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Differentiated Thyroid Carcinoma Is More Common in Reproductive Age Women but Is Not Clinically More Aggressive

Lee JC, Zhao JT, Clifton-Bligh RJ, Gill AJ, Gundara S, Ip J, Sywak MS, Delbridge LW, Robinson BG, Sidhu SB. Papillary thyroid carcinoma in pregnancy: a variant of the disease? Ann Surg Oncol. August 9, 2012 [Epub ahead of print]. doi: 10.1245/s10434-012-2556-3.

SUMMARY

Background

There are conflicting reports in the literature regarding the prognostic influence of pregnancy on patients with papillary thyroid carcinoma (PTC), and there is no literature on specific microRNA (miRNA) profiles of PTC in the context of pregnancy. The authors' aims were to determine whether pregnancy is an adverse factor in PTC and whether PTCs associated with pregnancy are biologically different from those in nonpregnant women in terms of their miRNA profiles. miRNAs are small molecules approximately 22 nucleotides in length; their profiles have been used to accurately identify the tissues of origin of poorly differentiated cancer tissues. In thyroid pathology, miRNA profiles have been used to classify thyroid tumor types and to differentiate malignant tumors from their benign counterparts.

Methods

Women diagnosed with PTC during or soon after becoming pregnant were recruited into the pregnancy group. Age-matched nonpregnant women were recruited into the nonpregnancy group. miRNA microarray was performed on the PTC tissue of pregnant patients (10), nonpregnant patients (10), and normal thyroids (5). There were 6 differentially expressed miRNAs from the microarray comparisons.

Results

There were 24 patients in the clinical pregnancy group (recruited between January 1995 and December 2010) and 30 in the nonpregnancy group (recruited between January 2004 and December 2005). Tumors from the pregnancy group were significantly larger and showed more regional lymph-node metastases. The microarray data showed a total of 27 miRNAs that were potential differentiators of PTC tissue samples from pregnant and nonpregnant patients. Of the 6 selected for validation, no significant difference in expression was found. There were no deaths in either group, and the disease-free survival rates were similar in the two groups (86.4 % in the pregnancy group vs. 91.3 % in the nonpregnancy group, P = 0.66), with mean lengths of follow-up of 44.7 and 44 months for the pregnancy and nonpregnancy groups, respectively. Also the rates of radioactive iodine ablation and mean doses given were similar in the two groups.

Conclusions

The data suggest that PTC during pregnancy may be more aggressive locoregionally. However, no difference in survival or recurrence is demonstrated. The miRNA profiles of the pregnancy-associated PTC have not been shown to be different from those of the nonpregnancy counterparts. This suggests that the differences seen clinically are related to patient factors rather than to the disease itself. The authors concluded that their data are in agreement with the majority of the published literature, which shows that pregnant women with PTC do not have a worse prognosis and that treatment can usually be delayed until postpartum, unless there are specific aggressive features or the malignancy is diagnosed very early in the pregnancy.

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ANALYSIS AND COMMENTARY

About 10 % of thyroid cancers diagnosed during childbearing age occur during pregnancy or in the 12-month postpartum period (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 1000 births. Also, 75% of these women are diagnosed during the 12-month postpartum period (2). Based on current guidelines from the American Thyroid Association (3) and the Endocrine Society (4), thyroidectomy may be postponed until after delivery for patients diagnosed with PTC during pregnancy whose disease does not show any aggressive features, although surgery is recommended during the second trimester if aggressive features are present. The only long-term retrospective study with a significant number of patients to justify the above conclusions was published in 1997 by Moosa and Mazzaferri (5). The authors showed no difference in long-term outcome in a group of patients with PTC who were undergoing surgery during pregnancy, as compared with those who were treated surgically in the 12 months after delivery. Whether pregnancy by itself is a risk factor for increased aggressiveness of PTC is controversial. In women with no evidence of residual PTC, pregnancy by itself does not affect the natural course of the disease; however, patients with evidence of persistent disease may show progression during pregnancy (6,7). On the other hand, Vannucchi et al. reported on a small number of patients and showed the negative prognostic effect pregnancy has on patients with thyroid cancer, attributing it to the presence of estrogen receptor alpha (ERa) on the majority of pregnancy-associated thyroid cancers and its absence in papillary lesions in nulliparous women (8).

In summary, as the authors stated, in the presence of conflicting clinical data, prospective molecular studies may be helpful in determining whether PTC in association with pregnancy is a more aggressive variant of the disease. As with other thyroid pathologies in pregnancy, a prospective long-term multicenter clinical trial with the support of molecular markers could solve the present clinical dilemma confronting the physician advising a woman who is pregnant or planning a pregnancy about the best therapy for a newly diagnosed or previously treated differentiated PTC.

— Jorge H Mestman, MD

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