Pregnancy Following Recent Radioactive Iodine Ablation in Thyroid Carcinoma Patient: A Case Report

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ABSTRACT

Well-differentiated thyroid carcinoma (DTC) is common among females of reproductive age. Pregnancy is associated with hormonal (TSH and HCG) and metabolic changes that might affect the thyroid gland. Information regarding the outcome of babies born to mothers who have recently undergone radioactive Iodine-131 ablation (RAI) is scarce. A 24-year-old pregnant woman with a history of thyroid cancer was consulted by the obstetrics and gynecology for further evaluation. She complained of a lump under the left jaw, and a thyroid nodule was found from further examination. Postoperative pathology of the right thyroid tissue revealed follicular and solid variant papillary thyroid carcinoma. Postoperative Thyroglobulin (Tg) level before ablation was 16.14 ng/mL. Ablation with Iodine-131 of 100 mCi was performed. Whole-body scintigraphy (WBS) indicated remaining functional thyroid tissue in the right thyroid field and thyroid tissue metastases in the left supraclavicular area. The patient was pregnant 3 months after the radioablation. Fetomaternal examination results 6 months pregnancy revealed fetal biometry according to gestational age (31 - 32 weeks) with an estimated fetal weight of 1787 grams and fetal doppler was normal. The patient is treated with levothyroxine 125 µg once daily, folic acid 400 µg twice daily, calcium lactate twice daily, and aspirin 80 mg once daily. The TSH level was 0.01 (0.55 - 4.78) µIU/mL and the fT4 was 1.14 (0.7 - 1.48) ng/dL. The latest thyroid ultrasound indicated no discrete mass in the thyroid fossa and non-specific lymphadenopathies. The baby was born normally, weighed 2680 grams, with normal thyroid function tests (neonatal TSH 1.02 µIU/mL, fT4 2.6 ng/dL).

Keywords: *Thyroid carcinoma, pregnancy, radioactive iodine ablation*

INTRODUCTION

Thyroid cancer is commonly diagnosed in younger individuals, especially in females of reproductive age. Papillary thyroid carcinoma (88%) and follicular thyroid carcinoma (9%) are the most common types of thyroid cancer, both categorized as DTC.[1,2] Over the past three decades, the incidence of DTC has increased by more than 5% per year globally. In addition to the raised awareness of the diagnosis, environmental variables (such as obesity and radiation exposure) are also responsible for this phenomenon.[2]

Due to its rising incidence, DTC became the second most common malignancy diagnosed in pregnancy, with a prevalence of 3.6 to 14 per 100,000 live births.[3] Approximately 10% of thyroid carcinoma cases are diagnosed during pregnancy or in the postpartum period. Pregnancy is associated with hormonal (TSH and HCG) and metabolic changes that might affect the thyroid gland. However, the relationship between these changes and the progression of thyroid carcinoma, especially DTC, is still controversial.[1]

The prognosis of DTC is favorable, with mortality less than 2% at 5 years; however, diagnosis of malignancy during pregnancy might raise anxiety regarding the optimal timing of the recommended therapies.[1] In general, the management of DTC consists of surgery (lobectomy and total thyroidectomy with or without lymph node dissection), selective use of radioiodine ablation, and levothyroxine suppression therapy.[2]

The 2015 American Thyroid Association (ATA) guidelines for adult patients with DTC recommend that women of childbearing age receiving RAI treatment should have a negative screening evaluation for pregnancy before RAI administration and avoid being pregnant for at least 6 months following RAI. This is due to the concern of increased risk for miscarriage and fetal malformation.[4] Therefore, our recent case report aimed to describe how pregnancy might affect the progression of DTC and the outcome of babies born to mothers who have recently (< 6 months) undergone RAI treatment.

CASE ILLUSTRATION

A 24-year-old pregnant woman with a history of thyroid cancer was consulted by the ob-gyn at our endocrine clinic for further evaluation. At the beginning of 2022, the patient complained of a lump under the left jaw. Upon ultrasound examination of the neck, in addition to a lump in the left sub-mandible, a nodule was discovered in the right thyroid. Then, surgery was performed to remove the lump in the neck and thyroid. The patient was given Iodine-131 ablation therapy at a dose of 100 mCi. Furthermore, the patient is being planned to repeat WBS with or without RAI. However, the patient was already pregnant three months after radio ablation therapy. The patient has no complaints of symptoms currently. Her history of illness was unremarkable. Her current medication was levothyroxine 125 µg once daily, folic acid 400 µg twice daily, calcium lactate twice daily, and aspirin 80 mg once daily. Her family history of illness was unremarkable.

Upon physical examination, the patient appeared well and alert. Her blood pressure was 118/84 mmHg, pulse was regular, 105 beats/minute, respiration rate 20 times/minute, and the axillary temperature was 36.8ºC. Her body weight was 68 kg with a height of 156 cm, and a body mass index of 27.94. Her head-neck examination was unremarkable apart from the postoperative scar tissue (Figure 1). Her latest thyroid function test (TFT) indicated a TSH level of 0.01 (0.55 - 4.78) µIU/mL and an fT4 level of 1.14 (0.7 - 1.48) ng/dL. The serum calcium level was 9.2 mg/dL. Her postoperative Tg level before ablation was 16.14 ng/mL. The WBS imaging following the administration of Iodine-131 ablation therapy indicated functional thyroid tissue remnants in the right thyroid field and thyroid tissue metastases in the left supraclavicular area (Figure 2). Detailed post-partial thyroidectomy pathology reports were as the following: right thyroid indicated papillary thyroid carcinoma (PTC), follicular and solid variant, with tumor size of 2.3 x 1.7 x 1.5 cm, without lymphangion-invasion nor perineural invasion (limited growth in the thyroid); left submandibular indicated fibro lipoma.

Fetomaternal examination results on 6 months pregnancy, revealed fetal biometry according to gestational age (31 - 32 weeks) with an estimated fetal weight of 1787 grams and fetal doppler was normal. Her current assessment was primigravida and stage I PTC (pT2N1M0, age < 55 years old) with intermediate risk of recurrence and indeterminate response of therapy. Then, she was prescribed levothyroxine 125 µg once daily along with previous medications, and a thyroid ultrasound examination was ordered. Two weeks later, the thyroid ultrasound revealed no discrete mass in the thyroid fossa and non-specific lymphadenopathies. Three weeks later, the baby was born normally, weighed 2680 grams, with normal thyroid function tests: neonatal TSH 1.02 µIU/mL (normal: < 9 µIU/mL), and fT4 2.6 ng/dL (normal: 0.83-3.09 ng/dL). During follow-up, a stimulated serum Tg level performed by stopping levothyroxine for 4 weeks revealed a negative result (< 0.04 ng/mL), with the anti-Tg level also negative (44.3 IU/mL). The patient was then classified as having an excellent response to therapy.

Figure 1. The head-neck examination showed postoperative scar tissue

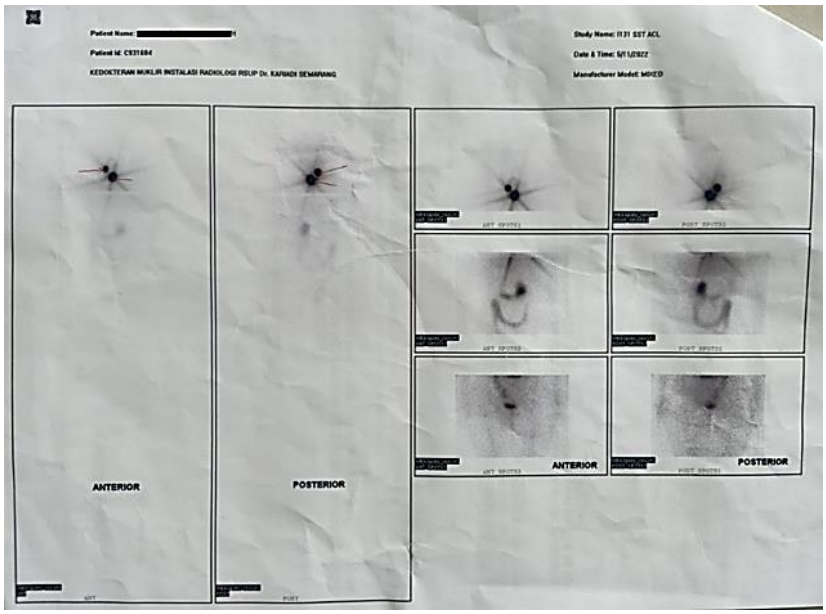

Figure 2. Whole-body scintigraphy imaging following administration of Iodine-131 ablation therapy indicated functional thyroid tissue remnants in the right thyroid field and thyroid tissue metastases in the left supraclavicular area

DISCUSSION

Papillary thyroid carcinoma is an epithelial neoplasm featuring evidence of differentiated follicular cells and a set of distinctive nuclear characteristics. There are several risk factors associated with PTC, namely ionizing radiation exposure (especially in childhood), genetics, obesity, and high dietary iodine intake. Papillary thyroid carcinoma is mostly diagnosed in middle-aged adults with a 3:1 female-to male ratio. RET protooncogene, NTRK1, and MET gene overexpression are several molecular derangements related to PTC. Mutation in the BRAF gene, particularly BRAFV600E, have also been identified in the pathophysiology of PTC and correlated with its prognosis.[5] Papillary thyroid carcinoma commonly presents as a painless thyroid lump with or without enlargement of cervical lymph nodes. Physical examination usually reveals a painless hard lesion that is less than 5 cm in size. Nodal metastases of ipsilateral lymph nodes are frequently reported in 27% of patients at presentation, although lateral lymph node

involvement is occasionally reported in some cases.[6]

The favored initial diagnostic approach for PTC is fine needle aspiration (FNA). Thyroid function tests have little role in the diagnosis of PTC because most patients have normal TFT at diagnosis. The preferred imaging technique for PTC is ultrasound, where microcalcification is a highly specific finding.[5] As primary treatment, the extent of surgery is decided after determining preoperative risk, which includes clinical, imaging, and cytological data. Following surgery, the risk of recurrence of the disease is determined according to ATA 2015 guidelines to decide further needs for RAI treatment. In general, low-risk patients do not need RAI adjuvant treatment, while intermediate and high-risk patients might be given RAI adjuvant treatment using selective doses. In this case, the patient has an intermediate risk of disease recurrence because of the presence of uptake in the neck on post-treatment WBS. Lifelong thyroid hormone replacement using levothyroxine is needed after thyroidectomy to achieve suppression of thyrotropin.[4]

Overall, the management of PTC during pregnancy can be categorized into two clinical scenarios: pregnant women who are newly diagnosed with PTC and pregnant or planning-to-be pregnant women with a history of PTC.[3] In our case, the patient has already received primary treatment (partial thyroidectomy) and has been given RAI treatment. Radioiodine (Iodine-131) administration during pregnancy is contraindicated due to the risks of fetal hypothyroidism, deformities, growth abnormalities, malignancies (leukemia), and other fatal changes. Additionally, it should not be administered to nursing mothers due to the significant accumulation of Iodine-131 in the lactating breast. Due to the slow-growing nature of PTC, further RAI therapy may be postponed allowing nursing for at least 6 to 8 weeks after the cessation of breastfeeding in nursing women.[3,4] Depending on the dose of Iodine-131 given, the patients need to be separated from the infant (approximately 6 feet) for at least 6 - 23 days.[7]

Before administering the first dose of RAI, it is recommended to measure the Tg level three to four weeks after surgery. A Tg level of > 30 ng/mL indicates disease persistence and is associated with recurrence, early treatment failure, distant metastases, and increased mortality. In a subset of patients with non-total thyroidectomy as primary treatment, the trend of Tg levels is used instead of a definite cutoff value.[4] However, Tg levels can significantly increase during pregnancy and return to preconception levels following delivery therefore, increasing levels of Tg should be interpreted carefully during pregnancy.[8] Neck ultrasound should be performed at 6 and 12 months, then the frequency is adjusted according to the patient's risk. Our present case was categorized as having an excellent response to therapy based on the nonspecific findings on imaging (neck US), and the stimulated Tg evaluation was negative following delivery. To maintain a TSH level in the range of 0.1 - 0.5 mU/L for appropriate thyrotropin suppression and to prevent fetal hypothyroidism, the levothyroxine dose should be adjusted every 4 weeks.[9]

The association between estrogen, HCG, and DTC has long been proposed due to the evidence that females of reproductive age are more likely to develop DTC.[10] Other studies also suggested the association between high parity and the increased risk of DTC.[11] In early pregnancy, the level of HCG increases, and simultaneously, the estrogen level also increases; therefore, theoretically, pregnancy will likely increase the risk of DTC. Some *in vitro* studies reported a proliferative effect of estrogen on thyroid cancer cells, while others reported the effect only on adenomatous and normal thyroid. Another study reported a higher incidence of DTC in women using estrogen oral contraceptives and hormone replacement therapy, while others did not.[12] Meanwhile, in a large cohort study, the use of clomiphene, a fertility agent, in parous women is not linked to an increased risk of DTC.[13] In this case, pregnancy-related hormonal changes did not seem to affect the progression of PTC, as the

result from the neck ultrasound evaluation indicated no structural evidence of disease.

The 2015 ATA guidelines for adult patients with DTC recommend that women of childbearing age should avoid being pregnant for at least 6 months following RAI due to the concern of negative pregnancy outcome.[4] A meta-analysis confirmed that the negative outcomes of pregnancies that occurred after a year following RAI treatment was not significant.[14] Another large-scale cohort study in Korea also reported the poor outcome of pregnancy after RAI was not significant if the interval was more than 6 months.[15] Following RAI administration, the ovaries are exposed to radiation from the blood, bladder, bowel, and, if any, metastases adjacent to the ovaries.[16] The effect of radiation absorbed by the ovaries can be categorized into deterministic effects, which are dose-dependent, and stochastic effects, which might occur at any radiation dose.[17] The 2017 ATA guidelines for the diagnosis and management of thyroid disease during pregnancy and the postpartum recommended all infants born to mothers with thyroid illness be screened for hypothyroidism 2-5 days after birth.[18] A neonatal TSH value of < 9 µIU/mL is considered normal and not associated with neonatal hypothyroidism, while the normal reference for fT4 in neonates is 0.83-3.09 ng/dL.[19] In this case, even though the pregnancy resulted in no apparent fetal malformation, further evaluation and active surveillance are needed for future negative outcomes. Women who recently underwent RAI also need to get effective contraception to prevent pregnancy under 6 - 12 months.

CONCLUSION

The management of intermediate-risk DTC in pregnancy following surgery and RAI treatment involves levothyroxine suppression therapy and active surveillance using Tg and neck ultrasound. Hormonal and metabolic changes during pregnancy might not affect the progression of intermediate-risk DTC. Recent radiation exposure (less than 6 months) due to RAI treatment to the female gonadal tissue might not increase the risk for miscarriage and fetal malformation in the pregnancy.

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