

# An unusual case of medullary thyroid cancer

## Nietypowy przypadek raka rdzeniastego tarczycy

### Authors' Contribution:

A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Manuscript Preparation  
E – Literature Search  
F – Funds Collection

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### ABSTRACT:

**Introduction:** Medullary thyroid carcinomas make up 9.4% of all cancers of the thyroid gland [1]. They can be divided into sporadic and familial forms. Sporadic forms are the most common ones. The rest of medullary thyroid carcinomas include familial forms; in most cases they are associated with MEN2a and MEN2b syndromes. If a neoplasm is associated with MEN2a or MEN2b syndromes, other tumors, such as pheochromocytoma or adenomas of the parathyroid glands, may also occur. Medullary thyroid carcinoma typically occurs as a solid tumor in the thyroid region of the neck. It can also produce pain in the thyroid region, dysphagia, hoarseness, or cervical lymphadenopathy. These symptoms are caused by adjacent tissues being infiltrated by the neoplasm and by metastases to cervical lymph nodes. The apparent absence of tumor in the thyroid region is very rare in patients who complain of signs associated with infiltration of the tumor, albeit in some cases lymphadenopathy can be the first sign of medullary thyroid carcinoma [2]. Even less commonly, no tumor can be visualized on CT scans of the thyroid gland with signs of cervical lymphadenopathy being present.

**Case report:** In this case report, we present a patient with metastases of medullary thyroid carcinoma within the neck, with no other findings in physical examination and additional tests.

### KEYWORDS:

branchial cyst, cervical lymphadenopathy, deep neck infection, medullary thyroid cancer, medullary thyroid carcinoma, metastases of medullary thyroid cancer, neck masses, peritonsillar abscess, serious soft tissue infection of the neck

### STRESZCZENIE:

**Wstęp:** Rak rdzeniasty tarczycy stanowi 9,4% wszystkich raków tarczycy [1]. Dzielimy go na występującego rodzinnie i sporadycznie. Najczęściej występuje jako postać sporadyczna. Pozostałe przypadki to postać rodzinna, która zwykle występuje w zespołach MEN2a lub MEN2b. Jeśli nowotwór jest związany z wcześniej wymienionymi zespołami genetycznymi, to mogą towarzyszyć mu inne guzy – guz chromochłonny nadnerczy oraz nadczynność przytarczyc spowodowana hiperplazją komórek gruczołowych przytarczyc lub gruczolakami przytarczyc. Typowo rak rdzeniasty tarczycy manifestuje się jako twarde guz na szyi. Innymi objawami mogą być: ból w okolicy tarczycy, dysfagia, chrypka. Związane one są z naciekaniem przez guz okolicznych tkanek. Rzadko zdarza się, aby w badaniu fizykalnym pacjenta, pomimo braku dolegliwości związanych miejscowo z tarczycą, nie wy badać guza w tarczycy, choć limfadenopatia szyjna może być pierwszym objawem raka rdzeniastego tarczycy [2]. Jeszcze rzadsze są przypadki, w których nie znajduje się guza, pomimo wykonania badań obrazowych.

**Opis przypadku:** Prezentujemy przypadek chorego z przerzutami raka rdzeniastego tarczycy do układu chłonnego szyi, przyjętego do Kliniki Otorinolaryngologii i Chirurgii Głowy i Szyi WUM, u którego po badaniu fizykalnym oraz po wykonaniu badań dodatkowych, nie znaleziono ewidentnej patologii w tarczycy ani nie stwierdzono objawów związanych miejscowo z tarczycą.

### SŁOWA KLUCZOWE:

guz szyi, infekcja tkanek miękkich szyi, limfadenopatia szyjna, przerzuty raka rdzeniastego tarczycy, rak rdzeniasty tarczycy, ropień okołomigdałkowy, torbiel boczna szyi

## INTRODUCTION

Medullary thyroid carcinoma (MTC) is derived from the C cells of the thyroid gland [3]. C-cells are responsible for producing calcitonin. MTC accounts for between 3.5% and 11.9% of all thyroid carcinomas. It is more prevalent in women than in men (7:1) [4]. Chong et al. report the age range of patients with MTC to be between 2 and 73 years, with the median age of 51 years [2]. MTCs can be classified into the following categories:

1. sporadic carcinoma (cases with negative family history of MTC) – according to Chong et al., this type accounted for 110 out of 139 cases;
2. genetic cancer (cases with positive family history of MTC) – according to Chong et al., this type accounted for 110 out of 139 cases:
  - MEN2a and MEN2b-related MTC (more common) [5, 6],
  - MEN2-non-related MTC (less common, no case reported among 139 cases described by Chong et al.).

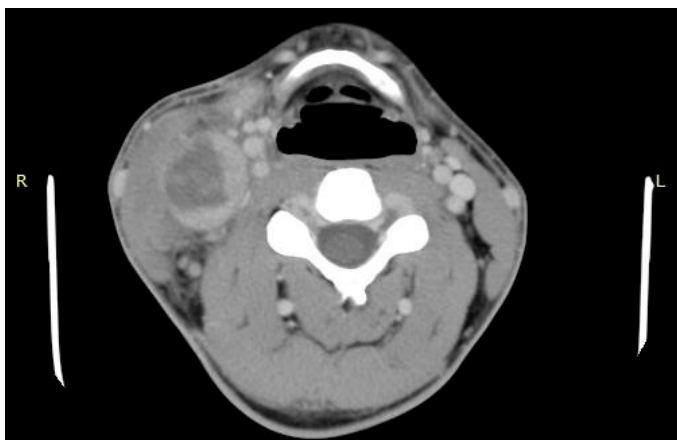


Fig. 1. Presentation of the tumor in preoperative contrast-enhanced cervical CT scan.

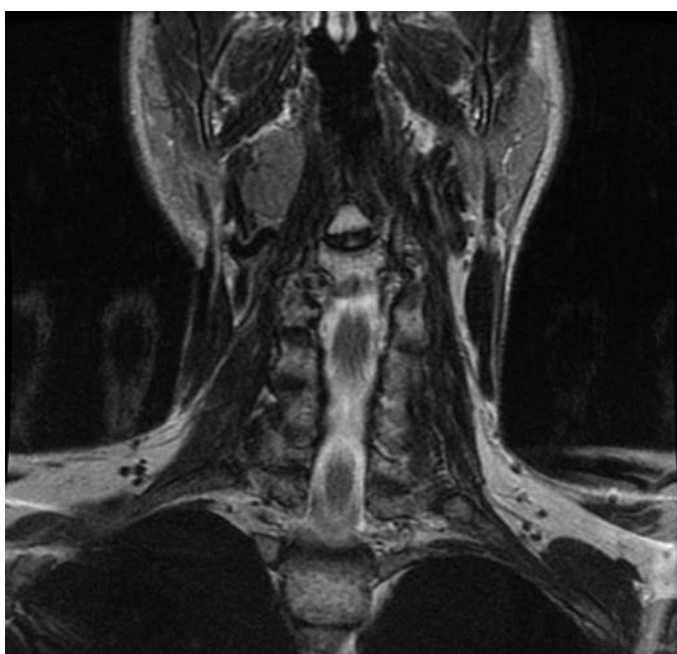


Fig. 2. Metastasis of the medullary thyroid carcinoma into the parapharyngeal space as visualized in cervical MRI scan.

Thyroid nodules are the most common MTC-related symptoms prompting the patient to seek medical assistance [2]. Although the first symptoms may vary, they are usually locally confined to the thyroid gland. These include pain in the thyroid region, dysphagia, hoarseness.

Systemic symptoms are rare, the most common being watery diarrhea [2]. Other generalized symptoms may be related to medullary adenoma and hyperactivity of the parathyroid glands. Hot flushes may be experienced by some patients [7].

In the presented case, the first symptom consisted in inflammatory infiltration of deep neck tissues spreading along the sternocleidomastoid muscle.

Purulent infections of the soft tissue within the neck are most commonly due to odontogenic infections or upper respiratory tract infections, including peritonsillar abscesses. However, the

origins of a significant number of purulent infections within the soft neck tissues remain unknown (according to some authors, this may pertain to more than one half of all cases) [8, 9].

## CASE REPORT

About 12 years ago, a 29-year-old male patient presented at the emergency department with a painful mass developing on the right side of his neck over the previous 3 days and fever of 39.4°C. To date, the patient had not been treated for any chronic disorder or had not taken any medicines permanently.

Physical examination revealed a hard, tender, non-fluctuant infiltrate spreading along the sternocleidomastoid muscle on the right side of the neck. Otherwise, no abnormalities were observed on physical examination.

Ultrasound scan of the neck was performed in the emergency mode to reveal 3 fluid reservoirs, the largest sized 83 × 60 mm, under the right SCM muscle between the mandibular angle and the supraclavicular fossa; the presentation might correspond to abscesses. An enlarged lymph node (32 × 16 mm) was also revealed in the mandibular angle region. Diagnostic imaging was extended to include contrast-enhanced CT scans of the neck, the findings including the presence of three fluid reservoirs; differentiation between cervical abscess and infected branchial cyst was suggested. The CRP level was 257 mg/dL, and leukocytosis of 12.5 K/ $\mu$ L was found in hematological investigations.

The patient was admitted to the Department of Otorhinolaryngology in an emergency setting; IV antibiotic therapy was initiated. Ceftriaxone 1 × 2 g. i.v. and metronidazole 3 × 500 mg i.v. were administered. After several days of antibiotic therapy, improvement in the general condition and normalization of inflammatory parameters were achieved. The dimensions of the neck lesion decreased significantly and the pain resolved. The patient was prepared for surgical removal of the neck mass. The surgery was performed after 10 days of antibiotic therapy. Macroscopic intraoperative presentation of the tumor was similar to that of merging lymph nodes. Due to this atypical macroscopic presentation, a decision was made to collect specimens for intraoperative histopathological examination. Emergency examination revealed reactive lymphadenitis. The tumor was dissected and removed as a whole. The postoperative period was completed without complications. The patient was discharged home to remain under follow-up of the hospital outpatient clinic. Final pathomorphological examination of the surgical specimen revealed medullary thyroid carcinoma (MTC).

After the neck wound had healed, the patient was referred to another center where thyroidectomy with radical modified right-sided cervical lymphadenectomy was performed. Following surgery, adjuvant radiotherapy was delivered. Following the completion of the treatment, the patient was followed up at the Oncology Center.

Twelve years after thyroidectomy and right-sided modified lymphadenectomy, when the patient was 41 years old, a follow-up

**Tab. I.** Symptoms of medullary thyroid carcinoma responsible for presentation at the physician's.

THE REASON FOR PRESENTATION	NUMBER OF PATIENTS
Painless thyroid nodule	69/139
Pain within the thyroid area, hoarseness, dysphagia	15/139
Cervical lymphadenopathy	15/139
Elevated calcitonin levels (screening examination in families with MEN2 burden)	13/139
Other	27/139

**Tab. II.** The causes of purulent infections of the soft tissues of the neck [8].

REASON	PERCENTAGE
Odontogenic infections	35.1
Tonsillitis	30.2
Injury (non-surgical)	4.1
Injury (surgical)	2.1
Sialolithiasis	3.1
Brachial cysts	0.6
SCC of the tongue	0.1
Unknown reason	24.1

contrast-enhanced MRI study of the neck revealed a tumor within the right parapharyngeal space. Examination revealed an intensely enhanced lesion sized 19 × 29 × 42 mm located anteriorly and medially from the internal carotid artery. Flow voids corresponding to blood vessels were observed within the tumor. No enlarged lymph nodes were reported besides the aforementioned tumor. The tumor presented with no restriction features in DWI scanning. The patient was admitted to the Department of Otorhinolaryngology for surgical treatment. No abnormalities were observed in the postoperative period following the removal of the pharyngeal tumor.

The patient was discharged on post-operative day 7 in general good condition, with no postoperative complications and normal cranial nerve function preserved on both sides. Medullary thyroid carcinoma tissue was reported following the postoperative histopathological examination of the excised tumor. Follow-up blood calcitonin level examination performed 20 days after surgery showed a clear decrease in hormone concentration from 2000 ng/L to 250 ng/L. The patient remains followed-up at the outpatient clinic of the Department of Otorhinolaryngology, Head and Neck Surgery of the Medical University of Warsaw.

## DISCUSSION

Incidentally detected mass within the thyroid region is the most common reason responsible for patients to be diagnosed with MTC reporting at their physician's for consultation. Other reasons include local symptoms within the thyroid region (thyroid pain, hoarseness, dysphagia) and cervical lymphadenopathy [2].

Of note is the fact that diarrhea was a common concomitant symptom reported by patients in the cited study (38 out of 139 patients). In 3 cases, diarrhea was the first symptom of the tumor. Diarrhea was more common in people with metastatic thyroid carcinoma [2]. Palpable thyroid mass was detected in as many as 80% of patients upon physical examination.

According to the National Comprehensive Cancer Network (NCCN) guidelines of February 2019, the diagnosis of thyroid tumors is started with the determination of TSH concentration and an ultrasound scan of the thyroid if thyroid tumor is clinically suspected. MTC presents as a solid tumor. For solid thyroid tumors, indications for biopsy include the mass size of more than 1 cm (if no alarming features, such as e.g. hypoechogenic lesion, microcalcifications, or non-smooth borders, are found in the US scan), or more than 1.5 cm (if no alarming features are found in the US scan). If the FNAB result confirms the diagnosis of MTC, recommendations include determination of the serum levels of calcitonin, CEA, and calcium, neck ultrasound (if not performed before), and determination of the motility of vocal folds. Each patient diagnosed with MTC should also be screened for the RET proto-oncogene mutation carrier status [10]. Approximately 6% of patients are carriers of the aforementioned mutation despite the absence of a positive family history of MTC [11, 12]. In addition, NCCN recommendations include the possibility of chest CT scan and triple-phase abdominal CT scan being considered in order to identify potential metastases. The management of MTCs is based on surgical treatment [13, 14]. MTC is not responsive to radioactive iodine since the thyroid C cells are incapable of absorbing iodine. TSH suppressive therapy, while being useful in other thyroid tumors, is ineffective

**Tab. III.** The causes of purulent infections of the soft tissues of the neck [9].

REASON	PERCENTAGE
Odontogenic infections	22.7
Upper respiratory tract infection	13
Peritonsillar abscess	3.8
Foreign body of the digestive tract	1.1
Head and neck surgeries	1.1
Skin infections	0.5
Parotid sialadenitis	0.5
Unknown	57.3

in MTC since the thyroid C cells lack TSH receptors. Chemotherapy is not widely used in the treatment of MTC as no good responses to chemotherapeutic agents were observed [15, 16]. Resection of the lymph nodes depends on the size of the thyroid tumor. For tumors smaller than 1 cm, resection of group VI nodes may be considered in addition to total thyroidectomy. If the tumor is larger than 1 cm, total thyroidectomy is always accompanied by the resection of group VI nodes. The elective resection of group II–V nodes may also be considered depending on the extent of the tumor and the changes within the lymph nodes as described in the cervical ultrasound scan. Elective resection of group II–V lymph nodes may be uni- or bilateral depending on changes reported in ultrasound scans [13, 14]. Post-operative radiotherapy is usually not performed since it has not been well studied in MTC treatment [15, 17, 18]. According to the NCCN, the follow-up of patients to screen for disease recurrence is based on the determination of calcitonin and CEA levels. If elevated CEA and calcitonin levels remain stable or if normal CEA and calcitonin levels are measured following surgery (the latter should be undetectable following thyroidectomy), these parameters should be monitored. In addition, imaging examinations of the neck or the chest and the abdomen should also be performed in patients with elevated CEA and calcitonin levels, as these are the sites where metastases are most commonly located. If no suspicious focal lesions are found, further follow-up including regular checkups of CEA and calcitonin levels is recommended. If new MTC foci are detected, repeated resection, radiotherapy, and kinase inhibitors (vandetanib, cabozantinib) are used to treat these lesions [19–22].

Now, let us take a look at the presented case from another perspective.

Purulent inflammation of the soft tissues of the neck might be the clinical manifestation of numerous diseases.

The most common causes of purulent infections of the soft tissues of the neck are odontogenic infections [23] and tonsillitis [24]. Other causes are much less common. It should also be noted that a large percentage of purulent soft tissue infections within the neck are of unknown origin. We therefore want to show how important it is to perform a thorough diagnosis of a patient in whom no evident point of origin is identified for the infection of

neck tissues. In the presented case, the proper diagnosis of MTC could only be made after histopathological examination of the tissue specimen. The diagnostics of inflammatory processes within the neck region consists of assessing the inflammatory parameters in the blood and in performing imaging studies such as neck ultrasound and contrast-enhanced neck CT scans. The imaging studies facilitate evaluation of the nature of lesions, their extent and location relative to cervical vessels. The treatment consists in intravenous broad-spectrum antibiotic therapy and, if fluid reservoirs are confirmed, incision and drainage of the infected area [25, 26]. In some cases, when a patient is incapable of receiving food by mouth due to dysphagia, the placement of a gastric feeding tube should be considered [27]. Another serious complication is dyspnea caused by the swelling of the airways; in such cases, tracheostomy should be performed. In some cases, when the purulent infection of the soft tissues of the neck is not too extensive, intravenous antibiotic therapy may be sufficient [27]. Antibiotic therapy alone is also used when the patient's condition permits it in cases when the suspected cause of the purulent inflammation is a branchial cyst. Surgical intervention in the course of acute inflammation makes the subsequent radical resection of the lesion, performed only after local inflammation has been controlled, more difficult [28]. A similar case is presented herein. The inflammatory infiltration mimicked a suppurated branchial cyst. Therefore, intravenous antibiotic therapy was chosen as the first line of treatment.

According to Jeffrey et al., 81% of patients in whom MTC was diagnosed following the detection of a palpable mass within the anterior part of the neck, presented with metastases to regional lymph nodes: 81% of patients presented with metastases to group VI nodes, 81% of patients presented with metastases to ipsilateral group II–V nodes, and 44% of patients presented with metastases to contralateral group II–V nodes [29]. The results reported by the authors of the study were supported by histopathological examinations of surgical specimens. Each patient included in the study was subjected to thyroidectomy, bilateral functional dissection of group II–V lymph nodes, and dissection of group VI lymph nodes. Resection of group II nodes was carried out to the level of the facial vein. In our case, a different approach was used, consisting in radical resection of the cervical lymph node system on the side of the tumor. Despite this radical treatment, cancer metastasis has occurred in an entirely atypical location.

## CONCLUSIONS

In the group of patients with purulent infections of the soft tissues of the neck, odontogenic infection and upper respiratory tract infections, including peritonsillar abscess, should be suspected first. One should keep in mind that inflammatory infiltration within the

neck may be a manifestation of numerous pathologies, including tumors. Therefore, thorough diagnosis including histopathological examination is required in patients without obvious points of origin of the inflammatory process within the neck. Further research is needed on the proper management of MTC. As of today, no uniform guidelines are available on the surgical treatment of MTC.

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