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Endocrine sequelae following chemo-immunotherapy and radiotherapy for triple-negative breast carcinoma: A case report

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I. INTRODUCTION:

Triple-negative breast cancer (TNBC) is managed with chemotherapy, immunotherapy, and radiotherapy. While survival has improved, these modalities can cause significant endocrine toxicities, including immune-mediated thyroid dysfunction and ovarian insufficiency. We present a case highlighting the complexity and evolution of endocrine disturbances following multimodal TNBC treatment.

KEYWORDS: Triple-negative breast cancer (TNBC),immune-mediated thyroid dysfunction, transient ovarian insufficiency, menopause.

II. CASE PRESENTATION:

A 45-year-old woman with TNBC underwent bilateral nipple-sparing mastectomy followed by carboplatin/paclitaxel, epirubicin/cyclophosphamide (EC), pembrolizumab, and adjuvant chest wall/axillary radiotherapy. One year after immunotherapy cessation, she presented fatigue, cognitive slowing, cold intolerance, and dysarthria. Laboratory evaluation revealed severe hypothyroidism (TSH 73.6 mIU/L, undetectable FT4), prompting levothyroxine therapy. Thyroid ultrasound showed an atrophic gland without autoantibodies, supporting immunotherapy-induced thyroiditis.

Gonadal assessment demonstrated elevated gonadotropins (FSH 43.9 IU/L; LH 86.5 IU/L) with paradoxically high estradiol (707 pmol/L). MRI pituitary imaging and pituitary hormone profile were normal.

Six months after the initial endocrine evaluation, the patient reported her first menstrual period in 2.5 years, accompanied by abdominal bloating. Repeat hormonal assessment showed increased estradiol (927 pmol/L). CT abdomen-pelvis showed left ovarian cyst and CA125 normal.

Urgent TVUS revealed: Overall normal findings apart from small fibroids of no major significance as well as right ovarian follicle.

Gynecology team concluded transient immunotherapy-induced ovarian insufficiency, suggesting potential ovarian recovery.

Pituitary Assessment:

Given abnormal gonadotropins and ovarian dysfunction, pituitary imaging and hormonal profiling were conducted. MRI demonstrated normal pituitary morphology without lesions. ACTH, cortisol, IGF-1, and prolactin levels were within reference ranges, indicating preserved pituitary function and excluding central endocrine causes of hypothyroidism or gonadal dysfunction.

Gonadal Hormones and Ovarian Assessment

Serial monitoring of gonadotropins and estradiol revealed perimenopause. Initial FSH and LH levels were markedly elevated, with paradoxically high estradiol. At six months, estradiol rose further, correlating with resumption of menses and imaging evidence of ovarian cysts and fibroid. By twelve months, FSH remained elevated; LH decreased, estradiol dropped, and AMH was undetectable, indicating progression toward menopause rather than transient ovarian insufficiency.

Timepoint	FSH (IU/L)	LH (IU/L)	Oestradiol (pmol/L)	AMH (pmol/L)	Interpretation
Initial	43.9	86.5	707	N/A	Disrupted ovarian function
6 months	36.4	80.1	927	N/A	Transient recovery suspected
12 months	80.1	36.4	<89	<0.2	Perimenopause confirmed

The patient's symptoms improved, with fatigue partially resolved. Ovarian function is consistent with menopausal transition. She was discharged from endocrinology follow-up after confirming hormonal stability and absence of ongoing complications.

MANAGEMENT AND OUTCOME:

Thyroid function is normalized on levothyroxine. Ovarian function exhibited transient recovery followed by biochemical decline toward menopause. Symptoms gradually improved, and the patient was discharged once endocrine parameters stabilized.

III. DISCUSSION:

This case demonstrates typical endocrine sequelae of modern TNBC therapy. Pembrolizumab-induced thyroiditis is well-documented and requires proactive monitoring and hormone replacement. Chemotherapy and radiotherapy contributed to ovarian dysfunction, with fluctuating gonadotropins and estradiol indicating evolving ovarian reserve before progression to menopausal transition. Preserved pituitary structure and function confirmed peripheral—rather than central—endocrine pathology.

IV. CONCLUSION:

Multimodal TNBC therapy can result in complex, evolving endocrine disturbances involving thyroid and ovarian axes. Longitudinal monitoring, early hormone replacement, and multidisciplinary coordination are essential to optimize survivorship outcomes.

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