



A case of acromegaly and disseminated follicular thyroid carcinoma

Przypadek pacjenta z akromegalią i rozsiałym rakiem pęcherzykowym tarczycy

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Abstract

Introduction: A particularly challenging case of concurrent acromegaly and follicular thyroid carcinoma in a patient of the Clinic of Endocrinology, UJCM in Krakow is discussed.

Case description: A 59-year-old male with post total thyroidectomy performed in 2005 and histopathologically confirmed metastases of the follicular thyroid carcinoma to the lungs was admitted to the Clinic in April 2006 for complementary ¹³¹I treatment. Acromegaly was treated in 1996 by trans-sphenoidal surgery. In December 2005 a relapse of pituitary adenoma was shown by MRI, which correlated with increased levels of hGH and IGF-1. Biochemical control of acromegaly was achieved with Sandostatin LAR. Pre-therapeutic whole-body scintigraphy (WBS) revealed numerous conjoined hot spots of ¹³¹I accumulation in both lungs and in thyroid remnants. In May and November 2006 the patient received ¹³¹I treatment. Post-therapeutic WBS in November 2006 revealed complete ablation of the thyroid remnants. Laboratory tests confirmed lowering of thyroglobulin concentration. In the years 2007, 2008, and 2009 the patient was qualified for therapy with ¹³¹I aided by rhTSH, achieving further reduction of Tg levels. Post-therapeutic WBS performed in 2009 revealed weak bilateral tracer uptake in the lung parenchyma. In 2010, chest CT revealed fibrosis in left lung segments, no infiltrative changes, and no lymph node enlargement. Patient follow-up continues at our Department.

Conclusions: Disseminated thyroid cancer in a patient with pituitary insufficiency may be successfully treated by rhTSH-supported ¹³¹I treatment. (*Pol J Endocrinol* 2010; 61 (5): 497-501)

Key words: acromegaly, disseminated follicular thyroid cancer

Streszczenie

Wstęp: W pracy przedstawiono interesujący i diagnostycznie trudny przypadek współwystępowania akromegalii i raka pęcherzykowego tarczycy u pacjenta Kliniki Endokrynologii UJCM w Krakowie.

Opis przypadku: Mężczyzna, lat 59, po operacji całkowitego wycięcia gruczołu tarczowego w 2005 roku, z potwierdzonymi badaniami histopatologicznymi przerzutami raka pęcherzykowego tarczycy do płuc, został przyjęty do Kliniki w kwietniu 2006 roku w celu leczenia uzupełniającego ¹³¹I. Akromegalię leczono operacyjnie z dojścia transsfenoidalnego w 1996 roku. W grudniu 2005 wykonano badanie MRI, stwierdzając wznowę gruczolaka przysadki, która korelowała z wysokim stężeniem hGH i IGF-1. Włączono leczenie Sandostatyną LAR, uzyskując kontrolę biochemiczną akromegalii. W preterapeutycznej scyntygrafii całego ciała (WBS, *whole-body scintigraphy*) uwidoczniło się bardzo liczne, zlewające się ze sobą ogniska gromadzenia ¹³¹I w płucach oraz gromadzenie znacznika w kikutach tarczycy. Pacjent w maju i listopadzie 2006 otrzymał leczenie ¹³¹I. Poterapeutyczna WBS z listopada 2006 wykazała pełną ablację kikutów tarczycy. W badaniach laboratoryjnych stwierdzono obniżenie stężenia tyreoglobuliny. W roku 2007, 2008 i 2009 pacjenta zakwalifikowano do leczenia ¹³¹I za pomocą rhTSH, uzyskując dalsze obniżenie stężenia Tg. W poterapeutycznej WBS z 2009 roku stwierdzono słaby wychwyty znacznika w miąższu płucnym obustronnie. W CT klatki piersiowej wykonanej w 2010 roku stwierdzono zwłóknienia w nadprzeponowych segmentach płuca lewego bez zmian naciekowych, węzły chłonne śródpiersia i wnęk nie powiększone. Pacjent pozostaje nadal pod opieką Kliniki. **Wnioski:** Chory z niedoczynnością przysadki po leczeniu operacyjnym akromegalii i rozsiałym rakiem tarczycy może być skutecznie leczony radiojodem ¹³¹I za pomocą rekombinowanego TSH. (*Endokrynol Pol* 2010; 61 (5): 497-501)

Słowa kluczowe: akromegalia, rozsiany rak pęcherzykowy tarczycy



Introduction

As suggested by several multicenter studies, acromegalic patients are believed to show a risk, higher than that in the general population, of developing benign and malignant tumours, mainly of the digestive tract (particularly colorectal), brain, prostate, breast, or thyroid gland [1, 2]. The aetiology of these tumours is unknown, but it may reflect the increased levels of growth hormone (hGH) and insulin-like growth hormone (IGF-1) in the blood.

The aim of this work is to present a diagnostically challenging case of concurrent acromegaly and disseminated follicular thyroid carcinoma in a patient of our Clinic of Endocrinology, UJCM in Krakow.

Case description

A 59-year-old male with histopathologically confirmed follicular carcinoma dissemination to the lungs was admitted to our Department in April 2006 for ^{131}I complementary treatment. Acromegaly in this patient was diagnosed in 1995 and treated in 1996 by trans-sphenoidal surgery. Follow-up of this patient was continued at the patient's permanent residence. In December 2005 a relapse of pituitary adenoma was diagnosed by MRI, correlated with increased levels of hGH (human growth hormone) and IGF-1 (insulin-like growth factor 1) and with no inhibition of hGH in oral glucose tolerance test (Table I). Treatment with octreotide LAR began with doses of 20 mg/month, followed by with 30 mg/month. Biochemical control of acromegaly was achieved, with present concentrations of hGH and IGF-1 listed in Table I. Over the last three years this patient has been treated with hypoglycaemic pharmaceuticals against type 3 diabetes. The presence of focal lesions in the lungs, probably of metastatic origin, was discovered in a routine chest X-ray examination in 2005 (Figs. 1 and 2); therefore, diagnostic procedures to establish the primary tumour location were initiated. Based on the diagnosis of

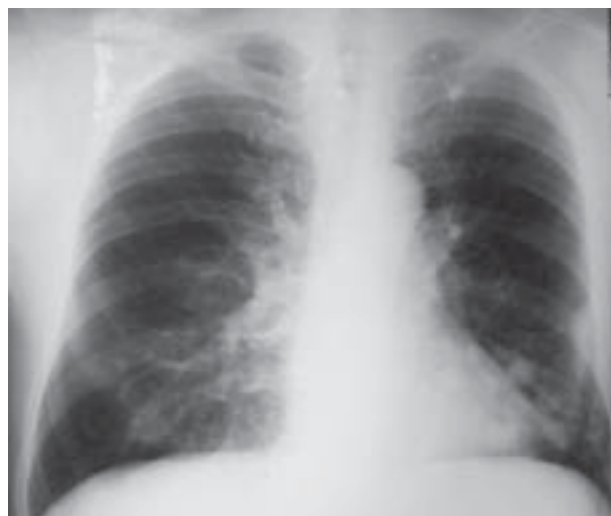


Figure 1. Chest X-ray from 2006, before ^{131}I treatment with pulmonary metastases

Rycina 1. RTG klatki piersiowej 2006 przed leczeniem ^{131}I z widocznymi przerzutami do płuc

nodular goitre, the patient was referred for thyroidectomy. In April 2005 total excision of the thyroid gland was performed. Based on histopathology and consultation at the Centre of Oncology in Gliwice, *adenoma microfollicularae necroticans glandulae thyroideae* was established. In a further search for the primary lesion, the patient underwent several diagnostic tests including bronchoscopy and transthoracic biopsy, which were not conclusive. Therefore, in February 2006 the patient was referred for open left lung biopsy whereby a fragment of the lingula, together with suspected foci, was excised. Follicular thyroid carcinoma was finally confirmed by histopathology of the excised samples. Following this diagnosis, the patient returned to our Department for further evaluation and treatment. From neck ultrasound, a 2.4 ml volume of thyroid remnants was evaluated, with a radioiodine uptake of 13% over the neck. Pre-therapeutic whole-body scintigraphy (WBS) revealed numerous conjoined hot spots of ^{131}I uptake in the lungs and in the thyroid remnants (Fig. 3A). Due to the advanced stage of the disease, the patient was qualified for radioiodine ^{131}I treatment. In May and November 2006 the patient received a total activity of 300 mCi (11.1 GBq). Post-therapeutic WBS in November 2006 demonstrated complete ablation of the thyroid remnants and a decrease in the number and intensity of focal isotope uptake (Fig. 3B), compared with the WBS of May 2006. Laboratory tests confirmed the decrease of thyroglobulin (Tg) concentration (Table II). The serum level of anti-thyroglobulin antibodies was 33.2 IU/mL (IRMA). As in this patient, who underwent pituitary adenoma surgery, the level of endogenously stimulated TSH did not exceed 25.0 $\mu\text{U/mL}$,

Table I. IGF-1 and hGH concentrations over the time of observation

Tabela I. Stężenia IGF-1 i hGH w czasie kilkuletniej obserwacji

| Date | hGH [ng/mL] (IRMA) | IGF-1 [ng/mL] (RIA) |
|---------------|-----------------------|------------------------|
| 2005 | 25.0 | 762.0 |
| November 2006 | 35.0 | 469.0 |
| April 2008 | 2.1 | 433.0 |
| November 2009 | 2.2 | 316.0 |
| February 2010 | 0.9 | 225.0 |

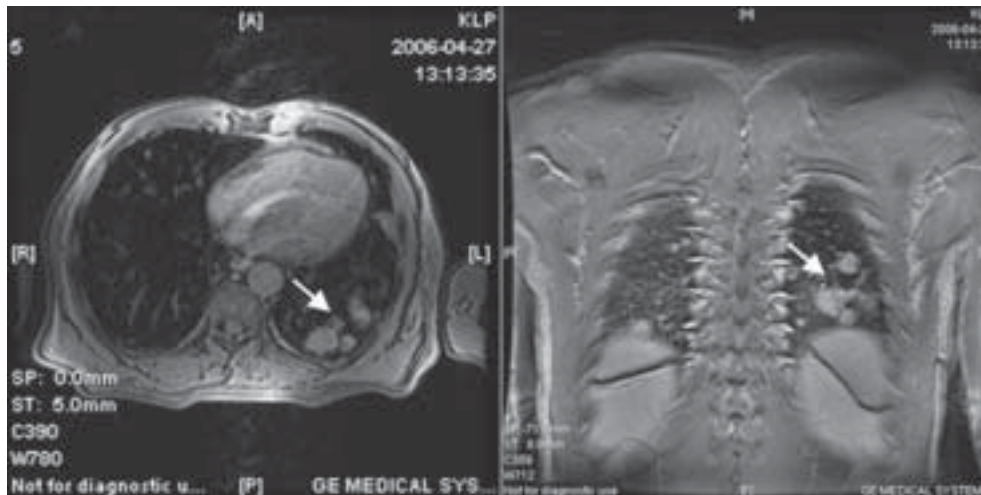


Figure 2. Chest MRI from 2006, before ^{131}I treatment. Lung metastases

Rycina 2. Badanie MRI klatki piersiowej 2006, przed leczeniem ^{131}I z widocznymi przerzutami do płuc

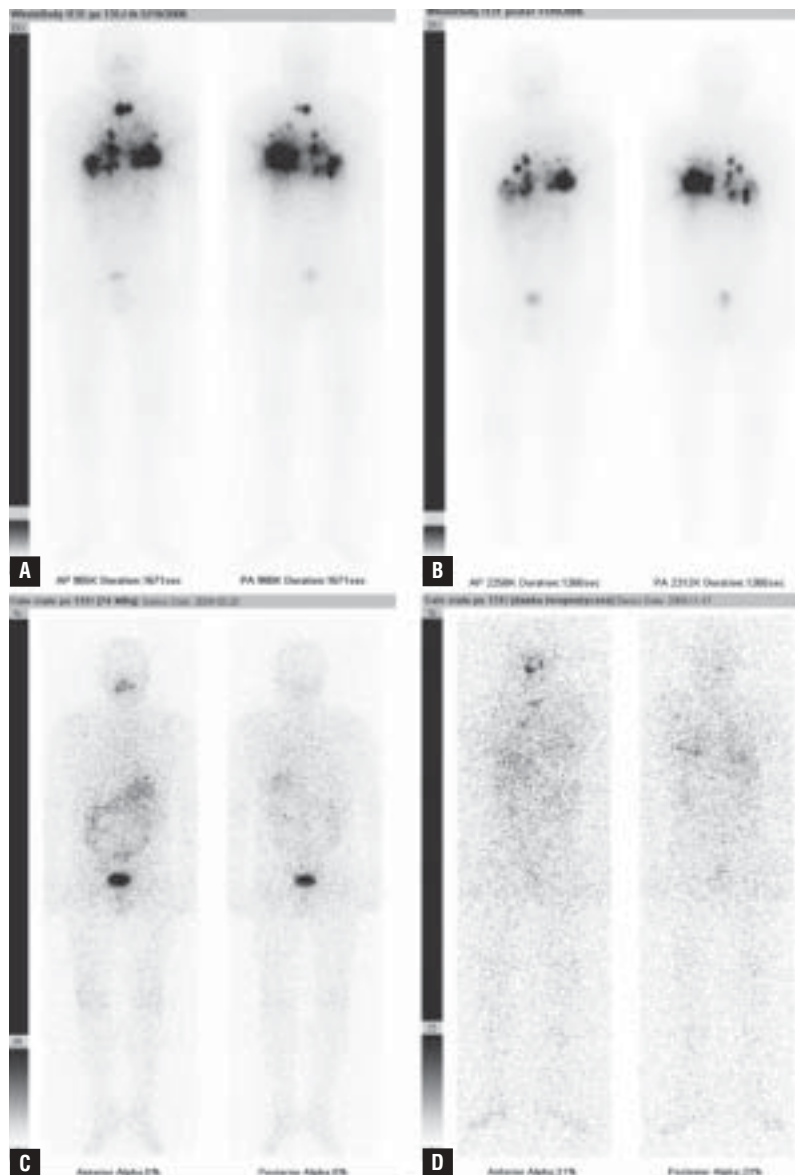


Figure 3. Whole body ^{131}I scintigraphy (WBS). **A.** Pre-therapeutic WBS (1 mCi; 37 mBq), May 2006. Tracer accumulation in multiple pulmonary lesions and thyroid remnants in the neck; **B.** Post-therapeutic WBS (150 mCi; 5.55 GBq), November 2006. No tracer accumulation in the neck, a decrease in the number and intensity of pulmonary tracer uptake; **C.** Diagnostic WBS (2 mCi; 74 MBq), August 2009. No tracer accumulation is seen in lungs or in the neck; **D.** Post-therapeutic scintigraphy (100 mCi; 3.7 GBq), November 2009. Weak, dispersed tracer accumulation in lungs and mediastinum

Rycina 3. Scyntygrafia całego ciała (WBS). **A.** Preterapeutyczna WBS (1 mCi; 37 mBq), maj 2006. Liczne ogniska gromadzące znacznik w płucach i w kikutach tarczycy; **B.** Poterapeutyczna WBS (150 mCi; 5,55 GBq), listopad 2006. Brak gromadzenia znacznika na szyi, zmniejszenie liczby ognisk i intensywności gromadzenia znacznika w płucach; **C.** Diagnostyczna WBS (2 mCi; 74 MBq), sierpień 2009. Brak gromadzenia znacznika na szyi i w płucach; **D.** Poterapeutyczna WBS (100 mCi; 3,7 GBq), listopad 2009. Dyskretne, rozproszone gromadzenie w płucach i śródpiersiu

Table II. Tg concentrations under suppressed or stimulated TSH observed over the course of treatment**Tabela II.** Stężenie Tg w czasie supresji i stymulacji TSH w okresie leczenia

| Date | Thyroglobulin [ng/mL] (ECL) | TSH [μ U/mL] (ECL) |
|-------------------------------|-----------------------------|-------------------------|
| May 2006 | 362.0 | 3.9 |
| September 2006 | 103.0 | 0.01 |
| November 2006 (T4 withdrawal) | > 1000.0 | 23.5 |
| April 2007 | 28.3 | < 0.001 |
| April 2008 (rhTSH) | 151.9 | > 100.0 |
| November 2009 | 15.2 | < 0.005 |
| November 2009 (rhTSH) | 318.0 | 217.0 |

over the years 2007, 2008, and 2009 recombinant human TSH (rhTSH)-aided 131 I therapy was performed, achieving a further reduction of Tg levels (Table II). In diagnostic WBS performed in August 2009 (Fig. 3C), no pathology in tracer accumulation was found, with continued high Tg serum concentration (Table II). Post-therapeutic WBS performed in November 2009 revealed weak bilateral tracer uptake in the lung parenchyma (Fig. 3D). In 2010, chest CT revealed fibrosis in left lung segments, no infiltrative changes, and no lymph node enlargement (Fig. 4). Patient follow-up is presently continuing at our Department.

Discussion

Concurrent acromegaly and disseminated follicular thyroid carcinoma is rare, and diagnosis and treat-

ment of the described patient were difficult and complicated.

Cancer is not a major cause of mortality in acromegalic patients [3] although it is suggested that the risk of developing benign and malignant tumours in acromegaly is higher than that in the general population.

Thyroid cancer is found in published analyses of prevalence of benign and malignant tumours in acromegaly, which most likely corresponds with hyperplasia of thyroid follicular cells. The frequency of goitre in acromegaly is high, constituting a risk factor for thyroid cancer. The frequency of simple and nodular goitre in this group of patients is estimated at 87.2% and 75.6%, respectively [4]. As confirmation, we also found nodular goitre by USG in 64/101 (63%) of our patients [5]. The prevalence of thyroid cancer in acromegaly is not known. In acromegalic patients, Tita et al. [6] and Ruchala et al. [4] estimated the prevalence of thyroid cancer at 5.6% (7/125) and at 5.8% (5/86), respectively. Thyroid cancer patients constitute 3% of all acromegalic patients registered in our Clinic of Endocrinology UJCM [5], as compared with the generally accepted 0.1% in the general population over iodine deficient areas.

The likely mechanism of these observations may be connected with increased levels of hGH and IGF-1 in the blood of patients with active acromegaly as hGH and IGF-1 are potent stimulators of normal or transformed cell proliferation. However, no causative proof of this is yet available. We observed no positive relationship between GH/IGF-1 concentration and thyroid volume [5]. Some authors associate the occurrence of colon neoplasms with elevated levels of hGH and IGF-1 [7]. Up to 50% of patients with acromegaly may develop colonic polyps, with increased prevalence in subjects over 50 years of age and a disease history of over

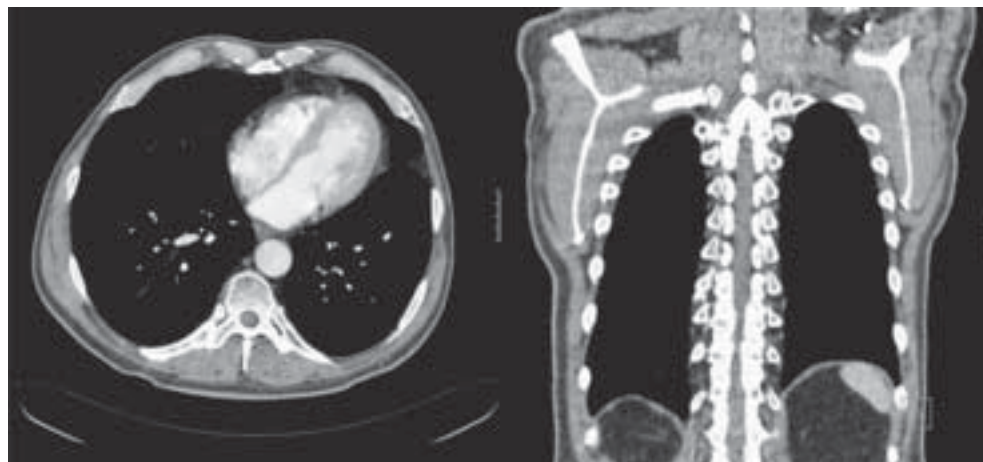


Figure 4. Chest CT, March 2010. Small fibrotic lesions in supradiaphragmatic segments of both lungs, no apparent metastases, no enlarged lymph nodes of the hili and mediastinum

Rycina 4. Tomografia komputerowa klatki piersiowej, marzec 2010. Drobne zwłóknienia w nadprzeponowych segmentach obu płuc, bez widocznych przerzutów, węzły chłonne wnek i śródpiersia niepowiększone

10 years [8, 9]. However, it is not possible to discern any increase of colon cancer in acromegalic patients from the available data even though colon polyps are precancerous lesions [10], perhaps because colon cancer is a relatively frequent disease (third in order of cancer occurrence in the general population). For thyroid cancer, epidemiological evidence seems even weaker as acromegaly is a rare disease of prevalence ranging between 50–70 cases /million and thyroid cancer in acromegalic patients is less frequent than colon cancer. Overall, thyroid cancer constitutes 3.1% of all malignant tumours in acromegaly [11]. Our studies [5] and those of Ruchala et al. [4] indicate that acromegaly enhances the risk of goitre. However, the prevalence of thyroid cancer is difficult to estimate as studied patient groups are small, making it difficult or impossible to apply standard epidemiological tools.

Following surgery, pituitary efficiency in the described patient was evaluated several times. No pituitary, adrenal, or gonadal axis substitution is required. However, being a thyroid cancer patient, suppression of TSH with L-thyroxine (LT4) at 200.0 µg/day was administered (Table 2). The first two therapeutic activities of ¹³¹I in 2006 were delivered following LT4 withdrawal. However, after LT4 was withdrawn, the TSH level did not exceed 25 µU/mL (Table 2), remaining below the Polish Society of Endocrinology 2006 recommendations [12]. From 2007 onwards we were able to apply rhTSH, which our patient received three times. Recombinant human TSH was introduced in differentiated thyroid carcinoma (DTC) treatment and follow-up as a safe and effective alternative to LT4 withdrawal. The first clinical applications of rhTSH were in diagnostics, to evaluate stimulated Tg concentration and WBS. In a multicentre randomized controlled study published in 2006 [13], rhTSH-aided ablation of thyroid remnants with 100 mCi of ¹³¹I was shown to be as effective as LT4 withdrawal in low risk patients. This was later confirmed in intermediate risk patients with lymph node metastases [14]. ¹³¹I treatment aided by rhTSH has not yet been approved for metastatic patients; however, several observations confirming the safety and efficacy of this treatment in advanced DTC have already been published [15, 16]. Recombinant TSH was safely used in metastatic thyroid cancer for radioiodine therapy in some special clinical situations, such as severe complications of hypothyroidism or in patients who are not able to endogenously stimulate TSH [17], which is the case for our patient.

As our case illustrates, multiple rhTSH treatment is efficient: decreased Tg level, negative neck US, weak tracer uptake in post-therapy WBS in 2009, and no evidence of disease in chest CT were stated. Our patient has evidently not been cured of thyroid cancer, since

Tg on LT4 therapy and rhTSH-stimulated concentrations continue to remain above 1.0 ng/mL. As our patient has so far received 600 mCi (22.2 GBq) and has retained I-¹³¹ uptake in his lung metastases, further radioiodine therapy is feasible; however, our patient's long-term prognosis remains uncertain. In macroscopic lung metastases only partial response or stabilization of the disease could be obtained with radioiodine treatment, as shown by Durante et al. [18] on a group of 444 DTC patients with distant metastases.

Conclusions

We believe that patients with a nodular goitre of the thyroid and with acromegaly should be carefully monitored by fine-needle biopsy and treated with rhTSH after pituitary gland surgery.

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