

# Metastases to the thyroid gland: seventeen cases operated on in a single clinical center

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## Abstract

**Background and aims** In spite of its rich vasculature, the thyroid gland is rarely the site of metastatic disease. The incidence of such metastases differs depending on the type of the analyzed material. In clinical papers, the incidence is low and, according to various sources, amounts to 2–3% of all malignant tumors of the thyroid. Most commonly, the primary tumor is located in the breast, bronchi, gastrointestinal system, (the colon, esophagus, or stomach) and kidneys. Usually, metastatic thyroid disease is identified upon autopsy, and only sporadic cases are encountered in clinical material. The authors present their experience in treating metastatic disease involving the thyroid gland based on the analysis of their clinical material consisting of patients operated on in a single center.

**Materials and methods** Seventeen patients presented with metastatic tumors of the thyroid. The material was further analyzed retrospectively. The group included four men and 13 women, with the male to female ratio of 1:4.25. The age of the patients ranged from 46 to 76 years, with the mean age amounting to  $62 \pm 9.78$  years. Eleven patients were diagnosed based on fine needle aspiration biopsy (FNAB). **Results** In 13 patients, the primary lesion was a clear cell carcinoma of the kidney, in one breast cancer, in another

one uterine carcinoma. In two patients, no primary focus location was established. All the patients were treated surgically. Twelve patients were consistently followed up after the surgery. Of this group, seven are still alive, including five individuals with metastases of renal carcinomas, but without recurrent disease. Five patients died due to disseminated neoplastic disease. No data are available on three patients. The mean follow-up time after thyroid surgery was 3.9 years. The longest followed-up survival time was 11 years.

**Conclusions** The most commonly clinically detected and treated surgically metastatic lesion of the thyroid gland is clear cell cancer of the kidney. In cases of renal cancer metastases to the thyroid gland, a total thyroidectomy seems to be warranted, although it does not affect the survival time.

**Keywords** Thyroid cancer · Thyroid metastases · Clear cell cancer

## Introduction

In spite of its rich vasculature, the thyroid gland is rarely the site of metastatic disease. The incidence of such metastases differs depending on the type of the analyzed material. In clinical papers, the incidence is low and, according to various sources, amounts to 2–3% of all malignant tumors of the thyroid [1, 2]. In postmortem examinations, the value ranges from 1.25 to 24.2% and is usually associated with cancer dissemination through blood from a distant focus or with a direct involvement of the thyroid gland by a neoplastic process situated in the adjacent organs [3–6]. The location of the primary focus is also diversified. Most commonly, the primary tumor is

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located in the breast, bronchi, gastrointestinal system, (the colon, esophagus, or stomach) and kidneys. Usually, metastatic thyroid disease is identified upon autopsy and only sporadic cases are encountered in clinical material [7].

Secondary thyroid tumors may be accompanied by synchronous metastatic lesions to other organs, e.g., to the lungs. Intravitaly, the most common observation is a metachronic metastasis of a clear cell carcinoma of the kidney, which accounts for more than one-half of metastases to the thyroid found in clinical material; only some of such lesions are manifested by clinical symptoms [8–10]. Metastatic involvement of the thyroid in the course of other cancers is rarely discernible clinically. The reason for such a phenomenon is primarily the rapid progress of the primary neoplastic disease (e.g., breast or bronchial cancer) [11, 12]. In the vast majority of cases, metachronic hematogenic metastases of renal carcinoma to the thyroid develop a long time after the surgical excision of the primary lesion, e.g., after a nephrectomy performed in a clear cell carcinoma of the kidney [2, 13], especially in cases of primary foci of a low clinical grade (15). The literature also provides clinical descriptions of metastases to the thyroid gland occurring in patients with other cancers such as cancer of the prostate, pancreas, uterus, ovaries, and melanoma [5, 8, 14–19, 24, 25].

Sporadic reports published to date and based on a scant material have prompted the present authors to describe and sum up their experience in treating metastatic disease involving the thyroid gland based on the analysis of their clinical material consisting of patients operated on in a single center over a period of the past 20 years.

## Materials and methods

In the years 1984–2003, at the Third Chair of General Surgery and subsequently in the Department of Endocrine Surgery, Collegium Medicum, Jagiellonian University, Cracow, 10,057 patients with various types of goiter were treated surgically. In this number, 812 individuals (8.1%) were diagnosed as malignant tumors of the thyroid gland. In this group, 17 patients (2.09%, and at the same time 0.17% of all the surgical patients) presented with metastatic tumors of the thyroid. Those patients were identified by search of a clinical register of thyroid malignancy, which has been run in the department since 1984. The material was further analyzed retrospectively including patients' demographic data, history of the disease including symptoms, extent of goiter surgery, postoperative examination of paraffin-embedded post-strumectomy sections, follow-up time, disease-free survival, and recurrence rate. The group included four men and 13 women, with the male to female

ratio of 1:4.25. The age of the patients ranged from 46 to 76 years, with the mean age amounting to  $62 \pm 9.78$  years.

## Results

In 13 patients, the primary lesion was a clear cell carcinoma of the kidney, in one breast cancer, in another one uterine carcinoma. In two patients, no primary focus location was established (Table 1). The dynamics of the disease process was diversified; in seven patients goiter had persisted for 10 years or longer, in eight, the medical history of goiter did not exceed 10 years, while in two patients, imprecise data did not allow for determining the duration of primary disease. The most common symptom reported by the patients was the sensation of pressure and increased neck circumference, in sporadic cases hoarseness and dysphagia (the latter was observed in two patients only). Eleven patients were diagnosed based on FNAB; in four individuals from this group, cytology was negative for tumor cells. In view of their serious clinical condition (rapidly progressing stridor), in two patients a decision was made to refrain from microscopic diagnostic management.

In the remaining four cases, the diagnosis of cancer was established only after postoperative examination of paraffin-embedded post-strumectomy sections. Histological results indicated poorly differentiated or anaplastic carcinomas in four patients, and clear cell cancers in the remaining 13 individuals. In the group with primary renal carcinomas, seven patients demonstrated intraoperatively a single metastatic focus, two showed multiple foci and one a concomitant tumor involving the left thyroid lobe and a metastatic lesion of the submandibular gland. The remaining three patients manifested extensive infiltrations of the thyroid gland. In one of these cases, a clear cell cancer involving one thyroid lobe occurred concomitantly with a primary focus of a papillary microcarcinoma situated in the contralateral lobe.

All the patients were treated surgically. In view of the more than a 20-year period covered by the presented retrospective analysis of patients operated on due to metastatic lesions of the thyroid, the surgical strategy used at that time changed. The principle underlying the surgical treatment of thyroid tumors is a total extracapsular thyroidectomy. A positive FNAB result combined with intraoperative histology of the tumor structure constitutes an indication for a total thyroidectomy. In the present material, such a procedure was performed in seven patients.

Of the remaining individuals, in view of the absence of firm signs indicating malignant character of the tumors, as assessed by intraoperative examination of frozen materials, four patients were subjected to total lobectomies with subtotal lobectomies on the contralateral side, while in

another three cases bilateral subtotal lobectomies were done. In two cases, taking into consideration the high clinical grade of the tumors with concomitant stridor and dysphagia developing shortly before the surgery, the procedures were palliative and were combined with tracheostomies. In another patient, in view of the massive involvement of the adjacent cervical structures, cytoreduction was used to reduce tumor mass and was combined with a tracheostomy.

Post-strumectomy complications were observed in two patients and were represented by unilateral transient paralysis of the recurrent laryngeal nerve and transient hypoparathyroidism, respectively. No perioperative mortality was noted.

Two patients received renal replacement therapy: one due to terminal right kidney failure after a left nephrectomy performed 16 years before, rapidly progressing nephropathy and signs of nephrotic syndrome persisting for 1 year, and another after a bilateral nephrectomy due to a clear cell renal cancer (the two nephrectomy procedures were performed 15 years apart).

Only 11 patients were consistently followed up after the surgery; this number constituted less than 65% of all the presented cases. No data whatsoever were available on three patients. Twice a year a telephone interview was kept with three other patients who lived far away from the hospital. Received dates contained information about general health condition or time and reason of death. Of the 11 followed-up individuals, seven are still alive, including five patients with metastases of renal carcinomas, but without recurrent disease. Five patients died due to disseminated neoplastic disease. The mean follow-up time after thyroid surgery was 3.9 years. The longest follow-up survival time was 11 years.

## Discussion

The thyroid gland is a rare site of secondary metastatic foci. Metastatic disease involving the thyroid is observed in the elderly individuals in their sixth and seventh decades of life. In the presently analyzed group of patients, the mean age was 62 years, being thus similar to that presented in the literature (15). Only in one case was the age of a female patient below 50 years. From a clinical point of view, as in the initial phase of primary tumors of the thyroid, metastatic tumors may present with scant symptoms, and the absence of firm local manifestations and documented neoplastic disease in medical history may at first lead to an erroneous diagnosis. In rare instances when the disease develops rapidly, metastases may be concurrent with local tumor growth manifested by hoarseness, dysphagia, or respiratory problems.

In the investigated group, only two patients did present with dysphagia combined with hoarseness. Intraoperatively, these individuals demonstrated high-stage local lesions with compression of the trachea, infiltration of the recurrent laryngeal nerve and adjacent tissues. Postoperative histology confirmed the clinical diagnosis of anaplastic carcinoma. In the remaining patients, the primary focus was detected in the course of a physical examination combined with an ultrasound of the neck. In a female patient, suspicion was raised as to the metastatic lesion originating from a primary tumor of the reproductive organs, while in two other patients, it was impossible to determine the site of the primary focus, and the diagnosis of a secondary thyroid tumor was established based on histopathology of the surgical specimen.

There is no complete agreement as to which cancers most frequently metastasize to the thyroid. Based on the analysis of the literature and their materials, the authors postulate that one of the most common cancers that metastasizes to the thyroid [2, 8, 9, 23] is clear cell cancer of the kidney, which was observed in as many as 13 (78%) of 17 patients in the present series. The literature reports synchronic metastases of clear cell cancer of the kidney as occurring in as many as 25% of cases (3). Metachronic metastases may develop after diversified latency periods after the occurrence of a primary focus in the kidney. Isolated metastases account for 1–4% of cases; of this percentage, 1% involves the thyroid (15).

In the present material, the latency period ranged between 2 and 17 years, with the mean time of 8.9 years. In view of the low dynamics of the neoplastic process and long latency period, such metastases may be detected by microscopic examinations of a surgically excised multinodular goiter or in less frequent instances, accidentally in the course of screening ultrasonography followed by cytology of material collected by FNAB. Multinodular goiter markedly hinders FNAB, leading to a decreased diagnostic accuracy of the procedure. In such a situation, the selection of a thyroid nodule to be biopsied is aided by a USG Power-Doppler evaluation of the vasculature. A neoplastic process is indicated by the presence of a vascular network within the nodule.

In the present material, goiter persisting for at least 5 years was noted in six patients. A prolonged history of thyroid enlargement or a highly dynamic goiter growth pattern leading to clinical signs starting from hoarseness through respiratory problems and ending with stridor were factors that necessitated the referral of the patient to surgical treatment. In 11 patients, the history of goiter was shorter than 1 year, and the metastatic lesion in the thyroid was detected “accidentally” in the course of a physical examination or ultrasonography. Renal cancer metastases, most commonly metachronic in character, are large in size

**Table 1** Clinical data of patients with metastatic involvement of the thyroid [patient outcome based on clinical presentation (follow-up in years)]

No.	No. of hist-path specimens	Sex	Age	Site of primary lesion	Year of surgery	Type of primary surgery	Interval between procedures (years)	Extent of metastatic thyroid gland involvement	Type of secondary thyroid surgery	Postoperative follow-up (years)	Survival
1	649/85	F	59	Kidney	1968	Left nephrectomy	17	Bilateral, multifocal masses	S	No data available	D-DDD
2	749/93	F	50	Kidney	1988	Right nephrectomy	5	Right lobe, solitary mass	S	11	A-NED
3	406/95	F	69	Kidney	1989	Right nephrectomy	6	Left lobe, solitary mass	TT	9	A-NED
4	2278/95	F	68	Kidney	1988	Left nephrectomy	7	Right lobe, solitary mass	TS	No data available	D-DDD
5	123/96	F	56	Kidney	1987	Right nephrectomy	9	Right lobe, solitary mass	S	No data available	No data available
6	496/97	F	46	Unknown		Not operated on	–	Left lobe, solitary mass	S	7	A-NED
7	1045/97	F	65	Reproductive organ (?)	1984	Hysterectomy	13	Multifocal masses	TT	1	D-DDD
8	560/98	M	54	Kidney	1982	Left nephrectomy	16	Bilateral, multifocal masses + papillary microca right lobe	TT	No data available	No data available
9	580/98	M	62	Kidney	1986 and 1997	Bilateral nephrectomy	12	Bilateral, multifocal masses	TT	6	D-DDD died in 2004
10	137/00	M	68	Kidney	1984	Right nephrectomy	16	Widespread masses; not specified	Palliative T	1	D-DDD died in 2000
11	806/00	F	72	Kidney	1998	Left nephrectomy	2	Right lobe, solitary mass	TS	4	A-NED
12	1822/01	M	77	Kidney	1994	Right nephrectomy	7	Widespread masses; not specified	cytoreduction + tracheostomy	1	D-DDD died in 2002
13	1875/02	F	71	Kidney	1990	Right nephrectomy	12	Right lobe, solitary mass	TS	No data available	No data available
14	1296/03	F	50	Kidney	1997	Left nephrectomy	6	Left lobe, solitary mass + left suprmandibular glandule	TT	2	A-NED

15	1649/03	F	75	Unknown	Not operated on	-	Widespread masses; not specified	Palliative TS + tracheostomy	1	D-DDD
16	2759/03	F	50	Breast	Left mastectomy	10	Multifocal masses	TT + lymphangiectomy	2	A-NED
17	2796/03	F	69	Kidney	Left nephrectomy	8	Left lobe, solitary mass	TT	No data available	A-NED

*D* dead, *A* alive, *DDD* dead with disseminated disease, *NED* no evidence of disease, *TT* total thyroidectomy, *TS* subtotal resection one lobe and total resection the second lobe, *S* subtotal thyroidectomy

(3–8 cm in diameter), which is what markedly facilitates their detection in the course of a routine physical examination. The foci detected by ultrasound were much smaller and the patients often did not report any complaints.

In such cases, the role of FNAB is very important in view of the fact that as a rule, only a single cold nodule is present in the thyroid gland. The value of FNAB in the diagnostic management of thyroid lesions is also emphasized by other authors [2, 8, 12, 26]. In the present material, only in four cases was the FNAB result negative and the diagnosis was established by postoperative histology only. In view of the highly advanced neoplastic process resulting in stridor, in two patients fine needle aspiration biopsy was not performed so as not to delay surgical treatment.

Preoperative diagnostic management should also include other organs in view of the possibility of the synchronous occurrence of renal cancer metastases. Similarly, as in the case reported in the literature, the present authors also noted in one woman a simultaneous metastasis to the submandibular gland, and the lesion was excised during the thyroidectomy [2].

The excision of secondary metastatic lesions in patients with clear cell renal cancer, including the lesions that are situated in the thyroid gland, improves late results of cancer treatment, and the latency period between the primary procedure and the diagnosis of a metastatic lesion may extend over many years. The postoperative follow-up duration is also diversified. In our material, the follow-up was 11 years. The mean survival time of all the patients included in the follow-up was 3.9 years, thus being similar to values reported in the literature [23, 27].

The management and the extent of surgery in metastatic involvement of the thyroid gland have not been firmly determined by a uniform international consensus. In view of the fact that in clear cell cancers of the kidney usually a single metastatic focus is encountered in the thyroid, the majority of authors recommend a lobectomy combined with an isthmectomy [8, 20–22]. Although there are no direct data based on comparative studies, which would prove the thesis that surgical excision of a clear cell renal cancer metastasizing to the thyroid prolongs the survival of the affected individuals, yet such a management policy has been accepted by some endocrinological surgeons.

In turn, in view of the common co-occurrence of thyroid lesions of the nodular proliferative type, the possibility of a multifocal metastatic lesion development and concomitant primary thyroid cancer, a total thyroidectomy seems to be necessary. A lobectomy and total thyroidectomy produce comparable oncological benefits [8], yet in the opinion of many authors, in such cases—similarly as in primary cancer of the thyroid gland—one should strive for a total thyroidectomy. Such a management policy is justified when the structure of a metastatic tumor in the thyroid has been

preoperatively confirmed by FNAB and when multiple metastatic lesions or a concomitant primary thyroid cancer is suspected.

In the presented material, positive preoperative cytology (FNAB) in seven patients was correlated with a postoperative diagnosis of metastatic lesions of the thyroid. However, it should be borne in mind that a firm diagnosis of metastatic clear cell cancer of the kidney involving the thyroid may be established solely based on histology of paraffin-embedded sections, as even an intraoperative examination does not fully guarantee an appropriate diagnosis in view of the numerous architectural similarities to various histological forms of primary thyroid tumors. Adenomas arising from “clear” cells that contain at least 75% of such cells in their mass are characterized by the fact that classic hematoxylin-eosin staining results in visualization of clear, empty spaces in their cytoplasm, which may correspond to deposits of glycogen, lipids, thyroglobulin, or mucus (15).

Thus, it is histology combined with precise clinical data that constitutes the appropriate basis for diagnosing metastatic tumors of the thyroid. Such management policy also allows for a safe postoperative levothyroxine substitution. Of importance here is also the possibility of metastases to the cervical lymph nodes, which were detected in one of post-thyroidectomy patients in the present series. On the other hand, when the diagnosis is established postoperatively only and based on histopathology of surgical specimens, striving at all costs for a secondary, radical procedure that would follow the previously performed subtotal thyroidectomy seems unwarranted. In the present material, in four patients, no confirmation was obtained by preoperative FNAB as to the tumor structure and hence the performed procedures were bilateral subtotal lobectomies.

Doubts are raised, however, when selecting a surgical method in patients with inoperable thyroid tumors due to the high clinical stage of the neoplastic process. In such cases, providing ventilatory support combined with an attempt at decreasing the tumor mass seems to be justified. In view of the absence of randomized prospective studies that would compare various treatment modalities, the selection of a management method in metastatic lesions of the thyroid gland is difficult and continues to depend on the experience of the surgeon and preferences of the center of thyroid cancer surgery. However, it should be emphasized that in all clinically and ultrasonographically confirmed cases of mostly isolated nodular lesions of the thyroid, one should absolutely strive for performing a fine needle aspiration biopsy. When combined with data on the past neoplastic disease, the procedure allows for establishing an exact final diagnosis. The detection of metastases to the thyroid gland is tantamount to a poorer prognosis, but still the prolonged, free-from-local-recurrent-disease survival of

patients may favor aggressive surgery as a method recommended in metastases of various cancer types to the thyroid gland.

## Conclusions

1. The most commonly clinically detected and surgically treated metastatic lesion of the thyroid gland is clear cell cancer of the kidney. The possibility of such a lesion should be borne in mind even a long time after a nephrectomy performed due to a clear cell renal cancer.
2. Excision of secondary metastatic lesions in the thyroid in patients with clear cell cancer of the kidney improves late therapeutic results. The latency time between the primary surgery and the diagnosis of a metastasis may extend over many years and its duration does not affect further prognosis.

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