7.1. MANAGEMENT OF DIFFERENTIATED THYROID CANCER DURING PREGNANCY

ROBERT J. AMDUR, MD AND ERNEST L. MAZZAFERRI, MD, MACP

Management of a patient with a thyroid nodule, or confirmed thyroid cancer, during pregnancy is controversial. The purpose of this chapter is to explain this controversy and make treatment recommendations. The paper by Moosa & Mazzaferri (1997) cites the major studies of this issue. Table 1 summarizes the main points from this chapter.

THE CONTROVERSY

Controversy about the management of pregnant patients with a thyroid nodule or thyroid cancer is based on disagreement about the effects that the hormonal changes of pregnancy have on the growth rate of thyroid cancer. Clinicians who believe that thyroid cancer is more aggressive during pregnancy take the position that the diagnosis of a thyroid nodule and, if necessary, thyroidectomy should be pursued during pregnancy and view termination of the pregnancy or premature delivery as necessary considerations. However, this is an older view of the problem, mainly based on isolated case reports or personal experiences in which pregnant women with thyroid cancer did not fare well (Kobayashi 1994). The contemporary view is that pregnancy has no major influence on the prognosis of thyroid cancer during pregnancy and that surgery and I-131 therapy can be delayed until after delivery in patients with well differentiated tumors (Herzon 1994; Moosa & Mazzaferri 1997; Driggers 1998; Vini 1999).

PREGNANCY STIMULATES THE GROWTH OF THYROID CANCER

A few case studies report aggressive features of differentiated thyroid cancers diagnosed during pregnancy. No prospective study demonstrates a difference in outcome compared

Table 1. Management of Thyroid Cancer During Pregnancy.

There is controversy about the prognosis of thyroid cancer during pregnancy:

- Some clinicians think that thyroid cancer behaves more aggressively during pregnancy
- Other clinicians think that pregnancy has no effect on the prognosis of thyroid cancer

There are data that suggest pregnancy may affect thyroid cancer behavior:

- There are reports that solitary nodules are more likely to be malignant during pregnancy
- There are in-vitro data that pregnancy hormones may cause neoplastic transformation of follicular cells, or stimulate proliferation of thyroid cancer

Data suggesting that pregnancy does not have an important effect on the behavior of thyroid cancer:

- Multiple clinical series with age-matched control groups find that the prognosis of differentiated thyroid cancer is the same in pregnant and nonpregnant women

Our policy:

- We recommend neck ultrasound and fine-needle aspiration at any stage of pregnancy for patients with a thyroid mass or adenopathy that is suspicious for cancer
 - We do not recommend diagnostic studies that involve ionizing radiation as part of the evaluation of a patient with thyroid pathology during pregnancy
 - In the absence of a history of rapid tumor growth or signs of problems that require immediate intervention (e.g., airway compromise), we do not recommend open biopsy or thyroidectomy if fine needle aspiration does not establish a diagnosis
 - When thyroid cancer is diagnosed during pregnancy, we recommend delaying additional workup and treatment until after the completion of pregnancy as long as the tumor does not have anaplastic features or a history of rapid growth, metastases or other aggressive features
 - In a patient with a large primary tumor or extensive adenopathy, we suggest completing the pregnancy as soon as the risk of premature delivery is low, otherwise we recommend letting the pregnancy take its normal course
 - We recommend that the diagnostic workup be completed, and the appropriate treatment initiated, soon after the completion of the pregnancy
-

to a control group. Concern about rapid growth of thyroid cancer during pregnancy is based on several observations:

Malignant nodules may be more common during pregnancy: There are reports that a solitary thyroid nodule during pregnancy is more likely to be malignant than a solitary nodule in a woman of similar age who is not pregnant (Rosen 1986.) and a weak association between parity and risk of thyroid cancer was found in an epidemiologic study (Galanti 1995). Ascertainment bias is likely a problem in all of these studies. Most contemporary opinions of the risk of thyroid cancer in thyroid nodules do not consider pregnancy to be a risk factor for thyroid cancer in an isolated thyroid nodule. This is summarized in the recent study by (Hegedus 2004) and in Chapter 1.

Pregnancy hormones may stimulate thyroid cell proliferation: There is good evidence that human chorionic gonadotropin binds to the TSH receptor of normal and neoplastic cells of follicular origin and that it may stimulate their growth (Hershman 1999). There is also evidence that malignant thyroid tissue may bind endogenous estrogens, but this finding has not been confirmed in all studies and its significance in patients with thyroid cancer has never been demonstrated.

THE DATA THAT PREGNANCY HAS NO SIGNIFICANT EFFECT ON THE PROGNOSIS OF THYROID CANCER

There are now several studies that use age-matched controls to evaluate the effect of pregnancy on the prognosis of patients with differentiated thyroid cancer (Herzon 1994; Moosa & Mazzaferri 1997; Driggers 1998; Vini 1999). These studies demonstrate that the prognosis of differentiated thyroid cancer is the same in pregnant and nonpregnant women of the same age.

OUR APPROACH TO PREGNANT WOMEN WITH THYROID NODULES OR THYROID CANCER

In our opinion delaying the diagnosis or treatment of a thyroid nodule in patient with an early stage, well differentiated thyroid cancer until pregnancy takes its natural course does not compromise the outcome to a degree that warrants interventions that increase the risk of a pregnancy complication. Neck ultrasound and fine needle aspiration are low-risk procedures. We attempt to obtain a diagnosis using fine needle aspiration at any stage of pregnancy in patients who present with a thyroid mass or adenopathy. In the absence of a history of rapid tumor growth, or signs of problems that require immediate intervention—such as airway compromise—we do not recommend open biopsy or thyroidectomy if fine needle aspiration biopsy is not able to establish a diagnosis.

When thyroid cancer is diagnosed during pregnancy, we recommend delaying additional workup and treatment until after delivery as long as the tumor does not have anaplastic features or a history of rapid growth. In a patient with a large primary tumor or extensive adenopathy, we recommend premature delivery as soon as the risk is low. Otherwise, we recommend that the pregnancy take its normal course.

At some point, delaying the treatment of a patient with differentiated thyroid cancer will compromise outcome. A separate chapter presents data on the effect of delay in diagnosis and treatment of differentiated thyroid cancer. To minimize the delay caused by pregnancy, we recommend a diagnostic workup and appropriate treatment within two months following delivery. Radioiodine therapy, and to a lesser degree diagnostic studies, disrupt family life because they require that the mother be isolated from her baby and often eliminate the possibility of breast feeding.

REFERENCES

- Driggers, RW, JN Kopelman, and AJ Satin. 1998. Delaying surgery for thyroid cancer in pregnancy—a case report. *J Reprod Med* **43**:909–912.
- Galanti, MR, M Lambe, A Ekblom, P Sparen, and B Pettersson. 1995. Parity and risk of thyroid cancer: a nested case-control study of a nationwide Swedish cohort. *Cancer Causes Control* **6**:37–44.
- Hegedus, L. 2004. Clinical practice. The thyroid nodule. *N Engl J Med* **351**:1764–1771.
- Hershman, JM. 1999. Human chorionic gonadotropin and the thyroid: hyperemesis gravidarum and trophoblastic tumors. *Thyroid* **9**:653–657.
- Herzon, FS, DM Morris, MN Segal, G Rauch, and T Parnell. 1994. Coexistent thyroid cancer and pregnancy. *Arch Otolaryngol Head Neck Surg* **120**:1191–1193.
- Kobayashi, K, Y Tanaka, S Ishiguro, and T Mori. 1994. Rapidly growing thyroid carcinoma during pregnancy. *J Surg Oncol* **55**:61–64.

- Moosa, M, and EL Mazzaferri. 1997. Outcome of differentiated thyroid cancer diagnosed in pregnant women. *J Clin Endocrinol Metab* **82(9)**:2862–2866.
- Rosen, IB, and PG Walfish. 1986. Pregnancy as a predisposing factor in thyroid neoplasia. *Arch Surg* **121**:1287–1290.
- Vini, L, S Hyer, B Pratt, and C Harmer. 1999. Management of differentiated thyroid cancer diagnosed during pregnancy. *Eur J Endocrinol* **140(5)**:404–406.