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CASE REPORT

A Rare Case of Metachronous Clear Cell Ovarian Carcinoma and Thyroid Carcinoma: Clinical and Pathological Insights

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Background: Clear cell ovarian carcinoma (CCOC) is a type of epithelial ovarian cancer, representing 5–11% of ovarian cancers. CCOCs tend to occur in the fifth to seventh decades of life, with only 10% of cases occurring in the fourth decade. On the other side, papillary thyroid carcinoma is the most common histology type of thyroid carcinoma and is associated with locoregional spread. Herein, we present a rare case of double-primer ovarian and thyroid cancer, which is a clear cell ovarian carcinoma metachronous with papillary thyroid carcinoma.

Case Report: A 47-year-old nulliparous woman presented to our Gynecology Oncology facility with an abdominal mass that had progressively increased in size over the last three months. She had a history of papillary thyroid cancer ten years previously and was treated with radioiodine (I-131). Physical examination revealed an immobile abdominal cystic mass measuring 20 × 18 × 15 cm. Ultrasound imaging revealed a cystic mass with a solid part, measured 16.1 × 10.9 × 12.84 cm, with M4 feature of the IOTA simple rule. CA-125 tumor marker levels were 190.1 U/mL. Ovarian cancer was suspected, and surgical staging with total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, frozen sectioning, and adhesiolysis was performed. Histopathological examination revealed a clear cell ovarian carcinoma.

Discussion: Papillary thyroid carcinoma tends to be a locoregional metastasis, whereas distant metastases are rare. Distant metastasis often occurs decades after the primary tumor, with the most common metastatic sites being the lungs and bones. This raises an important clinical question concerning the etiology of the ovarian carcinoma: whether it represents a metastasis from the pre-existing thyroid carcinoma or a distinct primary neoplasm. Determining the precise relationship between these malignancies is crucial for guiding treatment strategies and understanding the biological behavior of the tumors involved. In this case, clear cell ovarian carcinoma arose separately from papillary thyroid carcinoma.

Conclusion: Double primer cancer of the ovary and thyroid, which is a clear cell ovarian carcinoma metachronous with papillary thyroid carcinoma, is possible.

Keywords: ovarian cancer, thyroid cancer, metachronous

Introduction

Clear cell ovarian carcinoma (CCOC) is uncommon and is found in approximately 12% of women with epithelial ovarian cancer (EOC) in Western countries. CCOCs tend to occur in the fifth to seventh decades of life and account for only 10% of cases in the fourth decade.[1] The majority of CCOC cases are unilateral and diagnosed at an early stage (stages I–II). The prognosis of CCOC in the early stage is more favorable than that of serous ovarian cancer (SOC). In the advanced stages (stages III–IV), CCOC is associated with a poorer prognosis than SOC and is typically resistant to platinum-based chemotherapy.[2,3] Response rates of CCOC to platinum-based chemotherapy ranges from 11% to 56%, whereas in high-grade serous ovarian carcinomas (HGSOC), the response rate is >80%.[2] On the other thyroid carcinoma, the most common type of thyroid cancer. This disease is characterized by good

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prognosis and locoregional spread. Distant metastasis is rarely observed, but can occur decades after primary PTC is diagnosed. The most common metastatic sites are the lungs and bone. Rare metastatic sites include the brain, parotid gland, breast, liver, kidney, adrenal glands, ovaries, muscle, and skin.[4]

In a particular circumstance in which we diagnose thyroid cancer in advance of ovarian cancer, raises an important clinical question concerning the etiology of the ovarian carcinoma: whether it represents a metastasis from the pre-existing thyroid carcinoma or a distinct primary neoplasm. Determining the precise relationship between these malignancies is crucial for guiding treatment strategies and understanding the biological behavior of the tumors involved. In this case, clear cell ovarian carcinoma arose separately from papillary thyroid carcinoma. Herein, we report a rare case of double primary cancer of the ovary and thyroid, which was a clear cell ovarian carcinoma (CCOC) metachronous with papillary thyroid carcinoma (PTC).

Case Report

A 47-year-old nulliparous woman presented to our Gynecology Oncology facility with an abdominal mass progressively increasing in size over the previous three months. She had a history of papillary thyroid cancer ten years ago and had undergone radioiodine (I-131) treatment at the time.

Radioiodine therapy (I-131) was administered not for the abdominal mass but due to a recurrence of thyroid cancer, as indicated by the radioiodine (I-131) findings. The rationale for this treatment was the elevated TSH levels, measured at 42.8 μIU/mL (normal range: 0.3–5.0 μIU/mL), with a corresponding fT4 level of 0.8 ng/dL (normal range: 0.7–1.8 ng/dL). The patient received a cumulative NaI-131 dose of 805 mCi equal to 29.785 MBq. A whole-body scan performed 48 hours post-administration revealed multiple calcified lesions in the left thyroid field, the largest measuring 1.2 × 0.8 × 1.1 cm without radioactive uptake. Additionally, there were lymph nodes smaller than 1 cm in the submental, bilateral submandibular, and bilateral superior jugular areas did not demonstrate radioactive uptake, suggested a reactive process. However, there was pathological uptake in the bilateral ovaries, with the right ovary measuring 10.3 × 16.3 × 19.3 cm and the left ovary measuring 5.6 × 7.5 × 7.5 cm. No radioactive uptake was observed in the lungs, bones, or other areas of the body.

Radioiodine (I-131) Results are Shown (Figure 1):

1. Residual Malignancy in the Left Thyroid Field.
2. The appearance of lymph nodes in the submental, bilateral submandibular, and bilateral superior jugular areas may be caused by reactive processes.
3. Iodine-Avid Masses in Both Ovaries are Suspicious for Malignancy.

The treatment plan, according to the radioiodine (I-131) results, was the administration of suppressive doses of thyroid hormone at a dose of 1 tablet/day (100 μg/day) for 1 month. The dose is adjusted based on the results of the 3-week TSH level examination, then after 1 month (with a target TSH ≤ 0.1 μIU/mL), planned for gynecological consultation and removal of the ovarian mass 3 months after NaI-131 therapy if possible.

Physical examination in a gynecology oncology clinic revealed an immobile abdominal cystic mass measuring 20 × 18 × 15 cm. Ultrasound imaging revealed a cystic mass with solid part, measured 16.1 × 10.9 × 12.84 cm, with M4 feature of the IOTA simple rule. CA-125 tumor marker levels were 190.1 U/mL. Ovarian cancer was suspected, and surgical staging with total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, frozen section, and adhesiolysis was eventually performed, as shown in Figure 2. Histopathological examination confirmed the diagnosis of clear cell ovarian carcinoma (Figures 3 and 4).

Discussion

In a particular circumstance in which we diagnose thyroid cancer in advance of ovarian cancer raises an important clinical question concerning the etiology of the ovarian carcinoma: whether it represents a metastasis from the pre-existing thyroid carcinoma or a distinct primary neoplasm. Determining the precise relationship between these malignancies is crucial for guiding treatment strategies and understanding the biological behavior of the tumors involved.

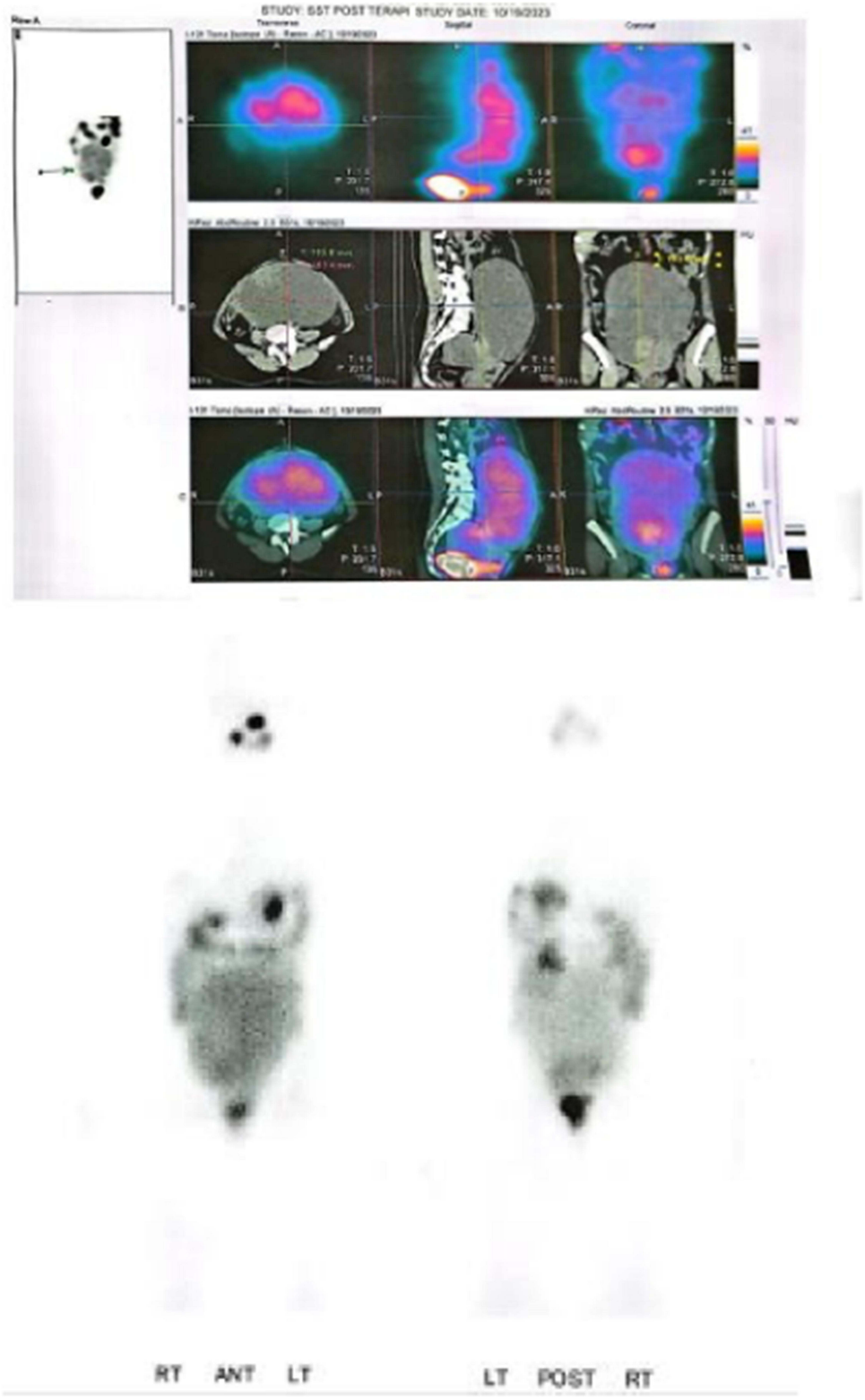

Figure 1 Nuclear radioiodine result showed an Iodine-avid masses in both ovaries are suspicious for malignancy (left) and residual malignancy in the left thyroid field (right).

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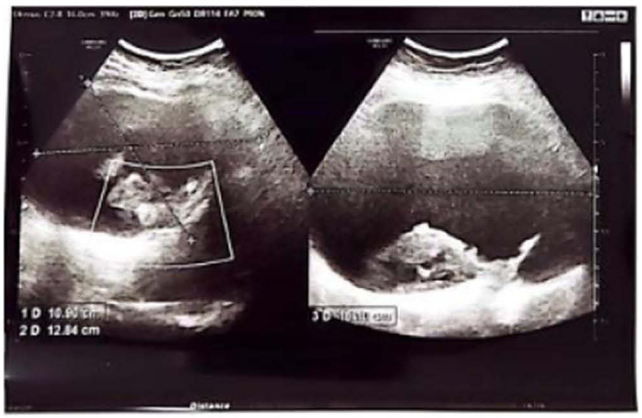

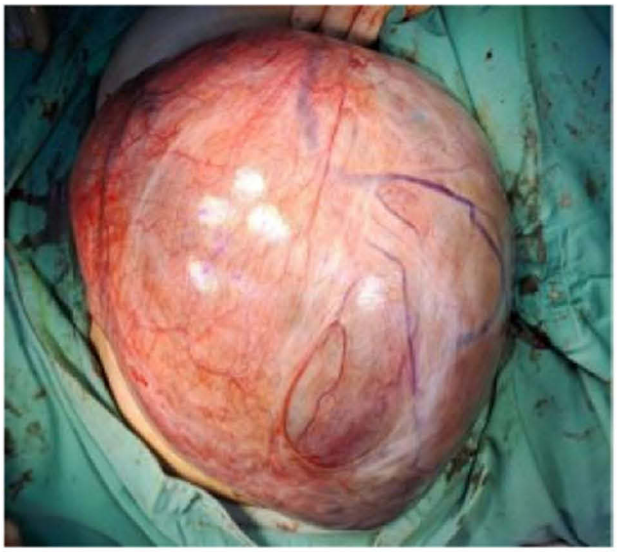

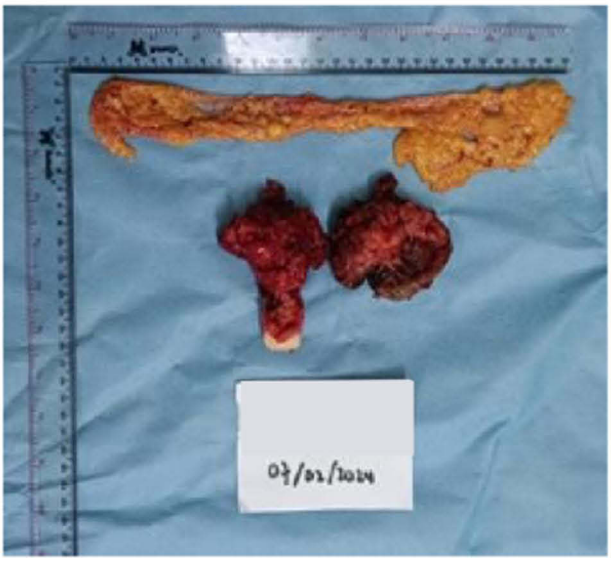

Figure 2 Abdominal ultrasound revealed a mixechoid mass, sized 16 × 12 × 10 cm (left); mass of the right ovary during operation procedure (middle); specimens of surgical staging (right).

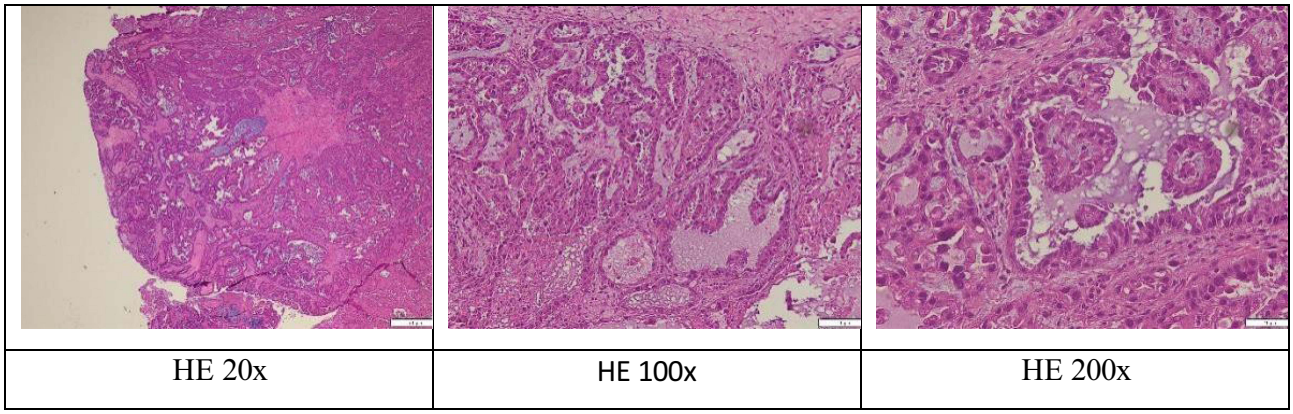

Figure 3 The histopathological results of the right ovary suggested a clear cell ovarian carcinoma.

Three major differential diagnoses were considered in this case of a woman who presented with a cystic ovarian mass ten years after total thyroidectomy for papillary thyroid carcinoma: cystic struma ovarii, papillary thyroid carcinoma arising in struma ovarii, and metastatic thyroid carcinoma.[5]

Metastatic ovarian tumors comprise approximately 5%–10% of all malignant ovarian tumors identified in the ovary. Thyroid carcinoma is rarely the primary tumor site. In a comprehensive autopsy study of 54 patients who died of known thyroid cancer, Silverberg et al found three cases of ovarian involvement, one medullary carcinoma, and two anaplastics. Tollefsen et al studied 70 fatal cases of papillary carcinoma of the thyroid, and did not find a single case of ovarian involvement. Young et al reported a case of follicular carcinoma that metastasized to the ovary and mimicked an ovarii. Logani et al reported a case of cystic ovarian metastasis from papillary thyroid carcinoma.[5–7]

None of the studies listed above have reported non-metastatic ovarian tumors arising after papillary thyroid cancer. In this case, histopathological analysis of the ovarian mass suggested clear cell ovarian carcinoma (CCOC) due to prominent hobnail cells found in the HE preparations. Subsequently, we wanted to determine whether the mass was secondary to papillary thyroid carcinoma (PTC) or was the primary tumor itself. Immunohistochemical examination revealed positive results for Napsin A, negative results for WT1, P53, PR, and TTF1. The conclusion from these results was that the ovarian mass was merely a CCOC and not a metastasis from PTC.

CCOCs are characterized by epithelial cells containing glycogen-rich clear cytoplasm and hobnail cells with varying degrees of fibrous stroma. CCOCs account for only 3% of ovarian epithelial tumors; however, almost all are malignant. This type of cancer tends to occur in the fifth to seventh decade of life (10% in the fourth decade). There has been an unexplained increase in the prevalence of clear cell carcinoma in Japan compared to that in Western countries. Two-thirds of the women with CCOC are nulliparous. More than half of the patients had associated endometriosis involving the ovaries or other pelvic sites. Most CCOC, even in advanced stages, are unilateral, and this type of malignancy is not graded.[1,8]

Various immunohistochemical evaluations have been performed to confirm the diagnosis of CCOC. Napsin A was 100% positive, and WT1 was 100% negative in CCOC. P53 was positive in only 76% of CCOC and 100% of (High Grade Serous Ovarian cancer (HGSOC).[9] Vang et al reported the characteristic immunoprofile of CCOC, which was positive for CK7, CAM5.2, 34βE12, CEA, Leu-M1, vimentin, bcl-2, p53, and CA-125; variably positive for ER and HER-2/neu; and negative for CK20 and PR.[10]

Thyroid transcription factor-1 (TTF-1) is a 38-kd homeodomain containing DNA-binding protein identified in the thyroid and lung as a regulator of thyroid-specific genes, surfactant, and Clara cell secretory protein gene expression. TTF-1 has been used as a reliable lineage marker for lung adenocarcinomas and thyroid carcinomas in surgical pathology studies.[11] In this case, TTF1 was used to distinguish whether the ovarian mass was secondary to PTC metastasis or whether it was the primary tumor itself. The TTF1 results were negative. Thus, we concluded that this case was a double-primer CCOC synchronous with PTC.

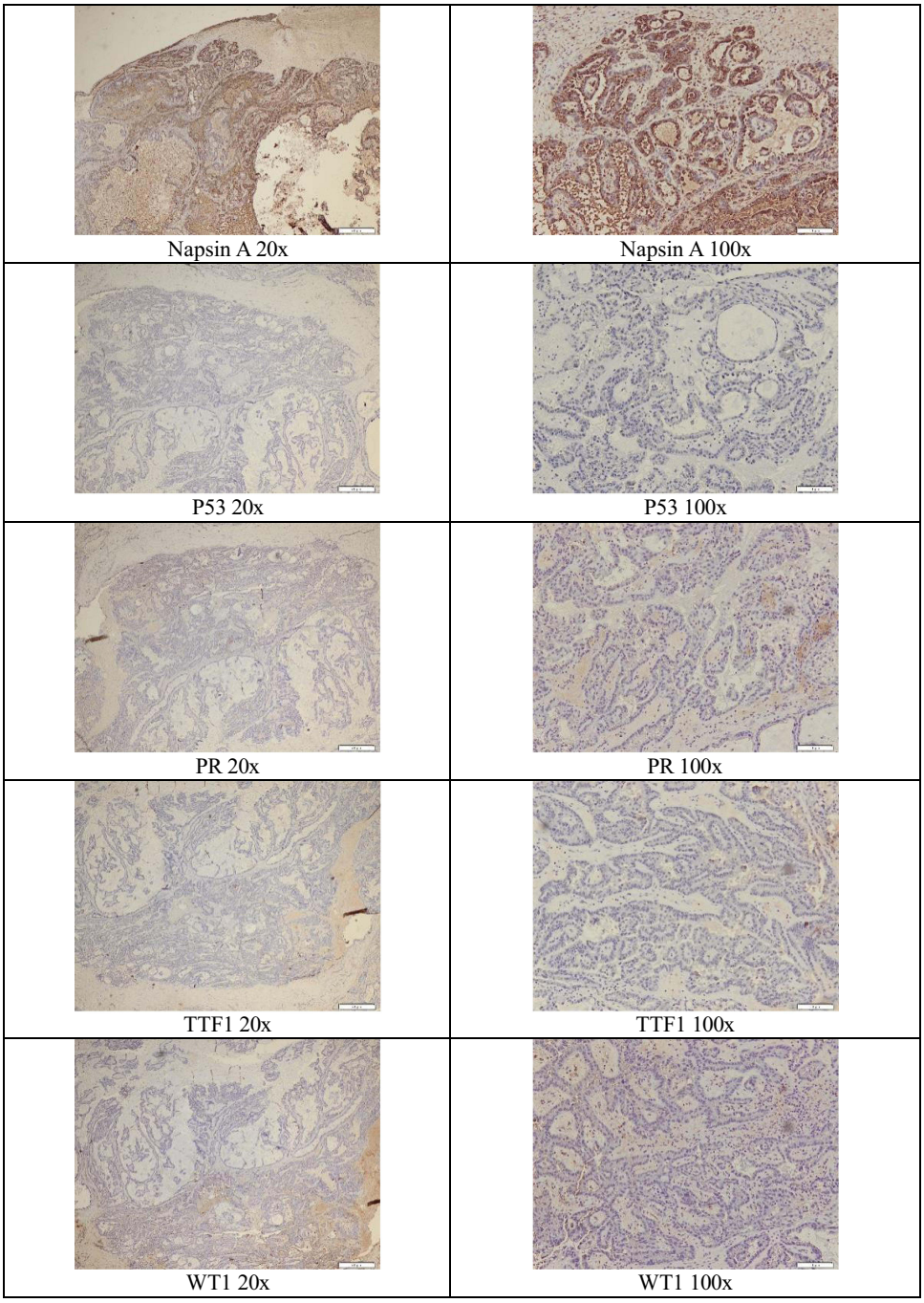

Figure 4 Serial immunohistochemical (IHC) examinations (Napsin A: positive; P53: negative; PR: negative; TTF1: negative; and WT1: negative) concluded that the mass is primer clear cell ovarian cancer, not a metastatic cancer.

The final diagnosis was clear cell ovarian carcinoma stage IC3 CCC with a metachronous papillary thyroid carcinoma. She was scheduled to receive intravenous platinum-based therapy (Paclitaxel-Carboplatin) 3-week interval. The outcomes of adjuvant chemotherapy remain unclear.

Conclusion

In a particular circumstance in which we diagnose thyroid cancer in advance of ovarian cancer, raises an important clinical question concerning the etiology of the ovarian carcinoma: whether it represents a metastasis from the pre-existing thyroid carcinoma or a distinct primary neoplasm. Determining the precise relationship between these

malignancies is crucial for guiding treatment strategies and understanding the biological behavior of the tumours involved. In this case, clear cell ovarian carcinoma arose separately from papillary thyroid carcinoma, and the conclusion was double-primer CCC metachronous with papillary thyroid cancer.

Ethics Approval and Informed Consent

The need for ethical approval was waived by the ethics institutional board. The patient was fully informed of the study's purpose prior to providing written consent, including the publication of any accompanying images. The patient agreed and signed a consent form to participate including publication of any accompanying images.

Author Contributions

SR, ABH, DS, AK, YMH, and KIM were involved in patient management. SR and KIM were involved in the conception, design, and writing of the manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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