

Early Miscarriage of Unwanted Pregnancy After Radioiodine Ablation in a Patient with Graves' Disease: Case Report

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ABSTRACT

Graves' disease in females of childbearing age is common. Radioiodine therapy (RAIT) is a definitive treatment for such a condition. The effect of radiation on germ cells and iatrogenic hypothyroidism following radioiodine therapy may cause a bad pregnancy outcome. We present an unfortunate case of miscarriage of early pregnancy in 7th gestational weeks following 7 months of RAIT and an approach to the clinical question 'How to manage Graves' disease with RAIT in women of childbearing potential'. Maintenance of an adequate interval and achieving euthyroid status after RAI ablation in Graves' disease in patients willing to conceive can reduce the risk of miscarriage and assure a good pregnancy outcome.

Keywords: Graves' disease, radioiodine therapy, pregnancy, iatrogenic hypothyroidism.

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INTRODUCTION

Graves' disease (GD), an autoimmune thyroid disorder, is common in young women. About 0.4–1.3% of women of childbearing age are affected before pregnancy and 0.2% during pregnancy (1). Poorly controlled or untreated hyperthyroidism in pregnant women with GD may cause a bad pregnancy outcome (1, 2). Radioactive iodine (RAI) ablation is regarded as the definitive treatment for Graves' disease. But radiation has a mutagenic effect on germ cells, which may result in abortion, premature birth, stillbirth, and genetic damage to offspring, including congenital anomalies or even malignancy (2, 3). Again, pregnant mothers and fetuses are at increased risk of complications like miscarriage, pre-eclampsia, placental abnormality, and post-partum hemorrhage secondary to hypothyroidism after RAI ablation (4). Hence, it is a big challenge for a physician to treat female patients with GD with childbearing potential and recommend the proper time or state to conceive for a safe, risk-free pregnancy outcome.

We report an unfortunate case of the unwanted but valuable pregnancy of a 23-year-old female patient with GD from a low socio-economic background who got pregnant after 5 years of marriage following 7 months of RAI ablation for GD. She ignored regular follow-ups after RAI therapy, took a low and irregular dose of levothyroxine, and presented with a recent history of miscarriage with abnormal thyroid hormonal status.

CASE REPORT

A 23-year-old woman from a low socio-economic background was previously diagnosed with Graves' disease (GD) for 4 years and presented with a history of miscarriage at 7 weeks of pregnancy in the thyroid clinic of the Institute of Nuclear Medicine and Allied Sciences (INMAS), Kushtia. She had a high triiodothyronine (T3) and thyroxine (T4) level, a low thyroid stimulating hormone (TSH) level, and positive TSH receptor antibodies (TRAb) at the time of the initial diagnosis. Then, she was treated with anti-thyroid drugs (ATD) for 2 years. TRAb levels became normal, but thyroid hormone levels rose after stopping anti-thyroid drugs. So, she received 12 mCi of radioactive iodine (¹³¹I) as ablation therapy. After 3 months of therapy, the follow-up hormone status revealed an elevated (61.70 mIU/L) TSH (normal range: 0.3-5 mIU/L), a decreased (1.50 pg/ml) free T3 (normal range: 2.0–4.4 pg/ml), and a decreased (0.53 ng/dl) free T4 (normal range: 0.8–2.5 ng/dl) level. Then, she was advised to take levothyroxine replacement therapy with about 100 micrograms per day.

She had been married for 5 years but was unable to conceive previously. She also had an irregular menstrual cycle before and following the RAIT and, hence, was not worried about a short amenorrhic state of about two months during the 7th month of RAIT. Then, she suffered from lower abdominal

pain, and an ultrasonographic finding revealed a case of missed abortion of about 7 gestational weeks, characterized by a deformed gestational sac with an indistinct fetal pole without any cardiac pulsation. After a complete abortion, the patient was sent to INMAS, Kushtia, for further management.

Patient had the history of irregular and inadequate (50 microgram) intake of levothyroxine tablets. On physical examination, the thyroid gland was found to be normal in size and shape. Mild exophthalmos was present. Biochemically, the patient's TSH was elevated (12.22 mIU/L), and free T3 was reduced (1.50 pg/ml). To exclude other probable causes of abortion, anti-Mullerian hormone, anti-nuclear antibody, and anti-cardiolipin antibody tests were done, and all the results came out as negative.

DISCUSSION

RAI ablation is a well-established treatment for GD. Studies have shown few cases of miscarriages immediately after RAIT in pregnancy. Otherwise, no evidence of radiation exposure affects the outcome of subsequent pregnancy and offspring, even in high doses of RAIT used in the treatment of differentiated thyroid cancers (5, 6). But the clinicians should focus on the importance of achieving an euthyroid state before conception following RAI ablation for a positive outcome of pregnancy. Iatrogenic hypothyroidism occurs within 1 year of RAI therapy in GD, and hypothyroidism accounts for miscarriage mostly before 20 weeks of pregnancy (4, 7). So, researchers recommended aiming for at least a 6-month interval to avoid the radiation effect and at least a 12-month interval to maintain a stable thyroid hormone level (3, 4, 6, 7). In our case, we could not detect the actual cause of the miscarriage. But we assumed iatrogenic hypothyroidism (over a 5-month interval of radiation therapy) was the main cause, as the patient did not take an adequate dose of levothyroxine and ignored routine follow-up. During miscarriage, our patient had elevated TSH and a decreased free T3 level, whereas the recommended ranges in the first trimester of pregnancy for TSH are 1–2.5 mIU/L and free T3 are 4.1–4.4 pg/ml (7). To ensure euthyroid status in patients with pre-pregnancy normal TSH levels, it is also recommended to increase Levothyroxine 2 doses per week after confirming pregnancy to prevent maternal TSH elevation (7). In patients with Graves' disease after RAI ablation, TRAb levels should be checked in early

pregnancy, at 20 weeks and 32 weeks, regardless of thyroid status (8). The reported patient ignored regular follow-up, and thus euthyroid status was not achieved and TRAb levels were not monitored. A clinical advice to patients of reproductive age about barrier methods of contraception to avoid unwanted pregnancies might be helpful.

A pregnancy test is advised for women with irregular menses who are unsure if they are

experiencing amenorrhea following RAI ablation, however this patient ignored all recommendations.

A proper approach for management of GD in female patients of childbearing age after radioactive iodine ablation includes: i) counseling about the importance of 6 months to 1 year interval between RAIT and conception ii) To avoid unwanted pregnancy, proper method of contraception advice iii) counseling about regular follow-ups and restoring the euthyroid state from the very beginning of pregnancy with proper dosage of levothyroxine iv) maintaining TSH < 2.5 mIU/L; v) checking thyroid function every 4-6 weeks and TRAb level in early pregnancy, 20th and 32 weeks (9, 10)). All these precautions and regular follow-ups result in a reduced incidence of miscarriage and other complications.

CONCLUSION

It is of utmost significance to maintain an adequate interval and remain in an euthyroid state after RAI ablation in Graves' disease for patients willing to conceive for a safe, uncomplicated pregnancy and the best possible outcome.

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