

Chapter 1

Current Concepts Regarding Thyroid Cancer during Pregnancy

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First Published **April 02, 2016**

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Abstract

Thyroid cancer is the second most common cancer diagnosed during pregnancy. According to several studies, DTC is detected three times more in women of reproductive age and the risk may be associated with high parity of pregnancy hormones. Total thyroidectomy should be performed in the second trimester only if there are factors that indicate instant surgery during pregnancy. Otherwise, surgery should be postponed to the post-delivery period. Follow-up for each patient must be considered as highly significant and be based on three basic steps :1) keep an adequate balance of maternal calcium and thyroid 2) preserve optimal levels of maternal thyroxin and 3) manage safe follow-up visits for the mother and make an additional treatment plan when needed.

Keywords

Thyroid Cancer; Pregnancy; Women; Differentiated Thyroid Cancer; Reproductive Age; Thyroid Function

Introduction

Thyroid cancer, the most frequent endocrine malignancy, is usually detected in young patients and is more commonly diagnosed in women. The diagnosis of a tumour during pregnancy observably causes distress about the most appropriate timing of suggested treatments and about both maternal and neonatal morbidity. Physiological changes which are considered to be normal during pregnancy and worries about fetal health pose significant

challenges to all aspects of thyroid cancer management. The treatment plan should be unique for each patient and the follow-up must be considered as highly significant. However, there are some discrepancies in the management of the two major histotypes: the differentiated thyroid cancer (follicular and papillary cancer DCT) and the medullary thyroid cancer (MTC) just as for non-pregnant patients.

Epidemiology

According to recent research, the second most common cancer diagnosed during pregnancy is DTC [1]. Therefore, thyroid cancer ranks among the most common cancers detected in pregnancy, with a prevalence of 3,6-14 per 100,000 live births. So, the detection of thyroid cancer in pregnant woman is quite common. In fact, an incidence of 10% of the thyroid cancers taking place during reproductive period are diagnosed during pregnancy or in the early post-partum period [2,3].

Pregnancy as a Risk Factor of Thyroid Cancer

Due to the homology between beta-subunits of human chorionic gonadotropin (HCG) and TSH, HCG is capable of stimulating the thyroid gland and may play a significant role to the enlargement of thyroid nodules and carcinomas. In a clinical study the researchers compared pregnant patients with a control group consisted of non

pregnant patients and indicated that the growth of PMC was higher in the first group [4]. Since DTC is detected three times more in women of reproductive age, it has been speculated that there are linkages between estrogen, human chorionic gonadotropin (HCG) and DTC. According to several studies, the risk of DTC may be associated with high parity of pregnancy hormones. Concluding, high parity is closely related with the risk of DTC; but the outcome of DTC in pregnancy is still lacking of clarity [1]. However, research indicated that the effect of estrogens on thyroid cancer in pregnancy was a risk factor of thyroid carcinoma in multiparous women, and these effects tend to be small [5]. It is recommended by a recent meta-analysis that women should be closely followed up so that the disease could be early detected. Pregnancy does not boost the possibility for lymphatic or distance metastasis [6].

DTC in pregnant patients shows higher recurrence, demonstrating that pregnancy could have a negative prognostic value in women with DTC. Further studies are required in order to clarify the underlying mechanisms that are still vague. Results suggest that in case of DTC diagnosis during or shortly after pregnancy, a more careful follow-up is needed [7]. However, it seems that pregnancy exert a risk for tumor recurrence or growth only in women with structural or biochemical disease present prior to the pregnancy [8]. Nevertheless, there are several studies that indicate that, in fact, pregnancy does not have

an influence on prognosis of thyroid cancer [9,2].

Management of Thyroid Cancer During Pregnancy

It is suggested by recent published ATA Guidelines that a nodule with cytology indicating papillary thyroid carcinoma, discovered early in pregnancy, should be monitored sonographically every three months. It is important to be mentioned that surgery should be performed in the second trimester even if the fetus is being at risk in case that papillary thyroid carcinoma grows essentially by 24 weeks gestation (50% in volume and 20% in diameter in two dimensions) or develops ultrasound evidence of extracapsular tumor invasion, compressive symptoms or lymph node metastases 1 cm, or larger [5,10-11]. However, it is advisable surgery to be performed after the delivery in case that the tumor is stable by midgestation or is diagnosed in the second half of pregnancy without negative impacted upon the patient's prognosis [12,13]. If surgery would not performed until the second trimester, thyroid hormone suppression treatment may be valuable for patients with an FNA biopsy diagnostic of a DTC. The aim of LT4 therapy is to maintain TSH in the low-normal range of 0.1–1.5 mU/L [8]. In principle, the characteristics of DTC in pregnancy are similar to general population of young adults, with good prognosis. Attention should be paid to avoid interventions that could cause adverse effects on the health of mother or fetus or even on preg-



An algorithm for the work-up and treatment of a thyroid nodule detected during pregnancy. [8] (Permission taken from the editor).

nancy progress. Total thyroidectomy should be performed only if there are factors that indicate instant surgery during pregnancy. Otherwise, surgery should be postponed to the post-delivery period [10].

It is greatly challenging to manage medullary cancer during pregnancy. Small medullary cancer with low serum calcitonin can be observed till the end of pregnancy. Larger medullary cancers with high calcitonin would require earlier surgical treatment in the form of total thyroidectomy, central compartment neck dissection, with ipsilateral neck dissection. As mentioned above, patients with rapid enlargement of tumor, aggressive pathological or clinical features and ultrasound features are considered to be at high risk and would need surgery before delivery [13].

Radioiodine scan is not permitted in pregnancy and breastfeeding [14].

Optimal timing for surgery and complications

There has been observed that during the first three months of gestation, when women with thyroid cancer have been operated, spontaneous abortion rates are relatively high. Moreover, in case of increased TSH levels – greater than 2,5mIU/liter-during the end of pregnancy, women are more vulnerable to breech presentation and

obstetrical complications such as fetal death [5]. Evidence from a retrospective, cross-sectional study in which 201 pregnant women suffering from thyroid and parathyroid cancer with age-matched nonpregnant controls showed that length of hospital stay, hospital costs, and rates general and endocrine complications were much greater in pregnant women than in typical patients. A more extended survey with a sample of almost thirteen thousand pregnant women supported the higher risk of spontaneous abortion in women who underwent surgery during gestation in contrast to those who did not. Another relative study made a comparison the outcomes of DTC between 61 women in pregnancy and 528, age matched, non-pregnant patients. Most of them were operated after giving birth but there were a few exceptions. The surgery was performed for one of them in the first trimester, twelve of the rest in the second, and one in the third trimester. Overall, after a median follow-up of 22,4 years, recurrence was similar in all four groups, no matter when the surgery was performed. Until now, researchers have not reached in agreement about the appropriate timing that a pregnant would undergo a surgery for DTC, and the specific time of surgery depends on patients' willing and other risk factors, though it is generally accepted that it is reasonable to delay surgery until after delivery when the disease is not aggressive [1,13].

Follow up

The most suitable clinical monitoring for pregnant women with thyroid cancer is based on three basic steps: 1) keep an adequate balance of maternal calcium and thyroid hormones in order to ensure the normal maturation of the foetal central nervous system; 2) preserve optimal levels of maternal thyroxine to stay away from potential recurrence or broaden of disease; and 3) manage safe follow-up visits for the mother and make an additional treatment plan when needed [2].

In any case of patient, either for those with first diagnosis or recurrent disease, post-operative therapy for DTC is based on the management of suprathysiologic “suppressive” oral doses of levothyroxine. The last forty years, this treatment has been widely used, with the statement that suppression of endogenous TSH deprives TSH-dependent DTC cells of the most significant growth factor. Thus, thyroxine treatment intends to suppress pituitary secretion of TSH, as indicated by serum TSH levels below 0.05 mIU/L. Many scientists have stated reduced number of tumour recurrence with thyroxine therapy in DTC. The required doses of L-thyroxine, to preserve maternal serum-free thyroxin concentrations within the upper third of the normal rates and for suppression of TSH levels, should be greater than 150/200 µg (at least 2 µg/kg/day). TSH should be kept under observation roughly every 4 weeks until 16–20 weeks of gestation and once be-

tween 26 and 32 weeks of gestation [8]. Since the end of pregnancy, it is acceptable to gradually decrease thyroxine dose in order to reach pre-pregnancy levels, while TSH levels should be continually under control [2].

In contrast, recent British guidelines for thyroid cancer in pregnancy, indicate that there is no data suggesting for or against suppression of serum TSH concentrations during pregnancy, when women choose to postpone the operative treatment for differentiated thyroid cancer (DTC) until after delivery [14].

For patients with MTC, whose tumours deriving from C cells are not TSH-dependent, there is no need for suppressive therapy, but just for thyroxine replacement treatment after surgery with same dosages as in hypothyroidism [2].

Patients that have undergone thyroidectomy often need support with calcium and D vitamin. It's important to avoid maternal and neonatal hypocalcemia not only for foetal bone development but also for health and disease prevention.

Furthermore, the follow-up should be added by neck sonography which is a method to detect loco-regional recurrences, followed by meticulous physical examination by experienced personnel and, when recommended, ultrasound-guided FNA to detect neck recurrence [2].

Conclusion

In conclusion, most authors claim that there is a weak link between thyroid cancer and pregnancy but it mainly concerns multiparous women or women with concomitant risk factors. Thyroid cancer in pregnancy and DTC in young adults have similar indolent course but pregnant woman seems to need a closer follow-up. In case of no sonographic evidence of capsular invasion or metastatic nodes, thyroid cancer may be followed by ultrasound without operative treatment until delivery. Nevertheless, when progressive disease is demonstrated, there might be a need for thyroidectomy. Generally, total thyroidectomy is safe but should be done during the second trimester. In case of diagnosis of medullary cancer, it is acceptable to use a more aggressive surgical approach [13].

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