



Management of metastases to the thyroid gland

Aleksander Konturek[^], Marcin Barczyński[^]

Department of Endocrine Surgery, Third Chair of General Surgery, Jagiellonian University Medical College, Kraków, Poland

Contributions: (I) Conception and design: A Konturek; (II) Administrative support: A Konturek; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: A Konturek; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Aleksander Konturek, MD, PhD. Department of Endocrine Surgery, Third Department of General Surgery, Jagiellonian University Medical College, 37 Prądnicka Street, 31-202 Kraków, Poland. Email: okont@mp.pl.

Abstract: The thyroid gland is rarely the site of metastatic disease because the vascularization, high oxygenation and high iodine of arterial blood content in the thyroid gland inhibit the growth of cancer cells. The incidence of the metastases depends on the type of primary tumor. Metastases to the thyroid gland account for 1.5–3% (approximately 2%) of all malignancies, with their autopsy-confirmed incidence rate ranging from 1.25% to 24.2%. Clinical material predominantly demonstrates metachronous metastases of clear cell carcinoma of the kidney, autopsy results show a predominance of metastases of the lung, colon and breast cancers. Metastases to the thyroid gland are most commonly unifocal metachronous tumors. Multifocal synchronous tumors are associated with a considerably poorer prognosis. The diagnostic method of choice is ultrasound-guided fine needle aspiration biopsy (FNAB) combined with immunohistochemically tests. Total thyroidectomy allows for a thorough evaluation of local tumor grade and is an important factor in oncological radicality of the surgical procedure. The role of multidisciplinary team is essential because balancing between the features of the primary tumor, status of the health (patient's comorbidities), age of the patient, clinical grade, histological structure and profile of metastases at the time of diagnosis are important factors influencing individualized survival rate.

Keywords: Metastases to thyroid gland; surgical management; thyroidectomy

Received: 31 May 2020; Accepted: 24 August 2020; Published: 30 September 2020.

doi: 10.21037/aot-20-46

View this article at: <http://dx.doi.org/10.21037/aot-20-46>

Introduction

Documented metastases of testicular cancer and posterior pharynx wall cancer to the thyroid gland demonstrating lesions resulting from multinodular goiter were described for the first time by Rudolf Virchow in 1871 in a 53-year old male and a 65-year old female. Metastases to the thyroid gland, despite its rich vasculature, are relatively rare. Most commonly they represent distant metastases spreading along blood vessels from other organs (the lung, mammary gland, colon, stomach, pancreas or ovary). Sporadically, apart from the phenomenon of infiltration itself, they may be a

consequence of metastasizing tumors involving neighboring organs, such as the pharynx, larynx, trachea or esophagus in patients with squamous cell carcinomas. Metastases from a primary tumor involving another organ to already existing lesions in the thyroid gland, e.g., to adenomas (tumor to tumor metastasis) are also highly uncommon. As it has been mentioned, in spite of rich vasculature, a metastatic focus rarely develops in the thyroid gland. As demonstrated by data from the literature on the subject, metastases to the thyroid gland account for 1.5–3% (approximately 2%) of all malignancies, with their autopsy-confirmed incidence rate ranging from 1.25% to 24.2%, being related both to blood-

[^] Aleksander Konturek ORCID: 0000-0001-8103-4082; Marcin Barczyński ORCID: 0000-0001-6062-1851.

associated cancer spread from a distant focus and the aforementioned thyroid invasion by a neighboring neoplastic process. It is difficult to unambiguously determine the pathophysiological foundations of the phenomenon; nevertheless, among the oldest hypotheses, two are stressed in particular:

- ❖ In view of the markedly high blood flow rate within the thyroid (in euthyrosis, the average rate is approximately 8 mL/100 g of tissue/sec., thus, the thyroid gland is one of the human organs with the best blood supply), cancer cells lose their adherence ability and ability to be subsequently implanted in the parenchyma of the gland;
- ❖ High oxygenation of arterial blood and high iodine content in the thyroid gland additionally inhibit the growth of cancer cells (1-8).

Clinical material predominantly demonstrates metachronous metastases of clear cell carcinoma of the kidney, which constitute a considerable majority of metastases to the thyroid gland. Only some of them are manifested by nodular lesions detected by palpation. Autopsy results show a predominance of metastases of the bronchus and mammary gland carcinomas which are rarely clinically manifested, mostly due to the rapid progress of the primary neoplastic disease. Since the decidedly most common route of neoplastic process spreading to the thyroid gland is the blood vessels, concomitant thyroid pathologies, such as multinodular lesions, isolated adenomas and thyroid fibrosis may constitute factors predisposing to occurrence of metastases, mostly due to a decelerated blood flow and decreased partial oxygen pressure in the microcirculatory system. Metastatic lesions are detected statistically more frequently in the female population (1.4:1) in the sixth and seventh decade of life. Metachronous metastases are most commonly single lesions (76%), but unfortunately they are very often concomitant with other primary focus metastases to other locations in the organism (79%) (9-12).

Diagnosis

Metastatic lesions to the thyroid gland may be preliminarily diagnosed based on conscientiously taken medical history aiming at obtaining information on past neoplastic diseases or current anti-cancer treatment. The majority of nodular lesions within the thyroid gland, especially when small in size, do not produce clinical symptoms, and detecting the focus is often incidental, happening in the course of routine

ultrasonography in diagnostic examinations of the cervical vessels or ultrasound breast examination. Enlarged neck circumference with signs of constriction, a fast growing unilateral tumor, symptoms of hoarseness, problems with swallowing and breathing represent late symptoms of thyroid diseases, most commonly associated with a poor prognosis. Nevertheless, such symptoms do not differ from the basic clinical picture illustrating primary lesions involving the gland. At times one may observe changes in hormonal activity of the thyroid, however, they are non-specific and may occur without concomitant alteration in the morphology of the gland. Usually a metastatic lesion of the thyroid is detected following the detection of a primary focus in another organ at various time intervals after primary surgical treatment (from 2.4 to 25 years). According to data presented in the literature on the subject, metachronous metastases predominate over synchronous lesions (metachronous/synchronous =2:1) (13-16).

Development of modern diagnostic imaging methods has decidedly affected the improvement of quality and accuracy of preliminary diagnoses. The method of choice is ultrasonography combined with fine needle aspiration biopsy (FNAB). Metastatic lesions are not characterized by their differing in ultrasonographic images from primary lesions of the thyroid gland, hence such symptoms as solid structure, blurred tumor outline, uneven shape, hypoechogenicity and microcalcifications may raise suspicions of neoplastic lesions. In case of isolated lesions in the thyroid gland, the sensitivity and specificity of the above imaging method are high and the positive and negative predictive values are 89% and 93%, respectively. The presence of nodular goiter markedly decreases ultrasound diagnostic accuracy; in such a situation, while selecting the biopsy site, of assistance may be evaluation of vasculature using Power-Doppler USG as well as the technique termed elastography. In case of metastases to the thyroid the use of molecular and immunohistochemical methods may be of a considerable help in differentiating between metastatic lesions and primary thyroid tumors. Of immunohistochemical tests employed in diagnostic management of lesions situated in the thyroid gland, one should emphasize: the first-line tests aiming at determining the theoretical primary origins of carcinomas of unknown primary sites based on staining for CK7/CK20: breast (CK7+/CK20-), colon (CK7-/CK20+/-), renal (CK7-/CK20-), prostate (CK7+/CK20-), hepatic (CK7-/CK20-), adrenal gland (CK7-/CK20-) and next step are separate specific markers:

- (I) Renal cancer (renal cell carcinoma): CD10+, PAX8+, Vimentin+, pVHL+, RCCMa+, Inhibin-, TTF1-, CEA-;
- (II) Colon cancer: SATB2+, CDH17+, TFF3+/-, Calretinin+/-, CDX2-/+ , CDX2: positive in 90–100% of colon adenocarcinoma cancer's,
 - i. 80% small intestine cancer's: CDX2+, CDH17+, Villin+/-, MUC5AC+/-;
 - ii. 70% of gastric cancer: CEA+, CDX2-/+ , MUC1-/+ , MUC5AC-/+ , CDH17+/-, TTF1-;
- (III) Breast cancer: ER+/PgR+, GATA3+, GCDFP15-/+ , MGB+/-, TTF1-;
- (IV) Lung cancer (mucinous): TTF1-/+ , CK7-/+ , CDX2-/+ , CK19 (subtype CYFRA21.1);
- (V) Pancreatic cancer: Maspin A+, S100P+, IMP-3+, pVHL-, SMAD4-/+ , MUC5AC+, CDX2-/+ ;
- (VI) Oesophagus cancer: CEA+, MUC5AC+/-, CDH17+, MUC1-/+ , CDX2-/+ ;
- (VII) Adrenocortical cancer's: Melan A+, Calretinin+, Inhibin A+, Synaptophysin+, Chromogranin-, CEA-.

Specific markers for thyroid cancers: PTC/FTC (papillary/follicular thyroid cancer): Thyroglobulin+, TTF1+ (and Napsin A for undifferentiated thyroid carcinomas); PAX8+ and for the medullary thyroid cancer: Calcitonin+, TTF1+, CEA+.

The BRAF V600E oncogene is an integral component of the kinase pathway and is present in: leukemia (58.33%); papillary thyroid carcinoma (56.55%), cutaneous melanoma and other localizations of melanoma (20.38%); colorectal adenocarcinoma (7.32%) and lung adenocarcinoma (17–28).

Despite progress in the field of cytological diagnostic management, the method continues to have limitations. After autoimmune inflammatory processes poorly differentiated and anaplastic thyroid tumors or lymphomas may pose considerable difficulties in differentiating between high grade metastases to the thyroid and primary tumors of the gland. Thus the selection of an enhanced diagnosis method (core needle biopsy, open biopsy of the thyroid gland) depends on the experience of the center and decision of the multi-specialist team, while patients subjected to non-diagnostic thin needle aspiration biopsy (FNAB) of lesions with high suspicion of malignancy should be always referred to urgent surgical treatment as only such a management procedure allows for determining proper diagnosis and choosing the best method of further therapy. The basis of treatment should be suspicion of metastatic lesions rather than the very fact of their occurrence (6–28).

Surgical treatment—management strategy

Metastases of a primary neoplastic focus to distant organs always raise considerable fears and deteriorate the prognosis. When detected intravitaly, synchronous and metachronous metastases of other tumors to the thyroid gland necessitate undertaking specific diagnostic and therapeutic activities. In spite of their rare incidence, in view of the specific structure of the thyroid gland, they constitute a problem and a therapeutic challenge. From the viewpoint of the patient the most important objective of all therapeutic modalities, including surgical treatment, is prevention of relapse. Such a standpoint renders a surgical procedure to be a step in therapy that should take into consideration the stage of the disease, thus reflecting the balance between the local and general state of the patient, showing possibilities and extent of surgical treatment; it should also evaluate quality of life as a significant factor of probability of surgical success.

In spite of the number of reported cases of distant metastases to the thyroid gland continuously increasing, there is no fully agreed upon and unambiguous consensus as to the management strategy and surgical treatment of metastatic tumors.

While analyzing the literature on the subject, one notes that the most common metastatic focus in the thyroid gland is single focus clear cell carcinoma of the kidney. All the authors agree that the extent of the surgical procedure should ensure oncological radicality, nevertheless, some recommend unilateral lobectomy and isthmectomy only, while others are in favor of total thyroidectomy. Although there is no unambiguous direct evidence supporting the idea that resection of a metastatic focus of carcinoma of the kidney from the thyroid gland is a contributory factor in prolonging survival time, such a management modality is fully accepted by surgeons. The continuing discussion addressing the extent of the procedure favors the solution accepted by the majority of authors showing the supremacy of total thyroidectomy over hemithyroidectomy (a decreased recurrence rate in the group of patients after total thyroid resection as compared to lobectomy =13% *vs.* 4.8%, $P < 0.005$). Concomitant nodular goiter, a possibility of multinodular metastasis or concomitant primary carcinoma of the thyroid gland speak for the necessity of performing total thyroid resection. This allows not only for a thorough evaluation of the local stage of the tumor, but also constitutes an important factor in oncological radicality of the procedure, especially in the case of patients with other multiple metastases of clear cell carcinoma of the kidney

to other organs (e.g., the pancreas). Total thyroidectomy may trigger an injury of the recurrent laryngeal nerves and hypoparathyroidism, nevertheless, the incidence rate of such complications in reference centers is low and comparable to that observed in thyroid surgery performed for other indications. A simultaneous involvement of the cervical lymph nodes in case of metastases to the thyroid is rare and this is why preventive lymph node resection is not recommended. However, the presence of the nodes should be always evaluated in preoperative examinations (US, angio-CT). In case metastases are present in the lymph nodes, lymphadenectomy should be performed taking into consideration the location of lesions in particular lateral and central compartments of the neck. A local high grade of the tumor that infiltrates the neighboring structures, what indicates that the lesion is non-operative, requires ensuring patency of the respiratory tract and possible respiratory support with an attempt at decreasing the tumor mass. In such cases, planning permanent tracheostomy is warranted. In view of the absence of thyroid iodine uptake of distant metastases to the gland, this treatment modality cannot be employed. Other alternative therapeutic methods (radiotherapy, chemotherapy) are of a low applicability due to lack of proven effectiveness of such modalities.

Thus, the selection of the therapeutic method continues to depend on the experience of the center and the surgeon, while prolonged survival of patients without local carcinoma recurrence may be an argument for the advantage of surgical treatment. In case of carcinomas other than clear cell carcinoma of the kidney metastasizing to the thyroid gland, a decisive role in the therapeutic success is fulfilled by grade of primary disease. Multiorgan resections decrease the percentage of local recurrent disease without increasing the survival time (18,29-33).

Non-surgical treatment

As it has been repeatedly mentioned, metastases to the thyroid gland are most commonly of a metachronous character and it is the stage of the primary disease that constitutes a decisive factor in therapeutic success. Synchronous metastases reflect the generalized stage of the disease and pronouncedly worsen the prognosis. Surgical treatment of a palliative character should be always considered in view of the time of survival with respect to comorbidities, as well as location and number of metastases. Thus, chemotherapy may be the treatment of choice in the group of patients with extensive distant metastases.

In case of breast cancer with numerous metastases to other organs or in the group with a very high surgical risk, positive effects have been achieved when systemic treatment has been introduced (adjuvant chemotherapy, hormonotherapy, immunotherapy, radiotherapy) in keeping with the international recommendations addressing high-stage breast cancer (taxane, anthracycline or with in resistant tumors - capecitabine, vinorelbine or eribulin are the preferred choices), while in case of HER-2 positivity, chemotherapy is based on trastuzumab and pertuzumab, and for HER-2 negative tumors—on bevacizumab. Pensabene *et al.* demonstrated in their report a positive effect of chemotherapy on intrathyroid metastatic foci, at the same time recommending the above therapy in cases of distant synchronous metastases, thus eliminating the need of thyroidectomy. It should be mentioned, however, that in the group of patients with multiple metastases to other organs and concomitant pressure signs, tumor cytoreduction combined with permanent tracheostomy are performed in order to eliminate total airway obstruction or prior to planned local radiotherapy (34-36).

In the course of colorectal cancer metastases to the thyroid, the customary treatment modality accepted by numerous centers is thyroidectomy that is particularly justified in the afore-mentioned airway compression. Nevertheless, when the primary disease promptly progresses, recommendations for surgical treatment are controversial and the prognosis is poor. Radioiodine therapy is not justified in view of no iodine uptake by metastases, while local radiotherapy should be considered in combination with chemotherapy. Positive effects have been noted in first-line treatment employing oxaliplatin and/or capecitabine in monotherapy or combined with a surgical procedure and/or radiotherapy in selected patients with metastases to the thyroid gland (37). No data that would recommend aggressive chemotherapy have been found in the literature on the subject, nevertheless, the average survival time of patients subjected to combination therapy was longer and the use of targeted immunotherapy (cetuximab; bevacizumab) increased the effectiveness of therapy in metastatic tumors (38,39).

Prognostic factors and prognosis

Negative prognostic factors in metastatic thyroid tumors:

- ❖ Age >70 years of life,
- ❖ High grade and high aggressiveness (high mitotic activity) of the primary focus,

- ❖ Synchronicity of carcinomatous lesions metastasizing from a primary focus to other organs,
- ❖ Multifocality of metastatic thyroid lesions,
- ❖ Local grade with infiltration of surrounding structures,
- ❖ Regional grade (lymph node involvement),
- ❖ Non-radical surgical treatment,
- ❖ Rapid development in medical history and rapid growth of metastatic focus.

Prognosis

Metastatic foci are accompanied by synchronous multiorgan foci in 35–80% (an unfavorable prognostic factor).

- ❖ Clear cell carcinoma of the kidney: in 20% of cases—synchronous tumors; in 80% of cases—metachronous tumors (in 30% of cases they develop within 5 initial years); general 5-year survival rate of approximately 51%, long-term remission in case of an isolated metachronous tumor long after surgical procedure performed in the primary focus (40–43).
- ❖ Non-small cell lung cancer: poor prognosis, in case of high-grade primary foci no cases of 5-year survival are noted, average survival time of 5–27 months (44,45).
- ❖ Breast cancer: in 5–10% of cases, the prognosis is generally poor (depending on the size of the primary focus and histological structure of carcinoma), especially in the course of aggressive primary focus (neoplastic emboli with thyroiditis), average survival time depends on primary focus grade: 5-year survival—single cases (34,46,47).
- ❖ Colon cancer: poor prognosis, 50% survival rate after 1 year (48–52).
- ❖ Melanoma: prognosis depends on treatment and grade of the primary focus, as well as on presence of synchronous metastases to the lymph nodes and other organs (53,54).

Summary

- (I) The most common malignant tumor metastasizing to the thyroid gland as confirmed by autopsy is lung cancer. The most common intravital (clinically) detected and surgically treated metastatic thyroid carcinoma is clear cell carcinoma of the kidney. Further places on the list of most frequent thyroid

- tumors are occupied by gastro-intestinal cancer (colon, gastric and pancreas cancers), breast cancer, laryngeal, pharyngeal, lung cancer, and melanoma.
- (II) Metastases to the thyroid gland are most commonly unifocal metachronous tumors. Multifocal synchronous tumors are associated with a considerably poorer prognosis.
- (III) The diagnostic method of choice is ultrasound-guided fine needle aspiration biopsy (FNAB) combined with immunohistochemical tests. Evaluation of local grade may be extended to include additional imaging examinations.
- (IV) Total thyroidectomy allows for a thorough evaluation of local tumor grade and is an important factor in oncological radicality of the surgical procedure, especially in case of concomitant multinodular goiter, suspected multifocal character of metastases and suspected primary thyroid carcinoma, but it does not affect survival time.
- (V) Prognosis depends on the age of the patient, clinical grade, histological structure and profile of metastases at the time of diagnosis. It also depends on time, number of metastatic foci and their location (multiorgan metastases).
- (VI) A careful balancing of mentioned factors and multidisciplinary discussion should determine individualized treatment approach (55).

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Thyroid* for the series “Recent Challenges in the Management of Thyroid Tumors”. The article has undergone external peer review.

Peer Review File: Available at <http://dx.doi.org/10.21037/aot-20-46>

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/aot-20-46>). The series “Recent Challenges in the Management of Thyroid Tumors” was commissioned by the editorial office without any funding or sponsorship. MB served as the unpaid Guest Editor of the series and

serves as an unpaid editorial board member of *Annals of Thyroid* from Oct 2019 to Sep 2021. AK serves as an unpaid editorial board member of *Annals of Thyroid* from Aug 2019 to Jul 2021. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

- Willis RA. Metastatic tumours in the thyroid gland. *Am J Pathol* 1931;7:187-208.
- Virchow R. Pathologie des Tumeurs. Aronsohn's French translation, 1871, 2, 283, 3243.
- Chung AY, Tran TB, Brumund KT, et al. Metastases to the Thyroid: A Review of the Literature From the Last Decade. *Thyroid* 2012;22:258-68.
- Nixon IJ, Coca-Pelaz A, Kaleva AI. Metastasis to the Thyroid Gland: A Critical Review. *Ann Surg Oncol* 2017;24:1533-9.
- Moghaddam PA, Cornejo KM, Khan A. Metastatic Carcinoma to the Thyroid Gland: A Single Institution 20-year Experience and Review of the Literature. *Endocr Pathol* 2013;24:116-24.
- Yumoto S, Baba Y, Nomoto D, et al. Thyroid metastasis from esophageal adenocarcinoma: a case report and literature review. *Surg Case Rep* 2019;5:137.
- Berge T, Lundberg S. Cancer in Malmö 1958-1969. An autopsy study. *Acta Pathol Microbiol Scand Suppl* 1977;(260):1-235.
- Brzozowski T. Fizjologia człowieka. Konturek. Edra Urban & Partner. 2019.
- Hegerova L, Griebeler ML, Reynolds JP, et al. Metastasis to the Thyroid Gland: Report of a Large Series From the Mayo Clinic. *Am J Clin Oncol* 2015;38:338-42.
- Surov A, Machens A, Holzhausen HJ, et al. Radiological Features of Metastases to the Thyroid. *Acta Radiol* 2016;57:444-50.
- Cichoń S, Anielski R, Konturek A, et al. Metastases to the thyroid gland: seventeen cases operated on in a single clinical center. *Langenbecks Arch Surg* 2006;391:581-7.
- Stasiak M, Michalak R, Lewinski A. Thyroid primary and metastatic malignant tumours of poor prognosis may mimic subacute thyroiditis - time to change the diagnostic criteria: case reports and a review of the literature. *BMC Endocr Disord* 2019;19:86.
- Papi G, Fadda G, Corsello SM, et al. Metastases to the Thyroid Gland: Prevalence, Clinicopathological Aspects and Prognosis: A 10-year Experience. *Clin Endocrinol (Oxf)* 2007;66:565-71.
- Can AS, Köksal G. Thyroid metastasis from small cell lung carcinoma: a casereport and review of the literature. *J Med Case Rep* 2015;9:231-4.
- Straccia P, Mosseri C, Brunelli C, et al. Diagnosis and Treatment of Metastases to the Thyroid Gland: A Meta-Analysis. *Endocr Pathol* 2017;28:112-20.
- Miyakawa M, Sato K, Hasegawa M, et al. Severe thyrotoxicosis induced by thyroid metastasis of lung adenocarcinoma: a case report and review of the literature. *Thyroid* 2001;11:883-8.
- Kim TY, Kim WB, Gong G, et al. Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. *Clin Endocrinol (Oxf)* 2005;62:236-41.
- Chen H, Nicol TL, Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland. *World J Surg* 1999;23:177-80.
- Zafar I, Buzad F, Weir E. Colon Cancer Metastatic to the Thyroid Gland in the Setting of Pathologically Diagnosed Papillary Thyroid Cancer: A Review and Report of a Case. *Cureus* 2020;12:e7314.
- Pusztaszeri M, Wang H, Cibas ES, et al. Fine-needle aspiration biopsy of secondary neoplasms of the thyroid gland: a multi-institutional study of 62 cases. *Cancer Cytopathol* 2015;123:19-29.
- Aron M, Kapila K, Verma K. Role of Fine-Needle Aspiration Cytology in the Diagnosis of Secondary Tumors of the Thyroid--Twenty Years' Experience. *Diagn Cytopathol* 2006;34:240-5.
- Falcone R, Ramundo V, Lamartina L, et al. Sonographic Presentation of Metastases to the Thyroid Gland: A Case Series. *J Endocr Soc* 2018;2:855-9.
- Liu H, Lin F. Application of immunohistochemistry in thyroid pathology. *Arch Pathol Lab Med* 2015;139:67-82.

24. Chernock RD. Immunohistochemistry of thyroid gland carcinomas: clinical utility and diagnostic pitfalls. *Diagnostic Histopathology* 2016;5:184-90.
25. Kawamoto H, Kaneko Y, Ryu K, et al. Thyroid metastasis from lung adenocarcinoma with EML4-ALK rearrangement. *BMJ Case Rep* 2016;2016:bcr2016217541.
26. Selves J, Long-Mira E, Mathieu MC, et al: Immunohistochemistry for Diagnosis of Metastatic Carcinomas of Unknown Primary Site. *Cancers* 2018;10:108-31.
27. The AACR Project GENIE Consortium. AACR Project GENIE: powering precision medicine through an international consortium. *Cancer Discovery* 2017;7:818-31.
28. Nakano K, Yamamoto H, Fujiwara M et al. Clinicopathologic and Molecular Characteristics of Synchronous Colorectal Carcinoma With Mismatch Repair Deficiency. *Am J Surg Pathol* 2018;42:172-82.
29. Hurlimann J, Gardiol D, Scazziga B. Immunohistology of anaplastic thyroid carcinoma. A study of 43 cases. *Histopathology* 1987;11:567-80.
30. Lin JD, Weng HF, Ho YS. Clinical and pathological characteristics of secondary thyroid cancer. *Thyroid* 1998;8:149-53.
31. Khaddour K, Marernych N, Ward WL, et al. Characteristics of Clear Cell Renal Cell Carcinoma Metastases to the Thyroid Gland: A Systematic Review. *World J Clin Cases* 2019;7:3474-85.
32. Russell JO, Yan K, Burkey B, et al. Metastasis to the Thyroid Gland: Case Series and Review With Observations by Primary Pathology. *Otolaryngol Head Neck Surg* 2016;155:961-8.
33. Ishikawa M, Hirano S, Tsuji T, et al. Management of metastasis to the thyroid gland. *Auris Nasus Larynx* 2011;38:426-30.
34. Zhou L, Chen L, Xu D, et al. Breast cancer metastasis to thyroid: a retrospective analysis. *Afr Health Sci* 2017;17:1035-43.
35. Cardoso F, Senkus E, Costa A, et al. 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4). *Ann Oncol* 2018;29:1634-57.
36. Pensabene M, Stanzione B, Cerillo I, et al. It is no longer the time to disregard thyroid metastases from breast cancer: a case report and review of the literature. *BMC Cancer* 2018;18:146-54.
37. Cheung WY, Brierley J, Mackay H. Treatment of rectal cancer metastases to the thyroid gland: report of two cases. *Clin Colorectal Cancer* 2008;7:280-2.
38. Mennet A, De Blasi V, Simoné G, et al. Thyroid Metastasis from Colorectal Cancer: A Case Report and Review of Literature. *Clin Med Rev Case Rep* 2016;3:141-4.
39. Froylich D, Shiloni E, Hazzan D. Metachronous colon metastasis to the thyroid: a case report and literature review. *Case Rep Surg* 2013;2013:241678.
40. Iesalnieks I, Winter H, Bareck E, et al. Thyroid metastases of renal cell carcinoma: clinical course in 45 patients undergoing surgery. Assessment of factors affecting patients' survival. *Thyroid* 2008;18:615-24.
41. Iesalnieks I, Machens A, Bures C, et al. Local recurrence in the neck and survival after thyroidectomy for metastatic renal cell carcinoma. *Ann Surg Oncol* 2015;22:1798-805.
42. Beutner U, Leowardi CH, Bork U, et al. Survival After Renal Cell Carcinoma Metastasis to the Thyroid: Single Center Experience and Systematic Review of the Literature. *Thyroid* 2015;25:314-24.
43. Jackson G, Fino N, Bitting RL. Clinical Characteristics of Patients With Renal Cell Carcinoma and Metastasis to the Thyroid Gland. *Clin Med Insights Oncol* 2017;11:1179554917743981.
44. Rossini M, Ruffini L, Ampollini L, et al. Synchronous thyroid metastasis from lung adenocarcinoma. *Ann Ital Chir.* 2015;86:560-2.
45. Salah S, Tanvetyanon T, Abbasi S. Metastectomy for Extra-Cranial Extra-Adrenal Non-Small Cell Lung Cancer Solitary Metastases: Systematic Review and Analysis of Reported Cases. *Lung Cancer* 2012;75:9-14.
46. Ghias AF, Epps G, Cottrill E, et al. Multifocal Metastatic Breast Carcinoma to the Thyroid Gland Histologically Mimicking C Cell Lesions. *Case Rep Pathol* 2019;2019:9890716.
47. Plonczak AM, DiMarco AN, Dina R, et al. Breast cancer metastases to the thyroid gland—an uncommon sentinel for diffuse metastatic disease: a case report and review of the literature. *J Med Case Reports* 2017;11:269:1-5.
48. Lièvre A, Leboulleux S, Boige V, et al. Thyroid metastases from colorectal cancer: the Institut Gustave Roussy experience. *Eur J Cancer* 2006;42:1756-9.
49. Ciriano Hernández P, Martínez Pinedo C, Calcerrada Alises E, et al. Colorectal cancer metastases to the thyroid gland: A case report. *World J Gastrointest Surg* 2020;12:116-22.
50. Mori K, Koinuma K, Nishino H, et al. Rectal cancer with a metastasis to the thyroid gland: A case report. *Int J Surg Case Rep* 2020;66:39-42.
51. Yamahara K, Moriki T, Katsura Y, et al. Surgical Treatment of a Patient with a Solitary Thyroid Metastasis from Primary Sigmoid Adenocarcinoma: A Case

- Report and Literature Review. *Case Rep Otolaryngol* 2019;2019:3208469.
52. Mori K, Koinuma K, Nishino H, et al. Rectal cancer with a metastasis to the thyroid gland: A case report. *Int J Surg Case Rep* 2020;66:39-42.
53. Kung B, Aftab S, Wood A, et al. Melanoma Metastatic to the Thyroid Gland: A Case Report and Review of the Literature. *Ear Nose Throat J* 2009;88:E7.
54. Costa MM, Belo S, Costa JC, et al. Malignant melanoma with synchronous thyroid metastases: case report and literature review. *Arch Endocrinol Metab* 2017;61:193-7.
55. Chen JY, Chen IW, Hsueh CH, et al. Synchronous diagnosis of metastatic cancer to the thyroid is associated with poor prognosis. *Endocr Pathol* 2015;26:80-6.

doi: 10.21037/aot-20-46

Cite this article as: Konturek A, Barczyński M. Management of metastases to the thyroid gland. *Ann Thyroid* 2020;5:19.