Thyroid Papillary Cancer Triggered by Pregnancy: Case Report

Gebeliğin Tetiklediği Tiroid Papiller Kanser

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ABSTRACT Differantiated thyroid cancer (DTC) is the second most common cancer seen during pregnancy. The mechanism of DTC development in pregnancy is still unclear. The incidence of DTC is tripled in women who are in childbearing age. It is believed that pregnancy increases the risk of DTC. However, there is no special monitoring guidelines at pregnancy for patients with benign thyroid nodules. In a 36 year old female patient that was monitored during pregnancy because of a benign thyroid nodule, the authors have detected a transition to thyroid papillary carcinoma in the 27th gestational week. The authors would like to underline the fact that malign transition can take place during pregnancy in women with previous benign thyroid nodules and that careful monitoring should be arranged for these subset of patients in pregnancy.

Key Words: Thyroid cancer, papillary; pregnancy; thyroid nodule


Anahtar Kelimeler: Tiroid kanser, papiller; gebelik; tiroid nodülü

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Thyroid cancer ranks as the 10th between solid organ tumors when incidence rates are compared, and its incidence is constantly increasing.1 Differantiated thyroid cancer (DTC) is the second most common cancer seen in pregnant women with a prevalence of 14 in 100 000.2 The fact that DTC is commonly seen during pregnancy has surfaced the notion that elevated hormones in pregnancy such estrogen, chorionic gonadotrophin (HCG) and others trigger the possibility of tumoral de velopment and growth. It is claimed that HCG, which is especially elevated in the early stages of pregnancy, may cause growth in the already existing nodule or may be responsible for a new nodule development.3 This case was presented because a 36 year old female patient that was monitored during pregnancy due to a benign thyroid nodule, was found
to progress to a thyroid papillary carcinoma in the 27th gestational week.

**CASE REPORT**

36 year old female patient (grada 3, para 2) was being followed due to a benign thyroid nodule. In her thyroid ultrasonography (USG), a 22x14x13 mm diameter hypoechogenic thyroid nodule of regular borders was present in the left lobe. The patient had no history of radiation therapy to the head and neck region. The patient had no history of thyroid cancer in the her family. The patient who had a hypoactive nodule in thyroid scintigraphy was evaluated as having a benign cytology in her thyroid fine needle aspiration biopsy (TFNAB). Her TSH levels were found to be 3.5 mIU/mL (normal range 0.27-4 mIU/mL) and a levothyroxine therapy of 100 mcg/day was started as a thyroid nodule suppression therapy. In her follow up examination held 6 months later, there was no growth in the thyroid nodule. Her TSH levels were found to be 0.21 mIU/ml. One year after her last visit, the patient showed for her yearly control at which time she was pregnant and in her 27th gestational week. In her physical examination, a 2 cm non-tender, firm, fixed lymphadenopathy in the left cervical region (Level VI) was detected. In her USG, a hypoechogenic nodule of 35x20x15 mm with irregular borders and microcalcifications was detected in the left lobule. There was a 25x20x18 mm lymphadenopathy with microcalcifications and small cystic areas in the Level VIth neck region without an indistinct hilus. TFNAB was performed on the thyroid nodule and lymphadenopathy that showed malignant signs ultrasonographically. Results of TFNAB were interpreted as thyroid papillary carcinoma with lymph node metastasis. As the patient was in the third trimester of pregnancy, surgical operation was planned for the early post partum period. L-thyroxine suppression therapy was continued. Her TSH levels were found to be 0.1 mIU/mL. Delivery was by caesarean section at the 38th gestational week according to the last menstrual period. Bilateral total thyroidectomy and central neck dissection was performed in the first post partum month. Pathology examinations revealed tumoral lesions in the left thyroid lobe of which the maximum had a diameter of 1.5 cm. There were no signs of lymphovascular invasion or necrosis in the tumoral regions. Tumor was found to be invasive till the capsule but otherwise limited to the thyroid gland. The capsule was intact. With the dyes, immunohistochemical S-100, high molecular weight keratine (HMWK) and cytokeratine 19 (Figure 1) that were applied to two different cross sections, there was staining in the tumoral regions. The final assessment was that it was a case of thyroid papillary cancer (T1b). In the serial sections of the lymph nodes, there were tumoral lesions that had papillary forms consisting of clear nuclei and random calcifications. Immunohistochemical HMWK, mezothelium antibody (HBME-1), Cytokeratine 19 and S100 were positive in tumoral regions and was naturally positive in Bcl-2 lymphoid tissue. Final judgement was in favour of “Papillary Thyroid Carcinoma with lymph node metastasis”. Following operation, there were no residual tissues seen in USG and scintigraphy. Thoracic computerized tomography (without contrast) and abdominal USG were performed for metastases screening. There were no signs in favour of metastases. The patient’s TSH level was 6.62 mIU/mL and her serum thyroglobuline (Tg) level was 3.81 ng/mL. Anti-Tg was found to be negative. L-thyroxin treatment of the patient was discontinued and radioactive iodine ablation (RAI) therapy was started. Following RAI ablation therapy, no recurrence was observed in the USG performed in the 3rd post therapeutical
month. Her serum Tg level was found to be 0.1 ng/mL.

**DISCUSSION**

In a 36 year old female patient that was monitored during pregnancy because of a benign thyroid nodule, a transition to thyroid papillary carcinoma was detected in the 27th gestational week.

There is a three fold increase in the incidence of DTC in women of childbearing age. Because of this statistics, the relationship between DTC and estrogen and HCG is currently being discussed.

Many studies have claimed a correlation between elevated births and DTC risk. In our case, the thyroid carcinoma developed during the third pregnancy in correlation with the literature data.

In some studies that assessed the relationship between estrogen and DTC, it was proposed that there was a significant increase in the risk whereas in some studies there were no statistically significant correlations between these two parameters.

It was claimed that estrogen increased this risk by pro-proliferative effects in the thyroid cell lines. In a in vitro study, it was shown that estrogens caused a significant increase in estrogen receptor alpha (ERα) expression in thyroid cancer cell lines.

Moreover, it was suggested that estrogen could trigger follicle development in TSH controlled thyroid in studies with neoplastic, hyperplastic and normal thyroid tissues. However, as a contrary opinion, it was claimed that even though estrogen had stimulatory effects in normal and adenomatous thyroid tissue, it did not trigger thyroid cancer.

Clinical studies show the same discrepancies about estrogen containing oral contraceptives and postmenopausal hormone replacement therapies. It has been shown that estrogens can increase the Tg production and Tg gene expression in DTC. Moreover, clinical studies show that serum Tg levels of pregnant women are high even without detectable tumor.

Thyroid tissue may secrete more than normal amounts of thyroid hormone during early pregnancy in response to HCG which has similarities with TSH. Elevated serum HCG levels cause an accelerated growth in thyroid tumor size especially in early pregnancy and at the same time can stimulate the growth of benign and malignant thyroid lesions. Although it is known that HCG increases the thyroid hormone production, there is no distinct relationship shown between HCG and DTC.

In cohort studies performed on women using fertility medicines, it was found that there was no increased risk of DTC resulting from HCG use.

There are contrasting views about increased thyroid cancer in pregnancy. Some investigators report that thyroid nodules discovered during pregnancy are more likely to be malignant than those found in women who are not pregnant. Some investigators report that thyroid nodules may enlarge, but the incidence of thyroid cancer is not increased during pregnancy. Kung et al. shown that pregnancy was associated with an increase in the size of preexisting thyroid nodules as well as new thyroid nodule formation. Some data show that pregnancy is not a risk factor for thyroid cancer development or recurrence.

There is no consensus on the optimal DTC operation time during pregnancy. It is found reasonable to delay the operation to postpartum period according to the patient’s will in absence of aggressive disease. Although it is thought that the timing of treatment affects the recurrence or progression of the disease, it is observed that there is no major effect on overall survival. There is no proof in favour of the fact that pregnancy should be discontinued when DTC is diagnosed. In our case, the operation was delayed till the postpartum period since the diagnosis was in the third trimester and the patient was willing to have the operation after giving birth.

Radioactive iodine therapy is contraindicated during pregnancy because of its toxic effects (fetal hypothyroidism, somatic growth disorders, leucemia etc) on the embryo or fetus. Radioactive iodine therapy should not be performed on breastfeeding women as it accumulates in the mother’s milk. In slowly growing thyroid cancers, radioactive iodine therapy may be delayed when there is breastfeeding. It would be wise to advise the pa-
patients to avoid pregnancy at least 6 months after I-131 administration.\textsuperscript{23} In our case, post operational RAI ablation therapy was started as the mother was not breastfeeding.

Ambiguity about DTC development in pregnancy is still going on.\textsuperscript{21} However, it is believed that pregnancy increases the risk of DTC. There is no special monitoring guideline at pregnancy for patients with benign thyroid nodules. As a result, we would like to stress the fact that malign transition can take place during pregnancy in women with previous benign thyroid nodules and that careful monitoring should be arranged for this subset of patients in pregnancy.

REFERENCES