



Infiltration of the thyroid gland by non-thyroid malignancy: A literature review reveals this to be an unusual cause of hyperthyroidism



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ABSTRACT

Background: Non-thyroid malignancies that metastasize to the thyroid gland are relatively rare. At one end of the spectrum they may only be identified at the time of autopsy. At the other extreme, they may be identified during the evaluation of a progressive malignancy. Most patients who are identified as having metastases to their thyroid gland are euthyroid, but some patients may have associated hypothyroidism or hyperthyroidism. This review examines cases of hyperthyroidism associated with metastases affecting the thyroid gland.

Results: Twenty four articles describing 26 cases of malignancy-associated hyperthyroidism were identified, with the cases presenting with features suggestive of a thyroiditis and with goiter. The solid malignancies (19 cases) were mostly breast and lung cancer. Hematologic malignancies (7 cases) were also reported with a similar thyroiditis-like presentation. Patients underwent the traditional work-up for a thyroiditis, but frequently underwent other radiographic studies, in addition to radioactive iodine imaging, and frequently also underwent thyroid biopsy. The course in most patients (22/26 cases) was progression from hyperthyroidism to hypothyroidism, as the underlying malignancy progressed or thyroidectomy was performed, or the patient succumbed to their malignancy. Some patients (4 cases) became euthyroid with successful treatment of their malignancy. A subset of patients (5 cases) initially presented with severe thyrotoxicosis. Many affected patients succumbed to their underlying malignancy.

Conclusion: Malignancy-associated hyperthyroidism has a similar underlying mechanism to subacute thyroiditis, in so much as there is damage or destruction of thyroid tissue. In cases of subacute thyroiditis this damage is self-limited, and there is recovery of thyroid function. In some cases of thyroiditis associated with malignancy there may be thyroid gland recovery as the underlying malignancy is treated and controlled. However, if the malignancy progresses, eventual hypothyroidism is likely to ensue.

Introduction

There are several common causes of hyperthyroidism or thyrotoxicosis which account for the majority of cases encountered in clinical practice. For the purposes of this review the terms hyperthyroidism or thyrotoxicosis are considered to be interchangeable. These common causes include Graves' disease, toxic nodular goiter, toxic nodules, and thyroiditis [1–4]. Less common causes of hyperthyroidism include human chorionic gonadotrophin induced thyrotoxicosis, typically caused by malignancies of reproductive origin such as gestational trophoblastic disease and testicular tumors, functioning thyroid cancer, struma ovarii, and TSH-producing pituitary adenomas [1,3–5]. With respect to sub-dividing thyroiditis into common and less common etiologies, Hashimoto's thyroiditis, silent thyroiditis, subacute viral thyroiditis, and drug-induced thyroiditis are probably the most

common [2,3,6], whereas infectious agents and other processes infiltrating the thyroid gland such as sarcoidosis and amyloidosis are probably less common causes of hyperthyroidism [7–10]. Radiation damage or mechanical insult to the thyroid gland are also other uncommon causes of thyroiditis with resulting hyperthyroidism [11–14]. Anaplastic thyroid cancer, as it presents with rapid enlargement of the thyroid gland, can also be associated with thyroiditis and temporary hyperthyroidism [15,16], as can primary thyroid lymphoma [17,18].

Infiltration of the thyroid gland by non-thyroid malignancies is an uncommon cause of hyperthyroidism and will be the focus of this review. As will be discussed, both solid tumors and hematological malignancies can infiltrate the thyroid gland and this process may be associated with euthyroidism, hypothyroidism, or hyperthyroidism.

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Table 1
Malignancies identified as a solid neoplasm* metastasizing to the thyroid gland.

Author and date	Country	Number of patients	Most frequent malignancy (number of cases)	Second most frequent malignancy (number of cases)	Third most frequent malignancy (number of cases)	Fourth most frequent malignancy (number of cases)
Lin, 1998	China single center	14	Lung (6)	Unknown (5)	Stomach (1) Breast (1) Lymphoma (1)	–
Kim, 2005	Korea single center	22	Breast (5)	Kidney (3) Colon (3) Lung (3)	–	–
Cichon, 2006	Poland, single center	17	Renal clear cell (13)	Unknown (2)	Breast (1) Uterine (1)	–
Papi, 2007	Italian pathology databases	36	Lung (9)	Gastrointestinal tract (7)	Breast (5) Renal clear cell (5)	Larynx (5)
Vardar, 2011	Turkey single center	3	Renal clear cell (1) Breast (1) Lung (1)	–	–	–
Chung, 2012	n/a literature review	374	Renal clear cell (1 8 0)	Colorectal (39)	Lung (31)	Breast (29)
Kim, 2014	Korea single center	13	Lung (9)	Unknown (2)	Cholangio-sarcoma (1) Penile (1)	–
Saito, 2014	Japan single center	29	Breast (10)	Lung (6)Gastrointestinal tract (6)	Renal cell carcinoma (3) Head and Neck (3)	Sarcoma (1)
Hegerova, 2015	US single center	97	Renal clear cell (22) Lung (22)	Head and Neck (12)	Breast (11)	Esophagus (9)
Straccia, 2017	n/a literature review	514	Renal clear cell (1 9 0)	Unknown (1 3 9)	Lung (1 2 3)	Breast (72)
Nixon, 2017	n/a literature review	495	Renal clear cell (1 2 4)	Lung (1 0 9)	Gastrointestinal tract (64) Breast (64)	–
Wang, 2018	China single center	21	Esophagus (7)	Breast (6)	Head and Neck (3) Unknown (3)	–
Falcone, 2018	Italy, single center	5	Lung cancer (2)	Renal clear cell (1) Breast (1) Esophageal (1)	–	–
Mistelou, 2019	Greece single center	36	Lung (12)	Lymphoma/leukemia* (9)	Breast (3) Renal clear cell (3)	–
Pastorella, 2019	n/a literature review	Not reported	Renal clear cell (not reported)	Breast (not reported)	Melanoma (not reported)	Sarcoma (not reported)
Khaddour, 2019	n/a literature review	147	Renal clear cell (1 4 7)	n/a, series examined only clear cell	renal carcinoma	

*Most series only included solid malignancies.

Methods

References for this review were identified through two searches of PubMed for articles published from January 1, 1960 to December 31, 2019. The first search used the MeSH terms “hyperthyroidism”, “thyroiditis”, and “neoplasm” and the second used the MeSH terms “hyperthyroidism”, “neoplasm”, and “metastases” respectively. Relevant articles were also identified through searches in the author’s personal files. Articles resulting from these searches and relevant references cited in those articles were reviewed. Preference was given to more recent articles and articles in English.

Results

Malignancy metastasizing to the thyroid, regardless of thyroid status

In order to provide a background regarding the types of malignancies that metastasize to the thyroid gland some of the available case series or reviews are summarized in Table 1 [19–34]. Autopsy series have found that the frequency of non-thyroid malignancies affecting the thyroid gland is 0.9% [26] – 2% [32] of autopsy cases. Most of the clinical series only examined solid tumors, and did not include hematological malignancies. There is some regional variation in the types of malignancies reported, with, for example, smaller series from some countries reporting more cases of lung and esophageal cancer. However, in the larger series clear cell carcinoma of the kidney is most frequently reported. The largest literature review that included 514 patients identified renal cell carcinoma (37%), cancer of unknown

origin (27%), lung cancer (24%), and breast cancer (14%) respectively as the most commonly reported malignancies [29]. Another literature review that included 495 patients reported the following frequencies of non-thyroid malignancies affecting the thyroid gland: renal cell carcinoma 25%, lung cancer 22%, gastrointestinal cancer 13%, and breast cancer 13% [32]. A recent review of malignancies that metastasized to endocrine glands, utilizing data from previously mentioned reviews [19,29,32,34], estimated the following frequencies of metastases to the thyroid gland: renal cell cancer 48%, colorectal 10%, lung 8%, and breast cancer 8% [35]. Another series involved 147 cases of renal cell carcinoma metastatic to the thyroid gland [33].

Most of these series, however, do not mention the thyroid status of the affected patients. Excluding patients documented as having thyroid disease that pre-existed their malignancy, those whose thyroid status is reported were mostly euthyroid with small numbers of patients being reported as hypothyroid, and even smaller numbers being reported as hyperthyroid. For example, using the report of cases of renal cell carcinoma as an example, no TSH was reported for 100 out of 147 cases, 42 cases had normal thyroid function, 3 cases were hypothyroid, and 2 cases were reported to be hyperthyroid [33].

Malignancies to the thyroid gland associated with hyperthyroidism

The first literature search resulted in 676 articles, whereas the second resulted in 231 articles. Any articles that described cases of patients with primary thyroid malignancies (differentiated thyroid cancer, medullary thyroid cancer, anaplastic thyroid cancer, primary thyroid lymphoma), pre-existing thyroid disease or positive thyroid

antibodies were excluded. Cases of human chorionic gonadotrophin induced thyrotoxicosis were excluded. In addition, cases of patients receiving tyrosine kinase inhibitor or immunoregulatory drug treatments that could affect thyroid function or produce thyroid auto-antibodies that could confound assessment of thyroid function were excluded [36]. Patients becoming hyperthyroid after receiving radiation therapy or receiving any drugs known to cause hyperthyroidism (e.g. immunotherapy) were also excluded. Cases in which symptoms of thyroiditis, such as thyroid pain and swelling, were reported, but a hyperthyroid state was not suggested or documented were also excluded. After these exclusions, and exclusions for lack of relevance to the topic, three relevant articles were abstracted from the first search and three were identified from the second search. Review of these included articles, some excluded articles, and personal files yielded an additional 18 articles. Thus, a total of 24 articles describing 26 cases were identified. Seventeen articles described 19 cases of hyperthyroidism due to solid malignancies. Seven articles described 7 cases of hyperthyroidism due to hematologic malignancies.

Solid malignancies

A summary of the 19 cases of hyperthyroidism associated with thyroid metastases from solid malignancies reported in the literature is shown in Table 2. Most of these are single case reports. Five cases of lung cancer [37–41], six cases of breast cancer [42–46], two cases in which the malignancy responsible was not clearly reported [47], and one case each of renal cell carcinoma [48], melanoma [49], pancreatic cancer [50], rectal cancer [51], leiomyosarcoma [52], and unknown primary [53] were documented. An additional case involving metastatic breast cancer with a presentation entirely consistent with acute thyroiditis and with tumor emboli found within the thyroid gland was excluded due to normal thyroid function [54]. Some patients were previously known to have a malignancy; in others the hyperthyroid presentation lead to the discovery of the malignancy. Twelve patients were female, four were male, and the gender was not reported for 3. Prominent features of these cases were the presentation of the patient with a painful goiter, sometimes with compressive symptoms, and degrees of hyperthyroidism ranging from subclinical to severe. Sometimes there was incomplete documentation of the details about the patient's thyroid testing and so the available information was provided. If performed, testing for thyroid antibodies was negative, iodine scanning showed absent radioactive iodine uptake within the thyroid gland, and computed tomography scanning of the neck showed diffuse goiter or nodular masses within the thyroid parenchyma. A unifying feature was fine needle aspiration of the thyroid gland showing malignant cells with characteristics of the primary malignancy, and thyroidectomy, if performed, confirming the thyroid metastases of the primary malignancy. Many of patients progressed on to hypothyroidism even if thyroidectomy was not performed, and most patients passed away from their malignancy within a year.

Hematologic malignancies

Table 3 shows a summary of the 7 cases of hyperthyroidism associated with thyroid metastases from hematologic malignancies reported in the literature. The malignancy was either reported as lymphocytic lymphoma [55,56], malignant lymphoma [57], lymphoma [58], anaplastic large cell lymphoma [59], B cell lymphoma [60,61], or chronic lymphocytic leukemia [62]. Most patients had pre-existing malignancies, but a few were first diagnosed with their malignancy when they presented with hyperthyroidism. Four women and 2 men were affected with gender not being reported in 1 patient. Similar to the cases with solid malignancies, patients presented with a goiter and compressive symptoms. Degrees of hyperthyroidism varied in severity among the cases. Thyroid antibodies were negative. When obtained, iodine scanning showed absent radioactive iodine uptake within the thyroid and

computed tomography scanning mostly showed diffuse goiter. Patient outcomes were mixed with 3 deaths, 1 “poor prognosis”, one remission, and the remaining outcomes not reported.

Discussion

When a non-thyroid malignancy spreads to the thyroid gland, it may reach the thyroid in three different ways. It may reach the thyroid by direct extension from an adjacent malignancy, such as has been reported for parathyroid carcinoma [63]. Lymphatic spread may occur, as might be expected with breast cancer. Alternatively, other malignancies may spread by the hematogenous route. Endocrine glands in general can be targets for metastases from several non-endocrine cancers: metastases to the pituitary, adrenal and thyroid gland have been described, likely due to their abundant blood supply [35]. Based on a review of these case studies of malignancies that metastasize to the thyroid gland and are then associated with thyrotoxicosis, it appears that the etiology of the thyrotoxicosis is development of thyroiditis, and that the thyroiditis has some features that are similar to the more common causes of thyroiditis, particularly subacute thyroiditis, but also has some different features.

It has previously been reported that metastases to the thyroid gland are more common in women than men [35]. That, indeed, did seem to be the case in the individuals reported here who developed hyperthyroidism due to thyroiditis, with women accounting for 16 of the 22 cases that provided the gender of the affected patient. The work up that was performed in the cases reviewed here was primarily the typical work up that would be performed to establish the diagnosis of subacute thyroiditis. This included measurement of TSH values, thyroid hormone levels, thyroid antibodies, and radioactive iodine uptake and scan studies. In these studies, in addition to low TSH levels and high thyroid hormone levels, the free thyroxine levels were generally proportionally more elevated than the elevation in the total triiodothyronine level, as would be expected with subacute thyroiditis. Thyroid antibodies were negative and uptakes on radioactive iodine uptake and scan studies were invariably low. Studies that were additionally performed as part of the work-up that would not generally be needed in an evaluation for subacute thyroiditis included imaging such as computed tomography of the neck or chest and thyroid fine needle aspiration or biopsy. In these cases, the imaging generally showed a goiter, often with compressive features, and a biopsy generally revealed malignant cells with features consistent with the primary cancer. As a generalization, based on these small numbers of cases, it appears that intra-thyroid metastases from solid malignancies usually result in a nodular pattern of metastatic infiltration, whereas hematologic malignancies seem to produce a goiter with a more diffuse infiltration pattern.

Similar to the case with a subacute thyroiditis, many of these cases documented a progression from hyperthyroidism to hypothyroidism. However, unlike subacute thyroiditis, the triphasic course with final recovery to euthyroidism was less often reported, unless the patient received chemotherapy for the underlying malignancy. In such treated cases, as the malignancy regressed, shrinkage of the patient's goiter was often reported, and thyroid function generally improved. In cases where the malignancy progressed, patients often required levothyroxine treatment for their hypothyroidism. Some patients underwent thyroidectomy for compressive symptoms, also necessitating thyroid hormone replacement.

In these cases of malignancy-associated hyperthyroidism, it is believed that the invasion of the non-thyroid cancer cells into the gland causes destruction of normal thyroid tissue with uncontrolled release of thyroid hormones, predominately thyroxine, into the circulation. While such infiltration could be initially associated with hyperthyroidism, it is logical that progression of the malignancy would be associated with a decline into hypothyroidism without recovery of thyroid function, unless treatment for the malignancy intervenes. A few of the cases described here (5 out of 26) were associated with severe hyperthyroidism

Table 2
Reports of metastases of solid malignancies to the thyroid gland associated with thyroiditis and hyperthyroidism.

Article Number	Author, Year	Number of patients	Patient Age (years)/ Gender (M/F)	Malignancy (Newly diagnosed [new] or known pre-existing [known])	Hyperthyroidism work-up	Cytology/pathology, and follow up
1	Tibaldi, 1986	1	39M	Lung (known)	Thyroid pain and swelling, extremely elevated thyroid hormone, I-125 uptake < 1%	Aspiration of thyroid showed cells similar to primary lung cancer. Patient's thyroid hormone levels later declined to hypothyroid range Metastatic lung cancer found at thyroidectomy
2	Kung, 1991	1	81F	Lung (known)	Painful swelling of thyroid gland swelling, TSH < 0.05, marked elevation of thyroid hormone and thyroglobulin	
3	Miyakawa, 2001	1	50F	Lung (known)	Thyroid enlarged, severe thyrotoxicosis based on TFTs (TSH < 0.05, markedly elevated thyroid hormones), I-123 uptake < 4%	Aspiration of thyroid showed cells similar to primary lung cancer. Patient later became hypothyroid
4	Shirahama, 2008	1	46F	Lung (new)	Painful thyroid swelling, laboratory diagnosis showing hyperthyroidism TSH 0.03, elevated thyroid hormones	Aspiration showed squamous cell carcinoma. Thyroid function normalized after chemotherapy
5	Wirtz, 2008	1	54M	Lung (new)	Painful thyroid gland swelling and hyperthyroidism (TSH < 0.01, elevated thyroid hormone)	Patient become hypothyroid. Biopsy showed metastatic lung cancer. Thyroid function improved after chemotherapy
6	Edmonds, 1978	1	25F	Breast (new)	Diffuse, firm goiter, TFTs showing undetectable TSH and elevated thyroid hormones, 2 and 24 hr I-131 uptake < 2%	Diffuse infiltration of thyroid with adenocarcinoma found after thyroidectomy
7	Trokouides, 1978 (also Rosen, 1978)	1	51F	Breast (known)	Rapidly enlarging thyroid, thyroid hormones upper normal, I-131 uptake 1%, further enlargement of thyroid and later became hypothyroid	Metastatic breast cancer found at time of sub-total lobectomy
8	Koev, 1987	1	52F	Breast (known)	Hyperthyroidism (described as tumor invasion of thyroid causing hyperthyroidism)	
9	Ferrara, 1997	1	58F	Breast (known)	Clinical presentation consistent with thyroiditis, elevated thyroglobulin	Immunohistochemistry of aspirated cells consistent with breast cancer
10	Skowrońska-Józwiak, 2010	2	Post-menopausal F	Breast (1 new, 1 known)	Hyperthyroidism and subclinical hyperthyroidism respectively, goiter, negative thyroid antibodies	Biopsy of the thyroid showing cells consistent with metastatic breast cancer
11	De Ridder, 2003	2	Not documented	Not clearly reported (breast, head & neck or renal cell carcinoma) (not documented)	TFTs showing hyperthyroidism	
12	Bacourt, 1980	1	65M	Renal cell carcinoma (known)	Presented with hyperthyroidism	
13	Costa, 2017	1	85F	Melanoma (new)	Subclinical hyperthyroidism, pre-existing multinodular goiter	Multiple melanoma tumor foci were found at the time of thyroidectomy, in addition to multinodular goiter
14	Eriksson, 1977	1	54M	Pancreatic (known)	Goiter and hyperthyroidism, I-131 uptake 0.6%	Biopsy of thyroid neoplastic cells. Thyroid function trended to normal. Thyroid completely infiltrated by pancreatic cancer at autopsy
15	Kim, 2007	1	61F	Rectal (known)	Firm, tender goiter, hyperthyroidism TSH 0.05), negative thyroid antibodies	Biopsy revealed malignant cells similar to original rectal cancer. Patient later became hypothyroid requiring levothyroxine
16	Ferrozzi, 1997	1	?	Leiomyosarcoma (?)	Mass within the thyroid gland, hyperthyroidism	Biopsy showed metastatic leiomyosarcoma, patient with lung metastases also
17	Watts, 1988	1	35F	Unknown primary (known)	Firm, tender goiter, hyperthyroidism (low TSH and elevated thyroid hormones), negative thyroid antibodies	Thyroid aspiration showed adenocarcinoma. Patient became hypothyroid requiring levothyroxine

Abbreviations: TSH = thyroid stimulating hormone, TFTs = thyroid function tests, I-123 = iodine I-123, I-125 = iodine I-125, I-131 = iodine-131.

Table 3
Reports of metastases of hematologic malignancies to the thyroid gland associated with thyroiditis and hyperthyroidism.

Article Number	Author, Year	Number of patients	Patient Age (years)/Gender (M/F)	Malignancy (Newly diagnosed [new] or known pre-existing [known])	Hyperthyroidism work-up	Cytology/pathology, and follow up
1	Shimaoka, 1976 (also Shimaoka, 1980)	1	40F	Lymphocytic lymphoma (known)	Diffuse thyroid enlargement, TFTs showing hyperthyroidism, I-131 uptake < 0.6%, negative thyroid antibodies	Became hypothyroid after radiation therapy
2	Compagno, 1980	1	?	Malignant lymphoma or other lymphoproliferative disorder (?)	Rapidly enlarging neck mass, hyperthyroid, hyperthyroid patient not described separately from other cases	Hyperthyroid patient not described separately from other cases
3	Gochu, 1994	1	35M	Lymphoma (known)	Goiter, hyperthyroidism, TSH 0–0.07, low uptake on I-123 scan	Open biopsy of thyroid showed lymphoma. Chemotherapy caused remission of goiter and euthyroidism. Patient then became hypothyroid. Patient expired of other complications.
4	Samuels, 1998	1	31F	Anaplastic large cell lymphoma (known)	Acute neck swelling and pain, severe hyperthyroidism, negative thyroid antibodies, neck CT showing diffusely decreased attenuation throughout thyroid	Patient deceased and autopsy showed anaplastic large cell lymphoma with destruction of normal thyroid tissue
5	Glasspool, 2001	1	37F	B cell lymphoma (new)	Presented with hyperthyroid, negative thyroid antibodies, iodine uptake absent in thyroid	Became hypothyroid with chemotherapy. Presented with recurrence, goiter, and recurrent hyperthyroidism. Returned to euthyroidism with second therapy
6	Choudhary, 2014	1	60M	Chronic lymphocytic leukemia (known)	Painful asymmetric neck swelling, very high thyroid hormone levels, elevated thyroglobulin	Imaging suggested lymphomatous nodules throughout the lungs, spleen, liver, kidney and thyroid gland. Patient deceased due to multiple complications including thyroid storm
7	McCarthy, 2016	1	61F	B cell lymphoma (new)	Neck swelling, TFTs showing hyperthyroidism, CT showed diffuse goiter, thyroid antibodies negative	Thyroid function normalized after chemotherapy. Patient in remission

Abbreviations: TSH = thyroid stimulating hormone, TFTs = thyroid function tests, I-123 = iodine I-123, I-125 = iodine I-125, I-131 = iodine-131.

[37–39,59], and even thyroid storm [62]. In contrast, subacute thyroiditis is rarely associated with severe hyperthyroidism or thyroid storm [64,65], perhaps reflecting the less precipitous progression of a subacute thyroiditis.

Some potentially distinguishing features of the cases described in this review is that although neck or thyroid pain and swelling was a prominent feature, the degree of thyroid enlargement was generally of a far greater magnitude than might be seen with a subacute thyroiditis, leading to the frequent imaging with computed tomography of the neck. In fact, evidence of noticeable, and even severe and progressive compressive symptoms, was seen in some cases. In keeping with the magnitude of the compressive symptoms, thyroidectomy was performed in some cases, with confirmation of the underlying malignancy infiltrating the parenchyma of the thyroid gland.

In contrast to subacute thyroiditis with its self-limited course, the cases described here obviously required treatment for their underlying malignancy which took the form of chemotherapy or radiation therapy as appropriate. Thyroidectomy was not universally performed, but was sometimes performed for relief of compressive symptoms. In marked contrast to cases of subacute thyroiditis, the outcomes of the patients affected by malignancy-associated thyroiditis were variable, with some patients responding positively to the treatment directed at their underlying malignancy, but also with patients succumbing to the malignancy. In most patients, metastases to the thyroid gland represented one of several metastatic sites, thus illustrating the advanced state of many of these malignancies.

A limitation of this analysis is the absence of the documentation of thyroid status in most cases of patients with malignancies metastatic to the thyroid gland. In addition, even if thyroid status is mentioned, it may not be completely documented, as illustrated by the information

available in Tables 2 and 3. For example, the incidence of hyperthyroidism appears to be higher for lung and breast cancer than renal cell carcinoma, but it may in fact be that the thyroid status has not been documented as clearly in some of the renal cell carcinoma cases. Many cases and case series have no documentation of TSH values. Painful thyroid enlargement was a prominent feature of the cases listed in Tables 2 and 3. Such cases were only included in this article if hyperthyroidism was documented and in other cases it may not have been documented. For example, the following case of painful thyroid enlargement with renal cell carcinoma has no documentation of the patient's TSH [66].

In conclusion, non-thyroid malignancies may rarely infiltrate the thyroid gland. A subset of affected patients may develop hyperthyroidism secondary to a thyroiditis caused by this infiltrative process. The degree of hyperthyroidism may range from mild to severe, and is usually preceded by goiter development. Successful treatment of the malignancy may be associated with a return to the euthyroid state, but progression of the malignancy usually is accompanied by development of hypothyroidism requiring thyroid hormone replacement. Overall outcomes for patients with a malignancy-associated thyrotoxicosis seem to be poor, presumably reflecting the advanced state of the underlying malignancy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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