Differentiated Thyroid Cancer and Pregnancy

Shiny Sherlie Varghese · Ashish Varghese · Chris Ayshford

Received: 6 December 2012 / Accepted: 3 January 2013 / Published online: 9 March 2013
© Association of Surgeons of India 2013

Abstract Thyroid cancer is second most common malignancy diagnosed during pregnancy. Differentiated thyroid cancer (DTC) is more common in reproductive age group due to its association with oestrogen and human chorionic gonadotropin. Evaluation and management of DTC has changed from an aggressive approach, now, to a more conservative approach. Management of DTC must be coordinated among the different specialists which include the surgeon, endocrinologist, radiologist, pathologist and, in pregnant patients, the obstetrician. Generally, DTC can be postponed till delivery, but exceptions include airway compromise, aggressive cytologic features, invasion of surrounding tissue, extracapsular spread and poor prognostic factors.

Keywords Differentiated thyroid cancer · Pregnancy · Risk stratification · Ultrasonography · Cytology

Introduction

Approximately 10 % of thyroid cancers diagnosed during childbearing age occur in pregnancy or the 12-month postpartum [1]. Thyroid cancer is reportedly the second most

common malignancy diagnosed during pregnancy (second only to breast cancer), at a rate of 0.144 cases per 1,000 births. Seventy-five percent of these women are diagnosed during the 12-month postpartum period [2]. Differentiated thyroid cancer (DTC) is three times more common in reproductive age and is thought to be due to an association between oestrogen and human chorionic gonadotropin [3]. This is further supported by studies which say that high parity and patients on fertility drugs have a higher risk of DTC. Late pregnancy also has increased the incidence of DTC [4].

Incidence

Ultrasound imaging for pregnancy, breast, head and neck with a routine look into thyroid has resulted in picking up of many asymptomatic thyroid nodules at an early stage. This is attributed to the increased incidence from 3.6 per 100,000 in 1973 to 8.7 per 100,000 in 2002, which is a 2.4-fold increase [5]. Chen et al. also [6] recognized a similar increase in DTC rates over the last two decades and concluded that the increase could not be explained solely on the basis of improved diagnostic methods. The recognition of DTC has certainly increased, forcing the need for clinical decision-making on a larger cohort of patients. A study of the California Cancer Registry linked to maternal/neonatal hospital discharge identified a thyroid cancer incidence of 14.4 per 100,000 [7].

Evaluation

In view of little supporting data for an aggressive approach for DTC, now a more conservative approach is the standard of care. While most thyroid nodules in pregnancy are non-

S. S. Varghese
Department of Obstetrics and Gynaecology, Christian Medical College, Ludhiana, Punjab, India

A. Varghese (✉)
Department of ENT–Head and Neck Surgery, Christian Medical College, Ludhiana, Punjab, India
e-mail: ashishvargheseent@yahoo.com

C. Ayshford
Department of ENT–Head and Neck Surgery, Worcestershire Royal Hospital, Charles Hastings Way, Worcester WR5 1DD, UK

obstructive, non-constrictive and non-functional, the main concern about thyroid masses is whether a cancer is present. The optimal diagnostic strategy for thyroid nodules detected during pregnancy is based on risk stratification. All women should have the following: a complete history and clinical examination, serum TSH testing and ultrasound of the neck. Diagnostic evaluation of the patient can be carried out as if there was no pregnancy except radioactive iodine scanning which is contraindicated [8]. The patient with a thyroid nodule should be asked about a family history of benign or malignant thyroid disease, familial medullary thyroid carcinoma, multiple endocrine neoplasia type 2, familial papillary thyroid carcinoma and familial polyposis coli [9]. Thyroid function test along with calcitonin is done as a diagnosis of medullary cancer would change the approach. Some of the medullary cancer occasionally may not produce calcitonin and so carcinoembryonic antigen is done. Ultrasound is a very accurate tool in detecting the nodule and determining the number, size and characteristic features, monitoring their growth and evaluating cervical lymph nodes. Features suggestive of DTC are hypoechoic lesions, irregular margins without peripheral halo, fine punctuate calcification, intranodular flow with multiple chaotically arranged vascular poles and infiltration of adjacent areas. The presence of two or more suspicious sonographic criteria identifies most neoplastic lesions of the thyroid gland (87–93 % of cases) [10].

Fine needle aspiration cytology (FNAC) is a critical test and is dependent on the ability of the cytopathologist and the adequacy of the specimen. Nodules smaller than 10 mm do not require a FNAC unless suspicious for malignancy on ultrasound or clinical grounds [11]. FNAC interpreted as ‘follicular neoplasm’ indicates a tumour that is most likely benign [12]. Young pregnant patients are unlikely to have pure follicular cancers as they are rare. In pregnancy, malignant follicular neoplasms are generally the follicular variant of PTCs, which are typically non-aggressive. Some authors feel that biopsy results suggestive of Hürthle cell carcinomas warrant more aggressive treatment, although the opinion that these tumours are more aggressive than non-Hürthle cell follicular carcinomas is controversial [13].

Surgery for DTC in Pregnancy

For most women with newly diagnosed DTC or those with resectable macroscopic recurrence, a decision about whether or not to perform surgery during pregnancy has to be made. A retrospective, cross-sectional study comparing 201 pregnant women undergoing thyroid and parathyroid surgery with age-matched non-pregnant controls reported that pregnant women had significantly longer hospital stay, higher hospital costs and higher

rates of general and endocrine complications [14]. Another large survey of almost 13,000 pregnant women reported a significantly higher risk of spontaneous abortion in women who underwent surgery during pregnancy compared with those who did not have surgery [15]. In a retrospective study which compared outcomes of DTC in 61 pregnant women with 528 age-matched non-pregnant controls found that of the pregnant women with DTC, 1 underwent surgery in the first trimester, 12 in the second and 1 in the third trimester, while most of the patients underwent surgery after delivery. After a median follow-up of 22.4 years, no significant differences in recurrence were observed between women who underwent surgery during or after pregnancy [16].

It is generally accepted that almost any cancer discovered in the third trimester may be observed until after delivery. Second trimester surgical intervention may be considered for aggressive variants of cancer and, in particular, for medullary cancer. Many reviews of thyroid cancer in pregnancy generally advise postponing surgery for well-differentiated thyroid cancer, but suggest that a more aggressive surgical approach may be warranted when medullary cancer is diagnosed [17].

Thyroid Surgery During Pregnancy

The management of medullary cancer in pregnancy presents unique challenges. Small medullary cancer with low serum calcitonin can be observed till the pregnancy is over. Larger medullary cancers with high calcitonin would require surgical treatment at the earliest in the form of total thyroidectomy, central compartment neck dissection, with ipsilateral neck dissection. A delay in the treatment decreases the chance of cure [17], also to some forms of well-differentiated thyroid cancers with aggressive behaviours such as tall cell and columnar cell. Patients with rapidity of growth, compressive symptoms and ultrasound features are stratified in high risk and would need intervention before delivery.

Surgery for thyroid carcinoma during the second trimester of pregnancy has not been demonstrated to be associated with increased maternal or foetal risk. Surgery performed in the first trimester is associated with altered organogenesis and spontaneous abortion and in third trimester, preterm labour and delivery [18]. Maternal hypothyroidism and hypoparathyroidism are also a risk post-thyroidectomy.

Monitoring of DTC During Pregnancy

When a decision has been made to defer surgery for well-differentiated thyroid carcinoma until after delivery, neck

ultrasounds should be performed during each trimester to assess for rapid tumour growth, which may indicate the need for surgery. Surgery in women with well-differentiated thyroid carcinoma may be deferred until postpartum without adversely affecting the patient's prognosis. Thyroid hormone therapy may be considered in pregnant women who have deferred surgery for well-differentiated thyroid carcinoma until postpartum. The goal of T4 therapy is a serum TSH level of 0.1–1.5 mIU/L. The pre-pregnancy TSH goal in women with DTC, which is determined by risk stratification, should be maintained during pregnancy. TSH should be monitored approximately every 4 weeks until 16–20 weeks of gestation and once between 28 and 32 weeks of gestation.

RAI Post-DTC Surgery

Following surgery for DTC the majority of patients will receive an ablative dose of radioactive iodine (RAI). The possible deleterious effects of radiation on gonadal function and the outcome of subsequent pregnancies have been evaluated by Sawka et al. [19]. There is no evidence that previous exposure to radioiodine affects the outcomes of subsequent pregnancies and offspring.

In order to avoid stagnation of ¹³¹I in the lactating breast and minimize the risk of breast radiation exposure, suppression of lactation through dopaminergic agents has been utilized, but this should only be used very cautiously after discussion with the patient [20].

Pregnancy should be deferred for 6 months following RAI treatment. LT4 dosing should be stabilized following RAI treatment before pregnancy is attempted.

Monitoring the Pregnancy Post-DTC Treatment

Ultrasound and thyroglobulin (Tg) monitoring during pregnancy in patients with a history of previously treated DTC are not required for low-risk patients with no Tg or structural evidence of disease prior to pregnancy. Ultrasound monitoring should be performed each trimester during pregnancy in patients with previously treated DTC and those who have high levels of Tg or evidence of persistent structural disease prior to pregnancy [21].

Conclusion

Management of DTC must be coordinated among the different specialists which include the surgeon, endocrinologist, radiologist, pathologist and, in pregnant patients, the obstetrician. Surgery when considered risky

to both mother and foetus must be considered. Generally, DTC can be postponed till delivery, but exceptions include airway compromise, aggressive cytologic features, invasion of surrounding tissue, extracapsular spread and poor prognostic factors. Small medullary cancer with low calcitonin can wait till pregnancy is over, but not so with large one with high calcitonin.

References

1. Yasmeen S, Cress R, Ramano PS, Xing G, Berger Chen B, Danielsen B, Smith LH (2005) Thyroid cancer in pregnancy. *Int J Gynaecol Obstet* 91:15–20
2. Smith LH, Danielsen B, Allen ME, Cress R (2003) Cancer associated with obstetric delivery: results of linkage with the California cancer registry. *Am J Obstet Gynecol* 189:1228–1235
3. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ (2007) Cancer statistics, 2007. *CA: A Cancer Journal for Clinicians* 57(1):43–66
4. Hannibal CG, Jensen A, Sharif H, Kjaer SK (2008) Risk of thyroid cancer after exposure to fertility drugs: results from a large Danish cohort study. *Hum Reprod* 23(2):451–456
5. Owen RP, Chou KJ, Silver CE, Beilin Y, Tang JJ, Yanagisawa RT, Rinaldo A, Shaha AR, Ferlito A (2010) Thyroid and parathyroid surgery in pregnancy. *Eur Arch Otorhinolaryngol* 267:1825–1835
6. Chen AY, Jemal A, Ward EM (2009) Increasing incidence of differentiated thyroid cancer in the United States, 1988–2005. *Cancer* 115:3801–3805
7. Smith LH, Danielsen B, Allen ME, Cress R (2003) Cancer associated with obstetric delivery: results of linkage with the California Cancer Registry. *Am J Obstet Gynecol* 189:1128–1135
8. Abalovich M, Amino N, Barbour LA et al (2007) Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 92(Suppl 8):S1–S47
9. Loh KC (1997) Familial nonmedullary thyroid carcinoma: a meta-review of case series. *Thyroid* 7:107–113
10. Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, Panunzi C, Rinaldi R, Toscano V, Pacella CM (2002) Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab* 87:1941–1946
11. Gharib H, Papini E, Valcavi R, Baskin HJ, Crescenzi A, Dottorini ME, Duick DS, Guglielmi R, Hamilton CR Jr, Zeiger MA, Zini M, AACE/AME Task Force on Thyroid Nodules (2006) American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *Endocr Pract* 12:63–102
12. Scilab GM, Staerkel GA, Shapiro SE et al (2003) Fine-needle aspiration of the thyroid and correlation with histopathology in a contemporary series of 240 patients. *Am J Surg* 186:702–710
13. Haigh PI, Urbach DR (2005) The treatment and prognosis of Hürthle cell follicular thyroid carcinoma compared with its non-Hürthle cell counterpart. *Surgery* 138:1152–1158
14. Kuy S, Roman SA, Desai R, Sosa JA (2009) Outcomes following thyroid and parathyroid surgery in pregnant women. *Arch Surg* 144(5):399–406
15. Brodsky JB, Cohen EN, Brown BW (1980) Surgery during pregnancy and fetal outcome. *Am J Obstet Gynecol* 138(8):1165–1167
16. Moosa M, Mazzaferri EL (1997) Outcome of differentiated thyroid cancer diagnosed in pregnant women. *J Clin Endocrinol Metab* 82(9):2862–2866

17. Massoll N, Mazzaferri EL (2004) Diagnosis and management of medullary thyroid carcinoma. *Clin Lab Med* 24:49–83
18. Mestman JH, Goodwin TM, Montoro MM (1995) Thyroid disorders of pregnancy. *Endocrinol Metab Clin North Am* 24:41–71
19. Sawka AM, Lakra DC, Lea J, Alshehri B, Tsang RW, Brierley JD, Straus S, Thabane L, Gafni A, Ezzat S, George SR, Goldstein DP (2008) A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors. *Clin Endocrinol (Oxf)* 69:479–490
20. Cooper DS, Doherty GM, Haugen BR et al (2009) Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 19(11):1167–1214
21. Hirsch D, Levy S, Tsvetov G, Weinstein R, Lifshitz A, Singer J, Shraga-Slutsky I, Grozinski-Glasberg S, Shimon I, Benbassat C (2010) Impact of pregnancy on outcome and prognosis of survivors of papillary thyroid cancer. *Thyroid* 20:1179–1185