



# Primary squamous-cell thyroid carcinoma — a successful treatment with five-year follow-up

Pierwotny rak płaskonabłonkowy tarczycy — opis przypadku skutecznego leczenia z 5-letnią obserwacją

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## Abstract

Squamous cell carcinoma is an extremely rare neoplasm of the thyroid (SCTC) that represents no more than 1% of all primary thyroid malignancies. We report a case of a 42-year-old woman with rapidly growing mass in the right lower neck, primarily diagnosed in fine-needle aspiration cytology as a low-differentiated carcinoma. After the surgery, exclusion of all the other possible primary tumour locations, and immunohistochemistry tests, the diagnosis of primary squamous cell carcinoma of the thyroid gland was established. Because of close surgical margins and metastatic neck node, the patient was referred to adjuvant postoperative irradiation. With five-year follow-up the patient is free of disease and still in very good condition. (*Endokrynol Pol* 2017; 68 (5): 592–596)

**Key words:** *squamous cell thyroid carcinoma, surgery, radiotherapy*

## Streszczenie

Rak płaskonabłonkowy tarczycy jest bardzo rzadkim nowotworem złośliwym tarczycy, dotyczącym poniżej 1% rozpoznanych przypadków raka tego gruczołu. W niniejszej pracy przedstawiono przypadek 42-letniej kobiety z wywiadem pod postacią szybko rosnącego guza prawego płata tarczycy, pierwotnie zdiagnozowanego w biopsji cienkoigłowej jako niskozróżnicowany rak tarczycy. Po zabiegu operacyjnym, wykluczeniu innych możliwych ognisk raka i badaniu immunohistochemicznym postawiono rozpoznanie pierwotnego, płaskonabłonkowego raka tarczycy. Uwzględniając obecność wąskich marginesów chirurgicznych i przerzutu do węzła chłonnego szyjnego, chorą zakwalifikowano do pooperacyjnej radioterapii. Po zakończonym leczeniu, od 5 lat pacjentka pozostaje w obserwacji onkologicznej bez cech nawrotu choroby i w bardzo dobrym stanie sprawności. (*Endokrynol Pol* 2017; 68 (5): 592–596)

**Słowa kluczowe:** *rak płaskonabłonkowy tarczycy, chirurgia, radioterapia*

## Introduction

Squamous cell carcinoma is an extremely rare neoplasm of the thyroid (SCTC) that represents no more than 1% of all primary thyroid malignancies. Squamous epithelial cells are not present in normal thyroid gland — only residual cells may be observed as remnants of thyroglossal duct or branchial clefts. SCTC may arise from these cells, but also be a component of anaplastic or undifferentiated thyroid carcinoma. Some authors observed that most cases of SCTC are associated with tall cell variant of papillary carcinoma. Another possible (and the most widely accepted) reason for SCTC origin is squamous metaplasia of thyroid cells [1, 2].

The differential diagnosis of SCTC is with squamous cell carcinoma extending into thyroid gland from the hypopharynx, larynx, or oesophagus or metastasising from lung, nasopharynx, or other primary locations. Before diagnosing SCTC, other primary focuses of squamous cell carcinoma must be excluded [3].

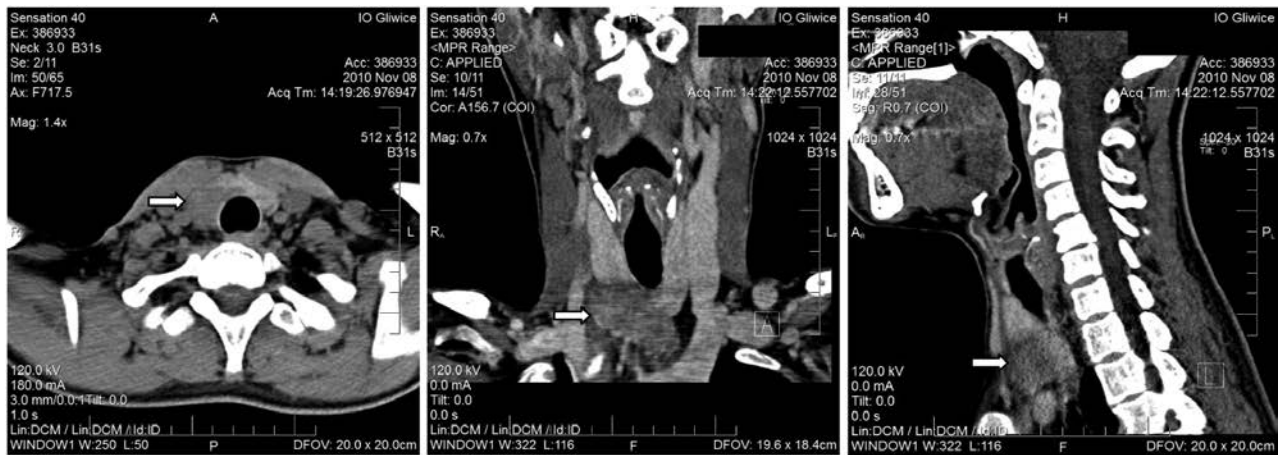
We report a case of thyroid cancer, which was initially diagnosed as low-differentiated carcinoma in fine-needle aspiration cytology (FNAC), but final pathological examination after the surgery revealed the diagnosis of SCTC.

## Case report

A 42-year-old woman with a negative thyroid gland malfunction observed a rapidly growing mass in the



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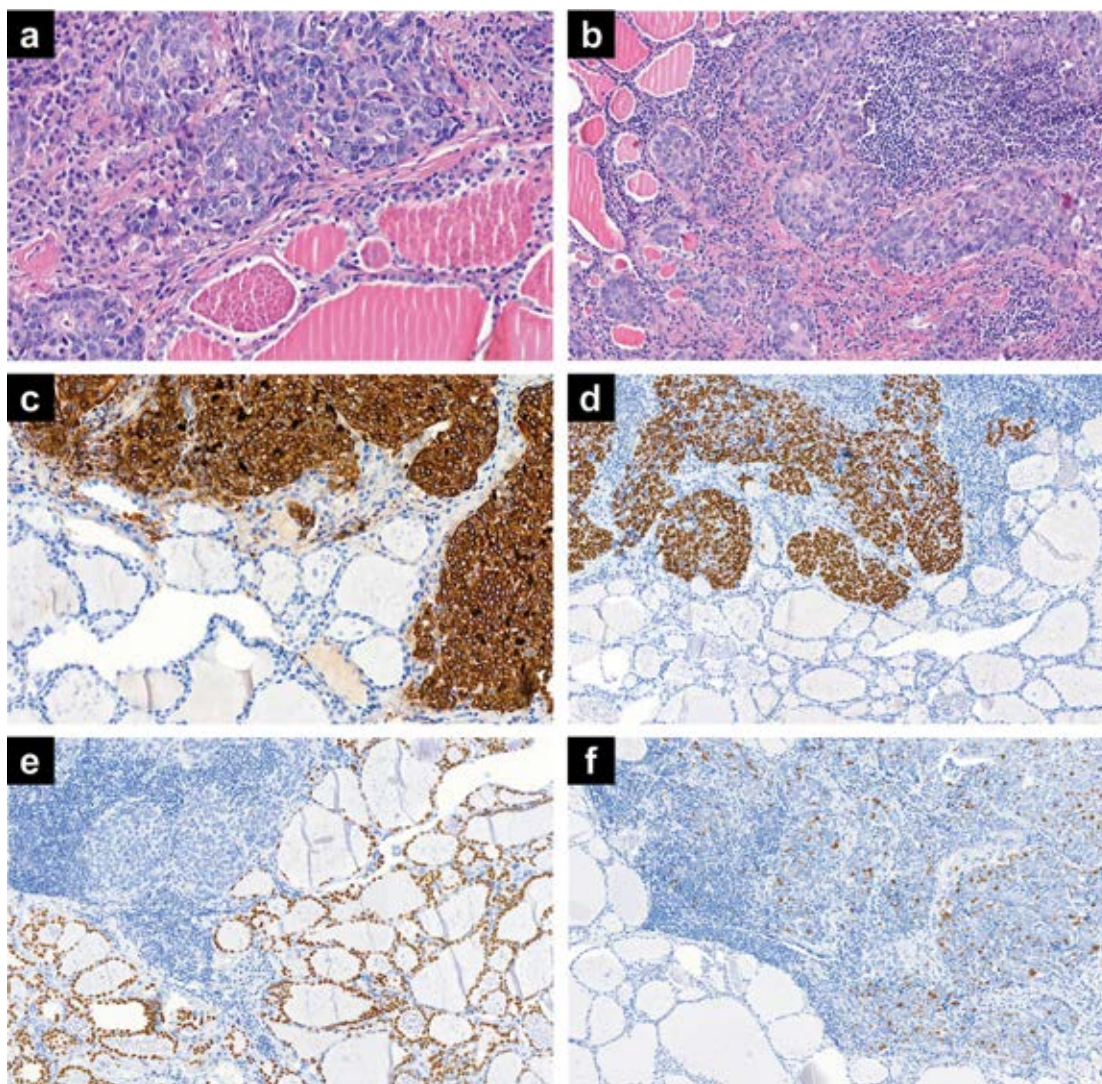
**Figure 1.** Contrast-enhanced computed tomography scans of the neck, showing soft tissue density mass arising from the inferior aspect of the right lobe adjacent to the trachea

**Rycina 1.** Obrazy tomografii komputerowej z kontrastem szyi w trzech projekcjach ukazujące miękкотkankową masę wyrastającą z dolnej części prawego płata tarczycy, przylegającą do tchawicy

right lower neck for three months. The patient visited a regional outpatient clinic in late September 2010, where diagnostic procedures were started. Cervical ultrasonography showed an irregular, hypoechoic tumour measuring 32.1 × 25.6 × 26.6 mm, located caudally in the right thyroid lobe and a small, radiologically benign, probably colloid tumour, with a diameter of 7 mm, located in the left lobe. FNAC was performed, suggesting thyroid anaplastic carcinoma. The patient was immediately referred to our institute to confirm the diagnosis and continue the treatment. During physical examination a solid tumour of the right thyroid lobe, penetrating down to the upper mediastinum, was palpated. Laboratory tests showed normal serum concentrations of TSH, fT4, and fT3. Also the findings of CEA, PTH, and calcitonin were within normal references. FNAC was repeated and also revealed a low-differentiated carcinoma. Contrast-enhanced computed tomography (CT) scan of the neck and thorax (November 2010) showed a soft tissue density mass arising from the inferior aspect of the right lobe, measuring 32 × 29 × 29 mm, adjacent to trachea without its infiltration (Fig. 1). No pathologies within the larynx, hypopharynx, and lungs with mediastinum and no suspicious neck nodes were diagnosed. Fibreoptic examination of the upper aerodigestive tract showed normal mucosa within the pharynx and larynx, without any pathologies suggesting a possible other primary tumour. The mobility of vocal cords was normal. Abdominal and pelvic ultrasonography showed no pathologies. The patient was planned for total thyroidectomy with medial neck dissection and biopsy of the right neck nodes. Recurrent laryngeal nerves and parathyroid glands were saved (November

2010). Postoperative pathological examination revealed a solid infiltration, macroscopically cream-coloured, encompassing the majority of the right thyroid lobe (maximal dimension of 41 mm), but also going through the isthmus to the medial part of the left lobe. Microscopic examination showed solid sheets of cells widely invading the thyroid parenchyma with two close surgical margins. Also, one metastatic adjacent neck node was diagnosed. All the tumour cells showed squamous morphology, and positive immunohistochemistry staining for such squamous differentiation markers as CK5/6 and p40. The positive staining for PAX 8 confirmed the thyroid origin of the neoplastic cells. TTF-1 was negative. The proliferation index Ki-67 was 30% (Fig. 2, 3) [4].

The diagnosis of primary squamous cell carcinoma of the thyroid gland was given and the stage of cancer was evaluated as pT3pN1aM0. The patient was referred to the postoperative radiotherapy. Before the irradiation, the re-examination of the patient, based on fibreoptic examination and magnetic resonance imaging (MRI), was performed to definitely exclude a possible primary tumour within the aero-digestive tract — no pathologies were found. Postoperative radiotherapy was performed between February 2, 2011 and March 12, 2011, with the intensity-modulated radiotherapy technique (IMRT). A total dose 60 Gy in 30 fractions (2 Gy) within the thyroid bed and adjacent metastatic neck lymph node bed and a dose of 50 Gy in 25 fractions (2 Gy) were given for bilateral lymph nodes groups (II, III, IV, VI, and upper mediastinum). The tolerance of radiotherapy was good — spotted and confluent mucositis was observed with no more than 50% of the irradiated mucosa within the hypopharynx and larynx.



**Figure 2A.** Squamous carcinoma infiltrating the thyroid parenchyma. Note the abundant lymphocytic infiltration (**B**); **C.** Cytokeratin 5/6 extensively positive in tumour cells\*; **D.** p 40 positive in tumour cells, negative in the accompanying lymphocytes\*; **E.** TTF-1 positive in thyroid parenchyma, negative in the tumour; **F.** Ki 67 proliferation index

\*IHC Markers of squamous differentiation

**Rycina 2A.** Rak płaskonabłonkowy naciekający miąższ tarczycy. Zauważalny obfity naciek limfocytarny (**B**); **C.** Intensywnie dodatnia cytokeratyna 5/6 w komórkach raka; **D.** Dodatnia reakcja markera p40 w komórkach raka, ujemna w sąsiadujących limfocytach; **E.** Dodatnia reakcja markera TTF-1 w miąższu tarczycy, ujemna w komórkach raka; **F.** Marker proliferacji Ki-67

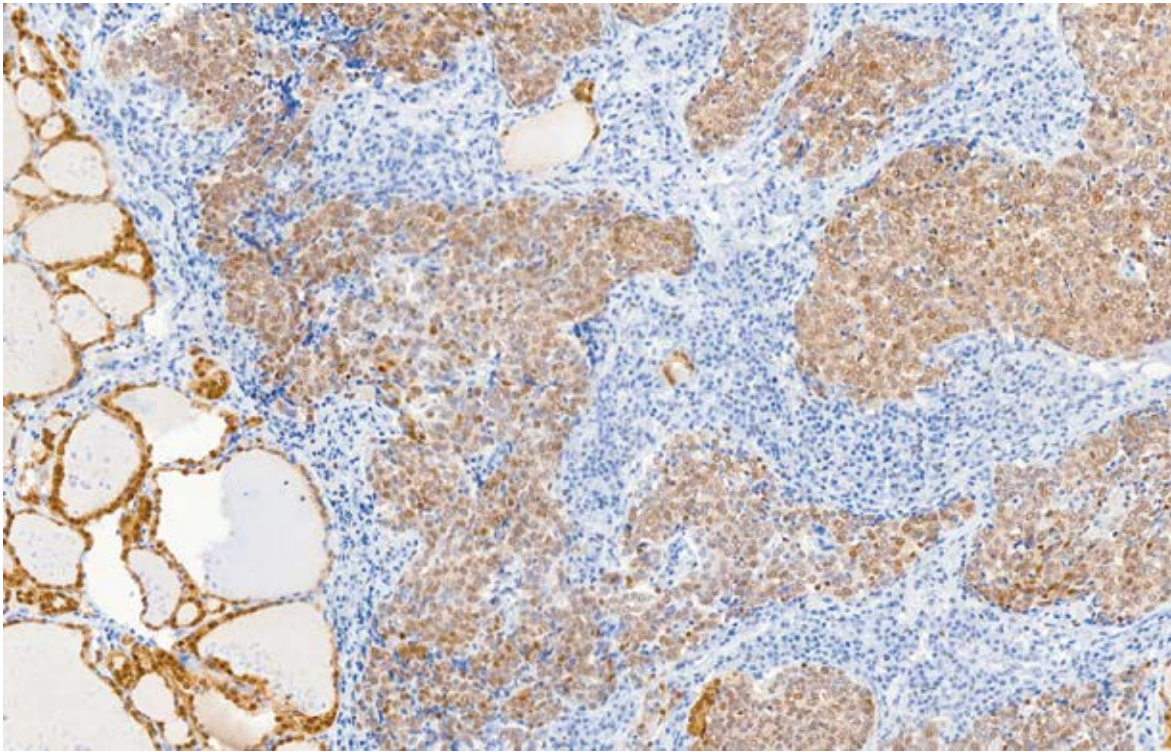
To date, the patient has survived 60 months following radiotherapy, with no evidence of recurrence.

## Discussion

Primary SCTC is an uncommon cancer of the thyroid gland. The incidence of pure SCTC in the English-language literature ranges from 0.2% to 1.1% of all neoplasms of the thyroid [5]. It usually occurs in the 5<sup>th</sup> to 7<sup>th</sup> decades of life with a mean age at diagnosis of 65 years (range 24–90 years) and female prevalence (female-to-male ratio 2:1) [5, 6]. Primary SCTC may coexist with papillary and anaplastic thyroid cancer.

Pure SCTC, occurring solitarily without other tumours, is extremely rare. Although controversial, squamous metaplasia is the most widely accepted aetiological theory of primary SCTC [1, 2, 7].

Patients with SCTC routinely present with rapidly growing neck mass and swelling. Based on the clinical symptoms, it is nearly impossible to distinguish SCTC from anaplastic cancer [7]. Predictability of diagnosis of SCTC with fine-needle aspiration biopsy is accurate in less than one-third of patients [1, 2, 6, 8–11]. As the disease progresses, dysphagia and hoarseness may occur [9]. SCTC is an aggressive, highly lethal neoplasm [7]. Metastases from primary SCTC are common, especially



**Figure 3.** Positive reaction of PAX 8, the sensitive marker for thyroid origin in tumour cells, as well as in the thyroid follicles

**Rycina 3.** Dodatnia reakcja PAX 8, czulego markera pochodzenia tarczycowego komórek nowotworu, obecna w komórkach raka płaskonabłonkowego i komórkach pęcherzyków tarczycy

to cervical lymph nodes (35%), but may occur in lungs, bones, liver, kidney, and heart [2, 5, 11].

Local relapse and progression to larynx and trachea causing dyspnoea and respiratory obstruction are the main reasons of treatment failure and death [7, 10, 12, 13]. Occasionally, cancer dissemination with pulmonary metastases may lead to death.

Because of the rarity of this disease, there are no standardised guidelines for the treatment of primary SCTC. Treatment modalities include surgical resection, which is the procedure of choice. However, operation alone is not a sufficient treatment for these cancers because of the high risk of tumour relapse. Although SCTC is regarded as relatively radio-resistant, adjuvant radiotherapy (50–66 Gy in 25–33 fractions, the dose depends on risk factors) should be a standard procedure. Chemotherapy has not been shown to be beneficial in SCTC [2, 12, 14], but in cases of positive surgical margins and pericapsular infiltration, postoperative radiotherapy combined with cisplatin, as in advanced head and neck squamous cell cancer, may be justified. To date, no sufficient information is available on its use in SCTC. If possible, debulking procedures with trachea reconstruction may be carried out in patients with advanced local disease to avoid suffocation caused by obstruction or bleeding [1, 2]. When radical surgery in

advanced cases is not possible, palliative radiotherapy (20 Gy in five fractions or 30 Gy in 10 fractions) may be beneficial to improve quality of life [15].

Prognosis of SCTC is very poor and the majority of patients die within one year after the diagnosis (the median survival is nine months; three-year survival is only 20%) [6, 7, 12]. Treatment should primarily be concentrated on surgical resection with negative margins. Complete surgical resection (R0) was the only significant prognostic factor in multivariable analysis [6, 14]. Although the benefit of adjuvant treatment was not proven, the results reported in the literature showed that patients with complete excision and postoperative radiotherapy had better survival when compared to patients with complete excision alone or incomplete excision with radiotherapy [2, 5, 13, 14, 16]. The presence of lymph node metastasis is also an important negative prognostic factor. Mean overall survival of patients with lymph node metastasis is shorter compared with patients without metastasis (10.8 vs. 16.4 months) [5].

We report a case of a female patient with primary SCTC treated with surgery and adjuvant radiation therapy with long, five-year follow-up without relapse. In our case, two close margins and one metastatic neck node were found, so adjuvant treatment was mandatory. Because of the lack of evidence of efficacy of

concurrent postoperative radio-chemotherapy in SCTC, we performed radiotherapy alone to an elective dose within neck nodes and escalated dose for the thyroid bed and metastatic lymph node bed. The long follow-up in our case shows that there is a possibility of successful treatment and cure in some patients with SCTC.

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