2*), and an increased lifetime ovulation (e.g., earlier age of first menstruation, late age of menopause, or never being pregnant). Recent epidemiological evidence has suggested that hyperthyroidism may also be associated with OC [2]. To date, this association has not been thoroughly examined. Here, we present a case of a female with OC and Graves' disease to highlight the potential significance of this association.

### Case Presentation

A 50-year-old female without significant past medical history presented to an emergency department with chest pain and shortness of breath and was found to have a pulmonary embolism. One month later, she presented again to the emergency department with abdominal pain and distension, and a CT scan revealed a 12 × 10 × 11 cm pelvic mass with large-volume ascites and evidence of carcinomatosis. She was diagnosed with stage III high-grade serous OC and underwent surgical resection and 6 cycles of intravenous and intraperitoneal cisplatin and taxol.

Four months after completion of therapy, she reported insomnia and jitteriness that had been present for nearly 10 years and managed with as-needed benzodiazepines. Laboratory studies revealed undetectable thyroid-stimulating hormone (TSH) and an elevated free T4 level of 2.3 ng/dL (normal range: 0.8–1.8). Subsequent laboratory evaluation 1 month later confirmed an undetectable TSH and a free T4 level of 4.4 ng/dL, consistent with a diagnosis of hyperthyroidism. Thyroid-stimulating immunoglobulin was found to be 531% of baseline (normal range: <140%). This confirmed a diagnosis of Graves' disease. Therapy with methimazole was initiated with normalization of her TSH and resolution of her symptoms.

### Discussion

In this case, given the long duration of symptoms prior to the diagnosis of OC and their resolution with appropriate therapy for hyperthyroidism, it seems likely that excessive thyroid stimulation had been present before the development of OC. The link between hyperthyroidism and OC remains evident only at an epidemiological level, and no mechanism of association has been demonstrated. The proposed mechanism involves increased levels of inflammation, which may mediate OC risk [2]. It has yet to be determined whether this asso-

ciation is causal and whether early treatment of hyperthyroidism could mitigate the risk of developing OC.

OC carries a high mortality rate when diagnosed at an advanced stage. Despite many attempts, no screening test is sufficiently sensitive and specific to be used in the general population at this time. It is essential that providers maintain an appropriate level of suspicion of OC in patients with nonspecific complaints. Identification of high-risk populations may allow screening tests to be used such that a positive result carries sufficient clinical significance.

### Conclusion

It is important for clinicians to be aware of the association between OC and hyperthyroidism and to have an increased degree of suspicion of OC among patients with known hyperthyroidism.

### Statement of Ethics

The authors have no ethical conflicts to disclose.

### Disclosure Statement

The authors have no conflicts of interest to disclose.

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