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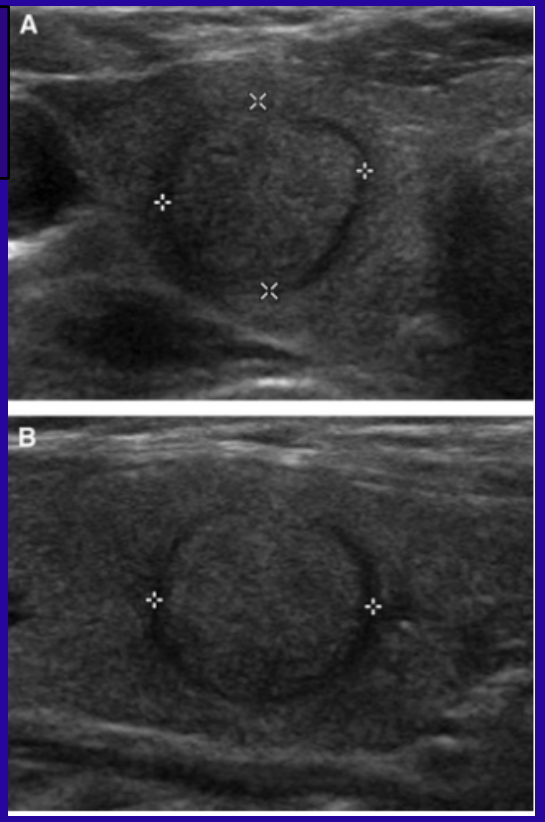
Thyroid Nodules and Cancer in Pregnancy

Clinical Case

An otherwise healthy 31-year-old G1P0 female patient is detected to have a firm 3 cm right thyroid nodule on clinical neck exam at 15 weeks gestation. She is completely asymptomatic, reports no history of head or neck radiation exposure, and has no family history of thyroid malignancy. What evaluation should be performed? What are her treatment options?

Definition

Discrete structural lesions that are distinct from the background thyroid parenchyma on ultrasound



Pseudonodules (Hashimotos thyroiditis)

ETIOLOGY

BENIGN CAUSES

- Adenomatous nodule (also called colloid nodule and hyperplastic nodule)
- Cysts
- Follicular adenomas
- Hurthle cell adenomas

MALIGNANT CAUSES

Carcinomas of thyroid follicular-cell origin

- Papillary carcinoma
- Follicular carcinoma
- Hürthle cell carcinoma
- Anaplastic carcinoma

Carcinoma of C-cell origin

- Medullary carcinoma

Lymphoma

Cancer metastatic to the thyroid (especially kidney, breast, lung, melanoma)

EPIDEMIOLOGY AND PATHOGENESIS OF THYROID NODULES IN PREGNANT WOMEN

The prevalence of thyroid nodules in pregnancy varies based on population iodine intakes. Thyroid nodules have been reported in **up to one-third** of pregnant women

Estradiol has been shown to stimulate the growth of benign and malignant thyroid follicular cells.

Human chorionic gonadotropin (hCG) may also contribute to thyroid nodule formation during pregnancy.

An increased prevalence of nodularity among women **previously pregnant** in comparison with **nulliparous** controls.

Initial Evaluation of Thyroid Nodules in Pregnant Women

1.History and physical examination

2.Measurement of serum thyroid-stimulating hormone (TSH)

3.Ultrasound to confirm the presence of nodularity, assess sonographic features, and assess for the presence of additional nodules and lymphadenopathy.

EVALUATION OF THYROID NODULES IN PREGNANT WOMEN

HIGH OR NORMAL TSH

- The indications for fine-needle aspiration (FNA) biopsy of the nodule are the same as in nonpregnant patient.

LOW TSH

Serum TSH should be reassessed, and if serum TSH remains <0.5 beyond 16 weeks gestation, further evaluation of the thyroid nodule should be deferred until after delivery given the possibility of a warm or hot nodule.

Recommendations for Radiopharmaceuticals Excreted in Breast Milk

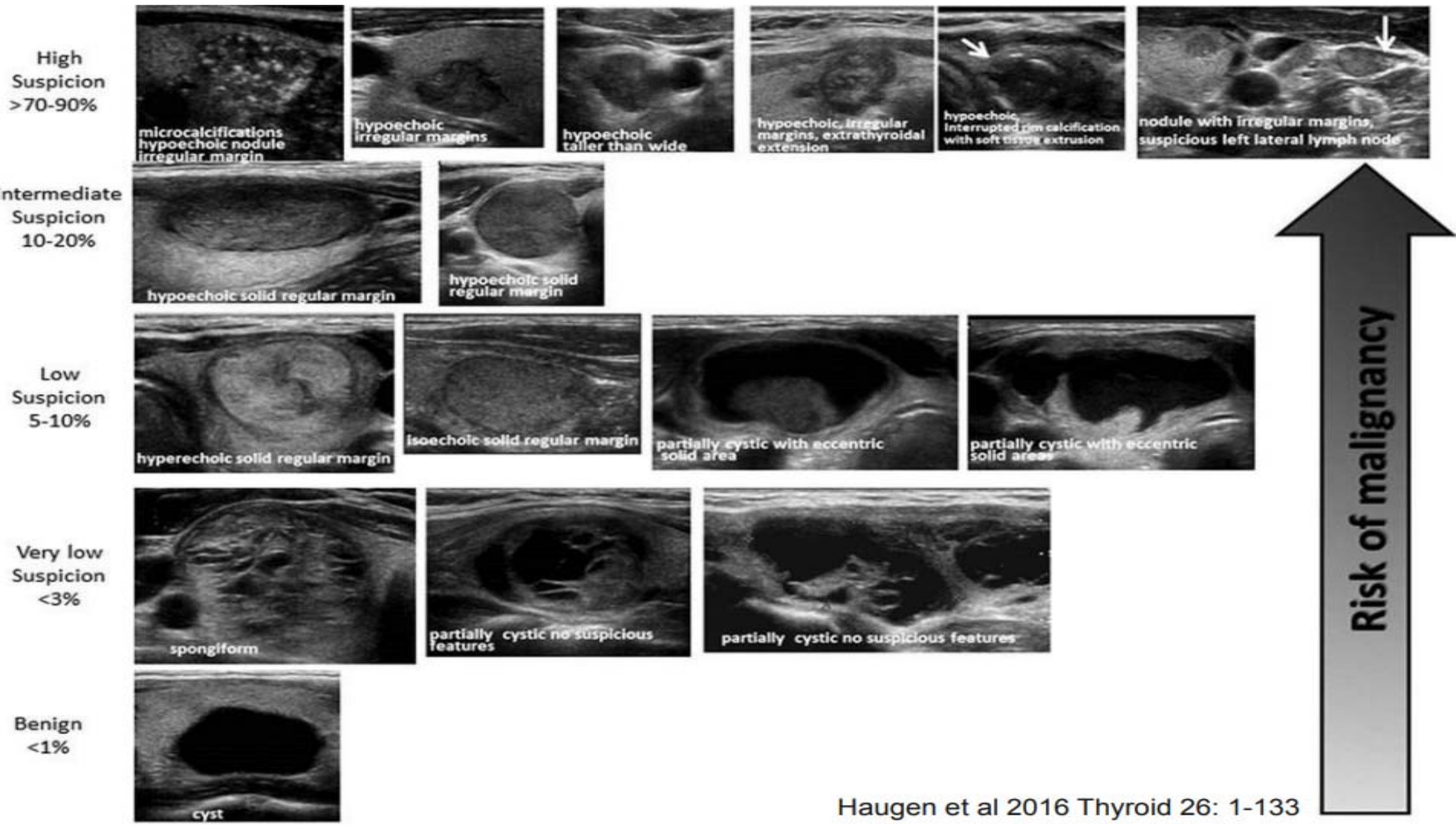
Women who are lactating and breastfeeding require special attention. NRC regulations stipulate that the patient must receive verbal and written instructions to that effect. For I-123, breastfeeding could safely be resumed after 2 days. For Tc-99m agents, 12 to 24 hours is sufficient

TABLE 16.4. Limits of activities that require instructions to breast-feeding patients and recordkeeping.[a]

Radiopharmaceutical	Activity above which instructions are needed mCi (MBq)		Activity above which record is needed mCi (MBq)		Recommended duration of cessation of breast-feeding
^{131}I-NaI	0.0004	(0.01)	0.002	(0.07)	complete cessation
^{123}I-NaI	0.5	(20)	3	(100)	–
^{131}I-MIBG	2	(70)	10	(400)	12 h (4 mCi/150 MBq)
^{99m}Tc-DTPA	30	(1000)	150	(6000)	–
^{99m}Tc-MAA	1.3	(50)	6.5	(200)	12.6 h (4 mCi/150 MBq)
^{99m}Tc-Pertechnetate	3	(100)	15	(600)	12 h (12 mCi/440 MBq)
^{99m}Tc-DISIDA	30	(1000)	150	(6000)	–
^{99m}Tc-Glucoheptonate	30	(1000)	170	(6000)	–
^{99m}Tc-Sestamibi	30	(1000)	150	(6000)	–
^{99m}Tc-MDP	30	(1000)	150	(6000)	–
^{99m}Tc-PYP	25	(900)	120	(4000)	–
^{99m}Tc-RBC in vivo	10	(400)	50	(2000)	6 h (20 mCi/740 MBq)
^{99m}Tc-RBC in vitro	30	(1000)	150	(6000)	–
^{99m}Tc-Sulfur colloid	7	(300)	35	(1000)	6 h (12 mCi/440 MBq)
^{99m}Tc-MAG3	30	(1000)	150	(6000)	–

TABLE 4.16 Recommendations for Radiopharmaceuticals Excreted in Breast Milk

Radiopharmaceutical	Administered activity mCi (MBq)	Counseling adivsed	Withhold breastfeeding
Ga-67 citrate	5.0 (185)	Yes	Cessation
I-131 sodium iodide	0.02 (0.7)	Yes	Cessation
I-123 sodium iodide	0.4 (14.8)	Yes	48 hr
I-123 MIBG	10 (370.0)	Yes	48 hr
Tl-201	3 (111)	Yes	96 hr
In-111 leukocytes	5 (185)	Yes	48 hr
Tc-99m MAA	4 (148)	Yes	12 hr
Tc-99m red blood cells	20 (740)	Yes	12 hr
Tc-99m pertechnetate	5 (185)	Yes	24 hr



Haugen et al 2016 Thyroid 26: 1-133

If there is no evidence of nodular growth, concerning ultrasound features (eg, extension beyond the thyroid or extension adjacent to the trachea or recurrent laryngeal nerve), or development of cervical lymph nodes during the period of observation, many endocrinologists defer FNA until after pregnancy.

Up to date

Most experts suggest that FNAB be performed during pregnancy according to nonpregnant criteria even if the patient would not elect surgery until postpartum so that a diagnosis can be determined and plans for postpartum management are not delayed.

jennifer L. Eaton Editor, Thyroid Disease and Reproduction A Clinical Guide to Diagnosis and Management

Timing of a follow-up ultrasound

Should be mid-second trimester if the nodule was first noted in early pregnancy.

If the nodule was first noted in later pregnancy, follow-up ultrasound can be deferred to the postpartum period

CYTOLOGY DIAGNOSES OBTAINED BY FINE-NEEDLE ASPIRATION BIOPSY OF THYROID NODULES AND MANAGEMENT RECOMMENDATIONS IN PREGNANT WOMEN

FNAB CYTOLOGY DIAGNOSIS	MANAGEMENT
• I. Nondiagnostic	Repeat FNAB, or defer until after delivery
• II. Benign	Routine follow-up
• III. Atypia of uncertain significance or follicular lesion of uncertain significance	Repeat FNAB, or monitor and defer until after Delivery
• IV. Follicular neoplasm or suspicious for follicular neoplasm	Monitor and defer until after delivery
• V. Suspicious for malignancy	Monitor and defer until after delivery
• VI. Malignant	Surgery in the second trimester, or defer until after delivery

Thyroid nodules with ***indeterminate cytology**** represent a diagnostic dilemma. Indeterminate thyroid nodules are not definitively malignant but when cancerous, often represent less aggressive variants of thyroid carcinoma. Harm due to delayed treatment of low-risk, well-differentiated thyroid malignancies in a pregnant patient is rare.

* When thyroid nodule fine-needle aspiration (FNA) cytologic results show follicular lesion of undetermined significance or atypia of undetermined significance (FLUS/AUS, Bethesda III) or follicular neoplasm (Bethesda IV), the results are often called indeterminate.

Thyroid Cancer and pregnancy

-Second only to breast cancer in pregnancy,

-Prevalence of thyroid cancer in pregnancy in a California Cancer Registry in 2003 : 14/100,000 live births.

-Mothers can be reassured that there are no data that postponing surgery until after delivery within 1 year of diagnosis affects survival and there are no data that suggest that the recurrence risk is altered by the timing of surgery as long as the cancer is well differentiated.

-About 10% of thyroid carcinomas occurring during the reproductive years are diagnosed during pregnancy or in the early post-partum period

Indications for Surgery in Pregnancy and Timing

-Most women with DTC can be reassured that waiting until postpartum does not appear to affect prognosis

-Preferred timing is in the second trimester after organogenesis has been completed and before viability (<23 weeks).

-In the third trimester: higher incidence of preterm labor

-Nodule is large and/or associated with suspicious lymphadenopathy or if patients are anxious and prefer that surgery be performed.

Patients with larger, more aggressive or rapidly growing cancers, or in the presence of extensive nodal or distant metastasis

UNUSUAL CASES

Medullary

Poorly differentiated

Anaplastic carcinomas

Advanced disease

Inadequate data are available

Surgical treatment → if the patient is <22 weeks,

Closer to 37 weeks, → beyond 23 weeks

Thyroid Hormone Suppression for Cancers or Suspicious Nodules

-Subclinical hyperthyroidism does not appear to pose a risk during pregnancy

-if the patient's TSH is >2 mU/L, it is reasonable to initiate thyroid hormone therapy

-The TSH should be maintained between 0.3 and 1.0 mU/L,

(The TSH should be maintained between 0.5 and 2.0 mU/L, up to date)

-Thyroid nodules that are benign and those for which cytology is indeterminate or not obtained should not be treated with suppressive therapy.

Pregnancy in **Previously treated**

- should be delayed for at least six months

-women without ultrasound or biochemical (thyroglobulin) evidence of persistent disease

-TSH should be measured as soon as pregnancy is confirmed, every four weeks until 16 to 20 weeks of gestation, and then at least once between 26 and 32 weeks of gestation

- women with persistent disease (structural or biochemical), disease progression may occur during pregnancy: periodic ultrasound and thyroglobulin (once each trimester) monitoring.

TSH GOALS IN PREVIOUSLY TREATED

Evidence of persistent disease (<0.1 mU/L)

Appears clinically free of disease (0.1–0.5 mU/L)

PREGNANCY IN PATIENT WITH DISTANT METASTASES

It is usually recommended that patients who have been properly treated for distant metastases be counseled that pregnancy is not contraindicated, even though some minor biochemical or structural disease progression is possible.

In seven patients with known pulmonary metastases reported in the Memorial Sloan Kettering Cancer Center cohort, only one of seven showed progression of distant metastases during Pregnancy.

RADIATION DAMAGE TO EMBRYO AND FETUS

Often it is suggested that a therapeutic abortion should be considered if an embryo receives ~10 rad (10 cGy) during the first 6 weeks after conception.

Half-life of I-131 is ~8 days (~40 days to near-completely clear in circulation) and would be highly destructive to the fetal thyroid if it is given within 40 days (after 7–8 weeks from LMP) of when the fetus begins to concentrate and make thyroid hormone at ~10–12 weeks.

I-131 Ablative Therapy in Breastfeeding Women

Lactation be discontinued for 1–2 months prior to 131-I treatment in order to avoid excess breast exposure

Clinical Case and Discussion

An otherwise healthy 31-year-old G1P0 female patient is detected to have a firm 3 cm right thyroid nodule on clinical neck exam at 15 weeks gestation. She is completely asymptomatic, reports no history of head or neck radiation exposure, and has no family history of thyroid malignancy. What evaluation should be performed? What are her treatment options?

Clinical Case and Discussion

A neck ultrasound confirms a 3.5 × 1.8 × 2.4 cm hypoechoic nodule in the right thyroid lobe with microcalcifications and irregular borders. *No abnormal lymph nodes are noted* in the central or lateral compartments of the neck.

Serum TSH is measured and is 1.5 mU/L.

The patient undergoes an ultrasound- guided fine-needle aspiration biopsy (FNAB) of the nodule, which confirms a diagnosis of PTC.

Clinical Case and Discussion

Given the lack of abnormal lymph nodes on neck ultrasound, the patient can be reassured that thyroidectomy can be postponed until after delivery without negatively impacting her survival or risk of recurrence. However, if preferred by the patient, there is also evidence that surgery can be safely performed in the second trimester after organogenesis has been completed and before viability (<23 weeks) without any significant increased risk to the fetus.

TSH suppression therapy with levothyroxine can be deferred until after thyroidectomy is performed given the normal serum TSH level.

Evidence to date suggests that in the vast majority of patients, pregnancy will not impact survival or overall thyroid cancer prognosis.

Rferences

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گفته ای از مولوی نامدار آخرین حرف است ای پروردگار

"گر خطا گفتیم اصلاحش تو کن مصلحی تو ای سلطان سخن"