Management of differentiated thyroid cancer diagnosed during pregnancy

Louiza Vini, Stephen Hyer, Brenda Pratt and Clive Harmer

Thyroid Unit, Royal Marsden NHS Trust, Downs Road, Sutton, Surrey SM2 5PT, UK

(Correspondence should be addressed to S Hyer, St Helier Hospital, Wrythe Lane, Carshalton, Surrey SN5 1AA, UK)

Abstract

Objective: To assess the outcome of thyroid cancer diagnosed during pregnancy.

Design: Retrospective analysis of patients diagnosed between 1949 and 1997 with thyroid cancer presenting during pregnancy.

Results: Nine women with a median age of 28 years were identified. A thyroid nodule was discovered by the clinician during routine antenatal examination in four cases, the remainder had noted a lump in the neck. In all patients, the nodule was reported to almost double in size during the pregnancy. One patient underwent subtotal thyroidectomy during the second trimester; eight were operated on within 3 to 10 months from delivery. Total thyroidectomy was performed in five and subtotal thyroidectomy in four. All tumours were well differentiated and ranged in size from 1 to 6 cm.

Outcome: The median follow-up was 14 years (5–31 years). One patient relapsed locally requiring further surgery. One patient developed bone metastases dying 7 years after presentation; her planned treatment had been delayed because of an intervening pregnancy. Eight of the original cohort of patients are currently disease free.

Conclusions: Differentiated thyroid cancer presenting in pregnancy generally has an excellent prognosis. When the disease is discovered early in pregnancy, surgery should be considered in the second trimester but radioiodine scans and treatment can be safely delayed until after delivery. In all cases, treatment should not be delayed for more than a year.

European Journal of Endocrinology 140 404–406

Introduction

Management of the pregnant woman with cancer is inevitably associated with considerable anxiety in both patient and clinician, mainly regarding the timing of any recommended treatment. In the case of thyroid cancer, this anxiety is compounded by reports that pregnancy may accelerate the course of the disease (1, 2). Recent evidence suggests that the prognosis of differentiated thyroid cancer in pregnancy is similar to that occurring in non-pregnant women of similar age (3).

The optimal timing of treatment, however, is still controversial, with some authors advocating surgery during the midtrimester whilst others recommend waiting until after delivery (3–5). We reviewed the records of pregnant women with thyroid cancer treated in our unit with particular regard to timing of treatment and outcome. We were interested to see if delayed treatment in these patients adversely affected survival.

Patients and methods

The Royal Marsden Hospital maintains a tumour registry of all thyroid cancer patients based on a

confirmed report of thyroid malignancy. The database captures all clinical information and other diagnoses, including pregnancy state. Between 1949 and 1997, 1398 patients with differentiated thyroid cancer were treated at the hospital, which serves as a tertiary referral unit for patients with thyroid disease. In nine patients, thyroid cancer had been discovered during pregnancy, representing 4.4% of women on the register actively trying to conceive.

Patient characteristics are shown in Table 1. The median age of the pregnant women at diagnosis was 28 years (range 24–31). Thyroid cancer was identified in the first trimester (one patient), in the second trimester (six patients) and in the third trimester (two patients) of their pregnancies.

An asymptomatic thyroid nodule was discovered by the clinician during a routine antenatal examination in four patients, the remaining five patients had reported a lump in the neck. In all cases the nodule was recorded to almost double in size during the pregnancy. No patients reported prior head and neck exposure to ionising radiation.

Fine needle aspiration confirmed malignancy in all cases. One patient underwent a subtotal thyroidectomy

Table 1 Patient characteristics.

Patient	Age (years)	Histology	Stage	Therapy	Recurrence	Survival (years)
1	24	P	T2N0	TT	No	6
2	24	P	T2N0	TT	No	14
3	26	P	T3N1a	TT, I ¹³¹	Local	5
4	27	P	T2N0	TT	No	7
5	28	P	T2N0	ST, I ¹³¹	No	24
6	28	P	T2N0	ST	No	31
7	30	F	T2N0	ST, I ¹³¹	No	18
8	31	F	T3N0	TT	Distant	Died (7 years)
9	31	P	T1N0	ST	No	30

P, papillary thyroid cancer; F, follicular thyroid cancer; TT, total thyroidectomy; ST, subtotal thyroidectomy.

T1, <1 cm; T2, 1–4 cm; T3, >4 cm. No, no lymph node metastasis; N1a, metastasis to ipsilateral cervical lymph nodes.

I¹³¹, radioiodine therapy.

during the second trimester of her pregnancy; the rest were operated on 3–10 months after delivery. One patient (patient 8, Table 1) had reported a lump in her neck in her first pregnancy, which recurred 16 months later in her second pregnancy and was investigated further. In this patient, planned treatment had been delayed by the intervening pregnancy and was initiated 25 months after the nodule had first been noticed.

Results and outcome

All tumours were diagnosed by experienced pathologists using established criteria (6). Total thyroidectomy was performed in five patients; subtotal thyroidectomy or lobectomy in four patients. Involved lymph nodes were resected in one case; in all other cases the tumour was confined to the thyroid gland. The thyroid cancer was well differentiated in all patients; seven were papillary and two follicular. Tumour size varied from 1 to 6 cm.

All patients were followed according to our thyroid cancer protocol at intervals increasing from 6 months to yearly. At each visit, patients were clinically assessed and serum thyroglobulin was estimated. Radioiodine ablation (3 GBq) was administered in three patients; one of them received two further therapy doses (cumulative activity 14 GBq) because of lymph node involvement. After surgery, patients received thyroxine treatment in doses sufficient to suppress thyrotrophin (TSH) levels.

Median follow-up was 14 years (5–30 years). During this period, thyroid cancer relapsed in neck lymph nodes in one patient and she was treated with modified neck dissection followed by radioiodine; 2 years later she remains disease free.

The patient with delayed treatment (patient 8) developed bone metastases 1 year following thyroidectomy and died 6 years later. In total, eight of the cohort of nine patients are alive and free of disease with normal serum thyroglobulin levels. Six children have subsequently been born to five of these patients.

Discussion

Papillary and follicular carcinomas of the thyroid are most common in women of childbearing age. Population-based surveys have suggested that up to 10% of thyroid cancers occurring in women during their reproductive years are diagnosed during pregnancy or in the first year after birth (7). In this series, 4.4% of thyroid cancers in young women were diagnosed in pregnancy. We have not included patients whose thyroid cancer was diagnosed up to a year after pregnancy as we were particularly interested in the influence of pregnancy on disease progression and treatment outcome.

It is suggested that high serum levels of human chorionic gonadotrophin, which has close homology with TSH, stimulates malignant thyroid tissue and may lead to rapid growth of thyroid carcinoma in pregnancy (8, 9).

In our series of nine patients, all reported an increase in tumour size; in two cases the tumour measured >4 cm and one patient had local spread to cervical lymph nodes. Only one of our patients underwent thyroidectomy during pregnancy; the rest underwent surgery less than a year after delivery. Outcome was good in all patients except in the one patient where planned treatment had been delayed beyond 2 years from initial presentation. This patient died with metastatic disease.

A good outcome for differentiated thyroid cancer (papillary or follicular) in young female patients is expected (10). In a large series of patients with thyroid cancer, the most important independent prognostic factor was age at diagnosis; tumour size, grade or histology were far less significant and only so in univariate analysis (11). The poor outcome in the patient who developed metastatic disease is likely therefore to be ascribed to the delay in treatment.

If treatment is delayed until after delivery and after the mother has stopped breast-feeding to avoid the risk of infant exposure to radioiodine, then patients with a

malignant thyroid nodule discovered early in pregnancy are likely to wait for a year or more.

We believe this would result in great anxiety to patients as well as putting them at increased risk, as delay in diagnosis for more than 1 year has been shown to increase the risk of death from thyroid cancer (10).

We recommend thyroidectomy in the midtrimester for thyroid cancers found early in pregnancy whilst those found later in pregnancy can safely be left until after delivery (3). In all cases, further investigation including whole body radioiodine scan and radioiodine therapy can be deferred until after the pregnancy and breast-feeding have been completed. Thyroid surgery in pregnancy is reported to be safe (12) although it is associated with increased fetal loss if more extensive surgery including neck dissection is performed (13).

In summary, evidence from this series and those previously published suggests that differentiated thyroid cancer discovered during pregnancy generally has an excellent prognosis but that treatment should not be delayed for more than a year.

References

- 1 Kobayashi K, Tanaka Y, Ishiguro S & Mori T. Rapidly growing thyroid carcinoma during pregnancy. *Journal of Surgical Oncology* 1994 **55** 61–64.
- 2 Rosen IB & Walfish PG. Pregnancy as a predisposing factor in thyroid neoplasia. *Archives of Surgery* 1986 **121** 1287–1290.
- 3 Moosa M & Mazzaferri EL. Outcome of differentiated thyroid cancer diagnosed in pregnant women. *Journal of Clinical Endocrinology and Metabolism* 1997 **82** 2862–2866.
- 4 Choe W & McDougall IR. Thyroid cancer in pregnant women: diagnostic and therapeutic management. *Thyroid* 1994 **4** 433–435.
- 5 Hod M, Sharony R, Friedman S & Ovadia J. Pregnancy and thyroid carcinoma: a review of incidence, course and prognosis. *Obstetric and Gynaecological Survival* 1989 **44** 774–779.
- 6 Rosai J, Carcangiu M & Delellis RA. Tumours of the thyroid gland. In *Atlas of Tumour Pathology*, 3rd series, vol 5, pp 302–310. Washington: Armed Forces Institute of Pathology, 1992.
- 7 Lambe M & Ekblom A. Cancers coinciding with childbearing: delayed diagnosis during pregnancy? *British Medical Journal* 1995 **311** 1607–1608.
- 8 Franceschi S, Fassina A & Talamini R. The influence of reproductive and hormonal factors on thyroid cancer in women. *Revue d'Epidemiologie et de Sante Publique* 1990 **38** 27–34.
- 9 Yoshimura M & Hershman JM. Thyrotropic action of human chorionic gonadotropin. *Thyroid* 1995 **5** 425–434.
- 10 Mazzaferri EL & Jhiang SM. Long term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *American Journal of Medicine* 1994 **97** 418–428.
- 11 Harmer CL & McCready VR. Thyroid cancer: differentiated carcinoma. *Cancer Treatment Reviews* 1996 **22** 161–177.
- 12 Hamilton NT, Paterson PJ & Bierdahl HD. Thyroidectomy during pregnancy. *Medical Journal of Australia* 1968 **1** 431–433.
- 13 Cunningham MP & Slaughter DP. Surgical treatment of disease of the thyroid gland in pregnancy. *Surgery, Gynecology and Obstetrics* 1970 **131** 486–488.

Received 16 December 1998

Accepted 7 January 1999