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Thyroid cancer diagnosed and treated surgically during pregnancy — a case report

Rak tarczycy rozpoznany i leczony operacyjnie w okresie ciąży — opis przypadku

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Abstract

Thyroid cancer has had an increasing prevalence over recent years and poses an extraordinary challenge when diagnosed during pregnancy. Although in the majority of cases in pregnant patients there occurs a well differentiated papillary carcinoma which has an excellent prognosis and for which surgery can be delayed until the postpartum period, in rare cases of advanced or rapidly growing tumour, and in a case of medullary or anaplastic cancer, surgery should be undertaken during pregnancy. Here, we present the case of a 30 year-old woman with Hürthle cell neoplasm recognised on cytology during the second trimester. Because of the neck lymph nodes metastases diagnosed on ultrasonography and cytology, which also could be seen as calcified foci on a chest X-ray examination performed three years earlier, she underwent surgery before the 22nd week of gestation. The course of surgery was successful and uneventful and she delivered a healthy child on term. An approach to pregnant patients with differentiated thyroid carcinoma is discussed. **(Endokrynol Pol 2013; 64 (2): 158–163)**

Key words: *differentiated thyroid carcinoma, thyroid surgery during pregnancy*

Streszczenie

Zapadalność na raka tarczycy w ostatnich latach wzrasta. Stanowi on szczególny problem wówczas, gdy zostaje wykryty u kobiety ciężarnej. W większości przypadków u ciężarnych występuje dobrze zróżnicowany rak brodawkowaty mający bardzo dobre rokowanie i leczenie operacyjne może być odłożone do okresu po porodzie. W rzadkich przypadkach raka rdzeniastego, anaplastycznego oraz zaawansowanego lub szybko rosnącego raka zróżnicowanego operację tarczycy należy przeprowadzić w okresie ciąży. Przedstawiamy przypadek 30-letniej ciężarnej, u której w drugim trymestrze ciąży w badaniu cytologicznym guza tarczycy stwierdzono nowotwór z komórek Hürthla, a badanie ultrasonograficzne i cytologiczne wskazywało na przerzuty do węzłów chłonnych szyi. Przerzuty do węzłów chłonnych szyi były również zauważalne w postaci uwapnionych ognisk na zdjęciu radiologicznym klatki piersiowej wykonanym 3 lata wcześniej. Podjęte przed 22. tygodniem ciąży leczenie operacyjne było skuteczne i niepowikłane. Pacjentka odbyła prawidłowy poród i urodziła zdrowe dziecko. W dyskusji poruszono problem chirurgicznego leczenia zróżnicowanego raka tarczycy u kobiet ciężarnych. **(Endokrynol Pol 2013; 64 (2): 158–163)**

Słowa kluczowe: *zróżnicowany rak tarczycy, operacja tarczycy u ciężarnej*

Introduction

Thyroid nodules are common thyroid disorders worldwide. The prevalence of palpable thyroid nodules reported by the Whickham and Framingham epidemiological studies is 5–6% in women and 0.5–1.0% in men and is higher in older and iodine-deficient populations [1, 2]. The prevalence estimated by high-resolution ultrasonography (US) is much greater: 19–67% of unselected individuals [3]. There are few studies evaluating an impact of pregnancy on thyroid nodularity, all derived from mild to moderate iodine-deficient areas [4–7]. The reported prevalence of palpable thyroid nodules in pregnant women is 3.6%, but US reveals thyroid nodularity in 15–30% of them. Pregnancy is associated with an increase in the size of pre-existing thyroid nodules and new nodules formation in 11–20% of women. In the majority of cases, the changes in thyroid morphology do not regress in the postpartum period, and an increased prevalence of thyroid nodules has been reported in multiparous women. Although most thyroid nodules are benign and only 5–15% appear to be malignant, the incidence of thyroid cancer is still growing. In the United States, annual incidence increased from 3.6 per 100,000 in 1973 to 8.7 per 100,000 in 2002, and it seems that improved diagnosis is not the sole factor accounting for this rise [3]. The retrospective study of the occurrence of cancer associated with

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obstetric patients conducted in California in 1991–1999 revealed nearly 4,500 cases of malignant disease among 4,846,500 obstetric patients (nearly 0.1%). Breast and thyroid cancer were the most common malignancies: 19 per 100,000 and 14 per 100,000 respectively [8]. Other reports have estimated that thyroid cancer affects 1 in 1,000 pregnant women [9, 10]. An approach to pregnant patients with thyroid nodules is similar to that in the general population with the exception of radionuclide scanning which is contraindicated during pregnancy and has some limitations during breastfeeding. All pregnant women should have a complete history with special attention given to previous head and neck irradiation and family history of thyroid malignancy, clinical examination, serum TSH testing and neck US. Fine-needle aspiration biopsy (FNAB) should be performed according to the general recommendations in any trimester. In most thyroid nodules that are diagnosed as follicular neoplasm, suspicious for malignancy or papillary cancer on FNAB, surgery may be deferred until the postpartum period. In the rare cases of medullary, anaplastic and advanced or rapidly growing differentiated thyroid carcinoma (DTC), surgery should be undertaken during pregnancy. Here, we present the case of an advanced DTC which was diagnosed in a pregnant woman and treated surgically in the second trimester.

Case study

A 30 year-old woman in the 22nd week of gestation was referred to the Endocrinology Department in Warsaw in October 2011 with suspected thyroid cancer (Fig. 1). The patient had no previous history of head or neck irradiation, nor any family history of any cancerous disease. Her first pregnancy was normal and she delivered a healthy child in 2008. The second pregnancy was uncomplicated until the 21st week when her obstetrician diagnosed nodular goitre. Then she was consulted by an endocrinologist, and a neck US with subsequent FNAB was performed. On the US there was multinodular goitre with a dominant nodule in the right lobe of 3 cm in diameter and calcified rim and several small isoechoic nodules throughout the whole gland. There were also several pathological foci in the right lateral neck compartment and in the right supraclavicular area suspected for metastatic lymph nodes (Fig. 2, 3). Cytological examination of the dominant nodule in the right lobe and two smaller nodules in the right and left lobes was described as II and III cytological group according to Bethesda classification.

These results seemed unsatisfactory and a second FNAB was performed of the dominant nodule in the right lobe and ipsilateral pathological lymph nodes.

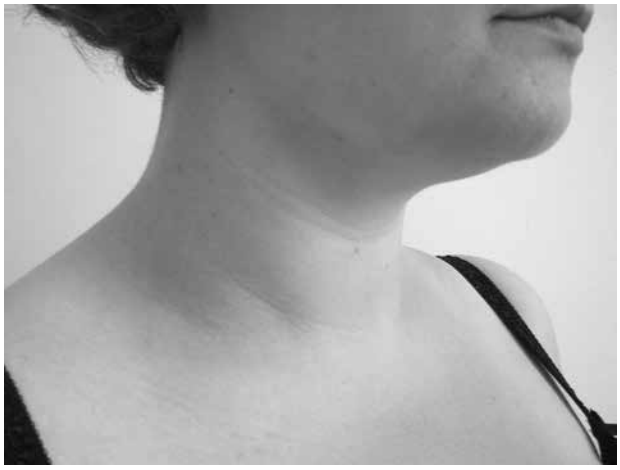


Figure 1. *Neck of the patient with visible right thyroid lobe enlargement*

Rycina 1. *Szyja pacjentki z widocznym powiększeniem prawego płata tarczycy*

The obtained results were suspicious for Hürthle cell thyroid carcinoma with metastases in lymph nodes. On examination in the Endocrinology Department, she presented as an overweight woman (height 168 cm, weight 85 kg) with visible and well palpated goitre. The dominant 3 cm nodule in the right lobe was hard but mobile, and several hard lymph nodes could be palpated in the right supraclavicular area and along the sternocleidomastoid right muscle. There was no hoarseness, dysphagia or shortness of breath. She did not demonstrate any signs or symptoms of thyroid dysfunction. Serum TSH, calcitonin and calcium were normal; 0.5 mIU/L (normal range 0.4–4.0 mIU/L), below 2.0 pg/mL (normal range below 2.0–8.0) and 2.2 mmol/L (normal range 2.09–2.54 mmol/L) respectively. Having analysed her medical history, the abnormal chest X-ray examination performed on 2009 was found with calcified foci within the right neck and right supraclavicular area (Fig. 4). She recalled that after she had learned that the pathological foci were not of pulmonary origin, she had abandoned further investigation. The decision was made for immediate surgery, and after obtaining the patient's consent, she was referred to a highly experienced surgeon. Successful total thyroidectomy with central and right lateral lymphadenectomy was undertaken (Fig. 5, 6) The pathological examination was indicative for papillary carcinoma in the right thyroid lobe with multiple metastases in the central and lateral neck lymph nodes. The postoperative period was uneventful: no postoperative hypoparathyroidism, recurrent laryngeal nerve injury, nor obstetric complications were observed. 150 micrograms of levothyroxine (L-T4) was instituted the next day

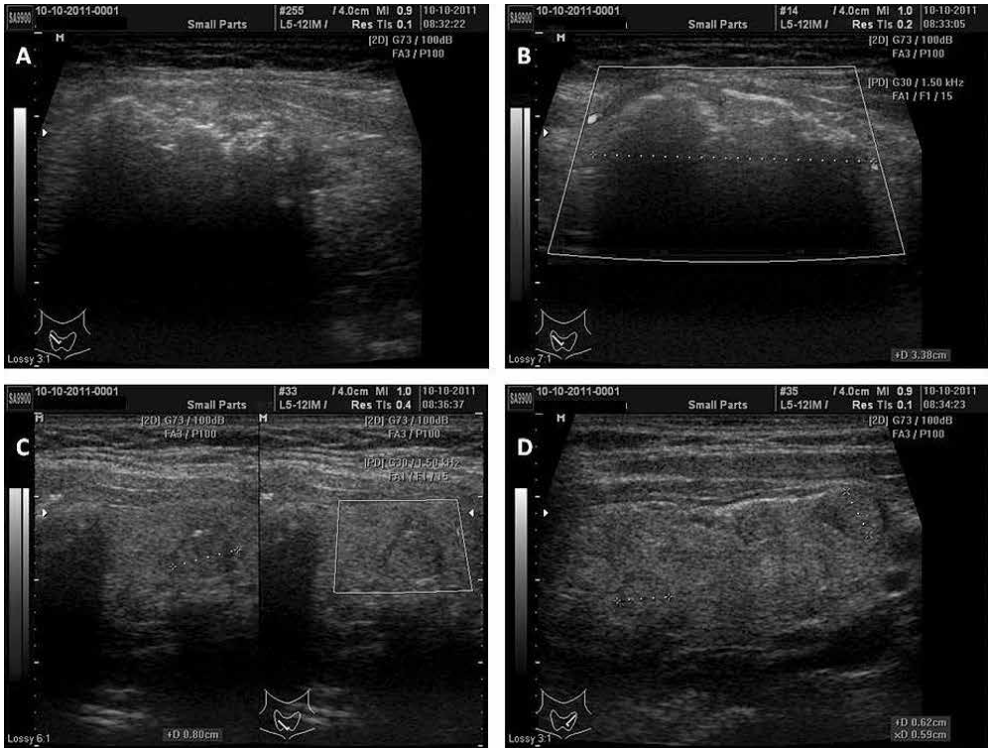


Figure 2. *US scan of thyroid: the dominant nodule in the right lobe with calcified rim and type I blood-flow on colour-Doppler imaging (***A, B***), small isoechoic nodules with type I blood flow on colour-Doppler imaging in the rest of thyroid gland (***C, D***)*

Rycina 2. *Ultrasonografia tarczycy: dominujące ognisko w prawym płacie z uwapnioną otoczką i I typem unaczynienia w badaniu kolor-Doppler (***A, B***), niewielkie isoechogeniczne ogniska w pozostałym miąższu tarczycy wykazujące I typ unaczynienia w badaniu kolor-Doppler (***C, D***)*

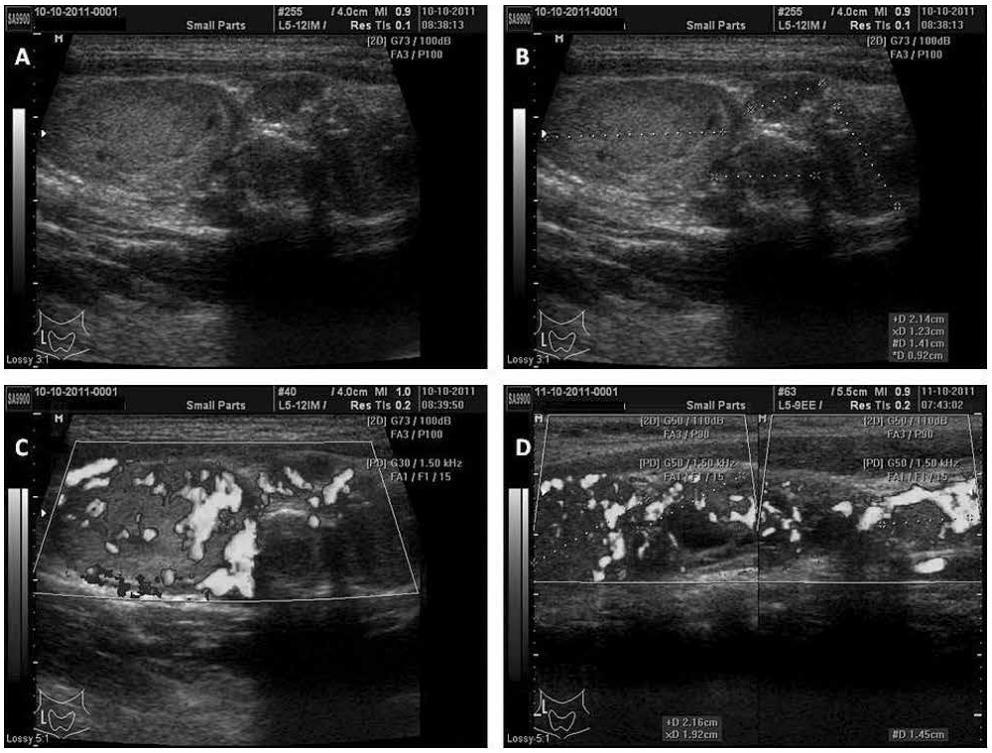


Figure 3. *US scan of the right lateral neck: metastatic lymph nodes along sternocleidomastoid muscle with macrocalcifications and type III blood flow on colour-Doppler imaging (***A, B, C, D***)*

Rycina 34. *Ultrasonografia prawego przedziału bocznego szyi: patologiczne węzły chłonne wzdłuż mięśnia mostkowo-obojczykowo-sutkowego z makrozwapnieniami i III typem unaczynienia w badaniu kolor-Doppler (***A, B, C, D***)*

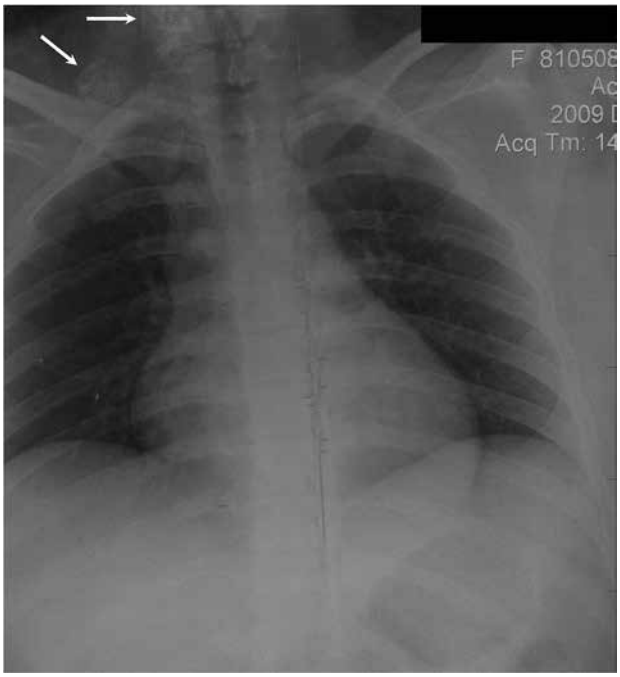


Figure 4. *Chest X-ray examination of the patient performed in 2009 with calcifications in the right region of the neck and right supraclavicular area*

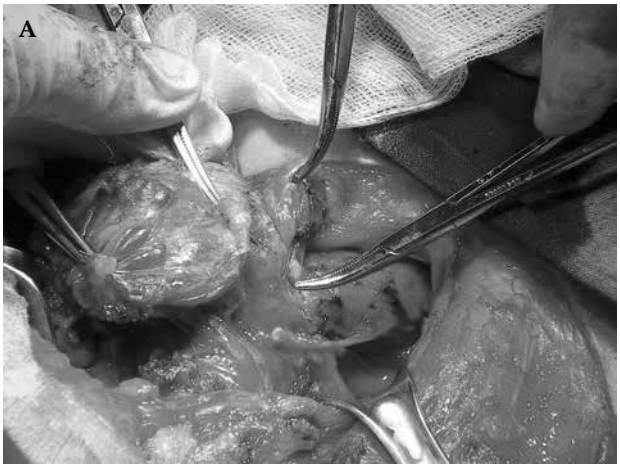
Rycina 4. *Zdjęcie klatki piersiowej pacjentki wykonane w 2009 roku: widoczne zwapnienia po prawej stronie szyi i w prawym dole nadobojczykowym*

after thyroidectomy; three days later, the dose was increased to 200 μg daily. In the second week after surgery, her TSH was 0.116 mIU/L and then it was kept below 0.1 mIU/L.

She had normal labour and delivered a healthy child who got 10 Apgar points. Three months later after having finished lactation, she was referred to the Oncological Unit to perform radioiodine (RAI) ablative therapy. No further information is available at this moment.

Discussion

Although most DTC recognised during pregnancy can be treated surgically in the postpartum period, the time of surgery depends on the tumour stage and its rate of growing, period of pregnancy when malignancy is identified, and the patient's decision. According to the current American Thyroid Association (ATA) recommendations, surgery for DTC in pregnant women should be undertaken in cases of rapid nodular growth or the appearance of lymph nodes metastases prior to midgestation [11]. In the reported case, some radiological signs of lymph nodes metastases within the neck had been present for three years, surgery could be performed in the optimal period of pregnancy i.e. the second trimester, and a consent from the patient was obtained. The impact of pregnancy on the course of DTC has been estimated in several retrospective studies and the conclusions of the majority of them is that a prognosis of DTC is the same in pregnant women as in nonpregnant controls [10–13]. In contrast, the observation of Vannucchi et al. [14] indicates that DTC diagnosed during pregnancy is associated with poorer outcome compared to nongravidic periods ($p < 0.0001$) and a diagnosis of DTC during the first year postpartum is the most indicative factor of persistent disease according to stepwise logistic regression analysis ($p = 0.001$). These results could be partly explained by the acceleration of DTC growth by oestrogens. The authors found a high oestrogen receptor-α expression in the tumours diagnosed during pregnancy and the first year after delivery (87.5%) compared to the tumours recognised one or more years after delivery (31%) and to the tumours diagnosed before pregnancy (0%). Also several *in vitro* studies have documented that oestrogens increase the expression of oestrogen receptor-α in thyroid cancer



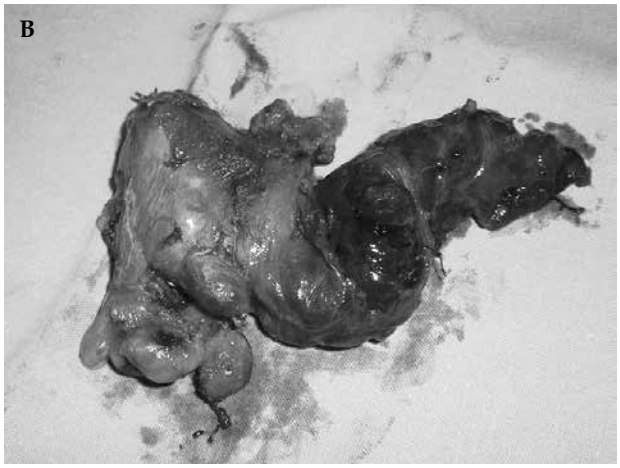


Figure 5. *Patient during thyroidectomy (**A**); excised thyroid gland and lymph nodes (**B**)*

Rycina 5. *Pacjentka w trakcie operacji (**A**), wycięty gruczoł tarczowy wraz z okolicznymi węzłami chłonnymi (**B**)*

cell lines and activate diverse intracellular signalling pathways [15, 16]. Unfavourable influence of human chorionic gonadotropin (hCG) with its potency for stimulating TSH receptor might also be considered, as serum TSH level is a recognised risk factor of thyroid carcinogenesis [17, 18].

While planning an operation in a pregnant woman, the risk of surgery and anaesthesia and potential difficulties in the treatment of hypothyroidism and hypoparathyroidism must be considered. Optimal timing for surgery is the second trimester when the risk for mother and foetus is the lowest. Operations should be avoided in the first trimester because of the potential teratogenic effect of general anaesthesia and the danger of spontaneous abortion. Surgery undertaken during the third trimester can cause a preterm labour.

Outcomes of thyroid surgery in pregnant women are not well characterised and results ranging from foetal death to no complications have been observed [19, 20]. Kuy et al. reported that after thyroid and parathyroid surgery, pregnant women had higher rates of endocrine (15.9 *v.* 8.1%; $p < 0.001$), surgical (23.9 *v.* 14.4%; $p < 0.01$) and general complications (11.4 *v.* 3.6%: $p < 0.01$), longer lengths of stay (two days *v.* one day; $p < 0.001$) and higher hospital costs ($6,873 *v.* $5,963; $p = 0.007$) compared to non-pregnant controls. The foetal and maternal complication rates were 5.5% and 4.5% respectively [21]. It appears essential to refer pregnant women to highly-experienced surgeons, as surgeon skill is a well-known predictor of patient outcome.

An important aspect of the management is the implementation of a full dose of L-T4 therapy immediately after surgery to avoid maternal hypothyroidism and achieve oncologic goals. Maternal hypothyroidism has well-characterised unfavourable foetal and obstetric effects [22–25], while subclinical hyperthyroidism seems not to carry any risk for mother and foetus. According to Endocrine Society guidelines [25] in pregnant women with DTC, serum TSH should be suppressed but detectable and high-risk patients need a greater degree of suppression compared to low-risk patients. The free T4 or total T4 levels should not be above the normal range for pregnancy. The more recent ATA guidelines [11] recommend in pregnant women with DTC who have surgery deferred until postpartum to keep serum TSH level of 0.1–1.5 mIU/L and in pregnant women with DTC treated prior to pregnancy to keep serum TSH at a level similar to the preconception period based on cancer stratification. According to the Polish Endocrine Society [26] in pregnant women with papillary carcinoma who do not undergo surgery until postpartum, serum TSH should be kept below 0.1 mIU/L. None of these recommendations refer to the case of pregnant women operated during pregnancy, but it seems reasonable to consider such cases to be of high-risk and keep serum TSH below 0.1 mIU/L if only such therapy is well tolerated.

Managing postoperative hypoparathyroidism in pregnant women poses a special challenge because prolonged maternal hypocalcaemia is a risk of foetal hyperparathyroidism and death and uterine atonia during labour. Inappropriate medication and maternal hypercalcaemia leads to foetal hypoparathyroidism and tetany after delivery. Both alfacalcidol and calcitriol are effective and safe, but the doses should be adjusted according to the serum ionised-calcium levels and calcium urine excretion.

In summary: an approach to a pregnant woman with thyroid cancer should take into account the maternal and foetal aspects and the decision as to the management should involve an interdisciplinary team of an endocrinologist, obstetrician, oncologist, surgeon and neonatologist.

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