Journal of Medical Case Reports

Breast cancer metastases to the thyroid gland - An uncommon sentinel for diffuse metastatic disease: A case report and literature review.

--Manuscript Draft--

Manuscript Number:	JMCR-D-17-00151R4
Full Title:	Breast cancer metastases to the thyroid gland - An uncommon sentinel for diffuse metastatic disease: A case report and literature review.
Article Type:	Case report
Funding Information:	
Abstract:	Background Metastases to the thyroid are rare. The most common primary cancer to metastasize to the thyroid is renal cell carcinoma, followed by malignancies of the gastrointestinal tract, lung and skin with breast cancer metastases to the thyroid being rare. Overall, the outcomes in malignancies that have metastasised to the thyroid are poor. There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Isolated thyroidectomy has been proposed as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway. Here, we present a case of a patient with breast cancer metastases to the thyroid gland and discuss the role of thyroidectomy in the context of the current literature. Case description A 62 year old Afro-Caribbean female was diagnosed with bilateral breast carcinoma in 2004, for which she underwent bilateral mastectomy. The pathology revealed multifocal disease on the right: T2N0 (0/20)M0 Gr1+2 invasive ductal carcinoma (IDC) and T3N1(2/18)M0 Gr 1 IDC on the left side. Surgery was followed by adjuvant chemotherapy and regional radiotherapy. The disease was under control on hormonal therapy until 2016, when the patient developed cervical lymphadenopathy. The fine needle aspiration cytology (FNAC) of the thyroid was reported as papillary thyroid cancer; and the fine needle biopsy of the left lateral nodal disease was more suggestive of breast malignancy. The patient underwent a total thyroidectomy and a clearance of the central compartment lymph nodes and a biopsy of the lateral nodal disease. The histopathological analysis was consistent with metastatic breast cancer in the thyroid and lymph nodes with no evidence of a primary thyroid malignancy. Conclusion A past history of a malignancy elsewhere should raise the index of suspicion of metastatic disease in patients presenting with a thyroid lumps with or without cervical lymphadenopathy. Detection of metastases to the thyroid generally indicates poor prognosis, obviating the need of surgery in an already compromised patient. The empirical thyroidectomy should be considered in select patients for local disease control.
Corresponding Author:	agata plonczak Imperial College London UNITED KINGDOM
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Imperial College London
Corresponding Author's Secondary Institution:	
First Author:	Agata Plonczak, MBBS BSc MRCS
First Author Secondary Information:	
Order of Authors:	Agata Plonczak, MBBS BSc MRCS
	Aimee DiMarco, MA MBBS PhD MRCS

	Dorothy Gujral, MBChB MRCP MSc FRCR PhD
	Roberto Dina, MD, FIAC, FRCPath
	Fausto Palazzo, MS, FRCS (Eng), FRCS (Gen)
Order of Authors Secondary Information:	
Response to Reviewers:	Dear editor, thank you for your comments. We tried to address all the points to the best of our ability. Please find it below. At the end of the Introduction there is a need to add a paragraph that explains why this case report is presented (what is unique and adds to the medical knowledge). This has now been amended: There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Isolated thyroidectomy has been proposed as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway. Here, we present a rare case of a patient with breast cancer metastases to the thyroid gland, and review the evidence for the role of thyroidectomy in the context of the current literature. (lines 87-92) More information is needed: Give complete past medical, social, family, and environmental history. What medication was the patient on prior to diagnosis? Additional information included: Her past medical history included hypertension, controlled by Amlodipine and Losartan and diabetes, on treatment with Metformin. (lines 96-7) The patient had no personal or familial risk factors for thyroid malignancy. (line 116=9-120) Give detailed physical and neurological examination on the primary admission. What was the temperature, pulse, blood pressure and temperature, on admission? Was urinalysis done? Is the editor referring to the initial diagnosis in 2004? Unfortunately, we do not have this information. Give all results of laboratory findings (i.e. CBC, liver and renal functions), serology, microbiology etc). What were the thyroid related laboratory results (TSH etc) Additional information included: Laboratory findings revealed a white cell count of 5.2 x109/L, haemoglobin of 115 g/L, and normal liver and renal function with an estimated glomerular filtration rate of 67ml/min/1.73m2. (lines 113-115). We did not do the TSH level. Give the duration and doses of all chemotherapeutic agent (lines 102-6, 122-3) This has now been included: Hormonal therapy initially consisted of 20mgs daily of Tamoxifen. After three years this was switched to an Aromatase inhibitor (Anastrazole 1mg daily) until 2009 when she completed 5 years of adjuvant endocrine therapy. The patient then subsequently relapsed with metastatic disease with lung nodules in 2008 and bone metastases were noted on bone scan four years later. She was commenced on 25 mgs once a day of Exemestane and 4mg intravenous monthly injections of Zoledronic acid in early 2014. Due to disease progression Capecitabine (1250 mg/m2 (based on total body surface area) twice daily) was commenced until after 6 cycles when it was discontinued due to Capecitabine-related toxicity and the patient was started on 2.5 mgs once a day of Letrozole and 150 mgs once a day of Ibandronic acid. The chemotherapy was switched to 500mg intramuscular monthly injections of Fulvestrant and she continues to take the Ibandronic acid.

	What medications (including doses) were administered at discharge. Did she receive Synthroid (what dosage?). The patient was discharged on daily 125mcgs of Levothyroxine. (lines 131-2) In the Discussion - describe what is unique in this case compared to what is available in the literature. Additional information included and the paragraph now amended: There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Our patient with breast metastasis to the thyroid and co-existing lung and bone metastatic deposits, was managed with a total thyroidectomy with a good outcome. Isolated thyroidectomy has been proposed in previous studies [20, 37] as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway [37]. It has been also suggested that this may be beneficial for a selected group of patients with clinically significant and relatively isolated metastatic disease of the thyroid especially from a renal primary [25]; however, in the absence of prospective trials this is at best speculative. (lines 187-194)

Title Page

Title: Breast cancer metastases to the thyroid gland – An uncommon sentinel for diffuse metastatic disease: A case report and literature review

Agata M. Plonczak[1] (MBBS BSc MRCS) agata.plonczak@gmail.com

Aimee N. DiMarco[1] (MA MBBS PhD MRCS) aimee.dimarco@imperial.nhs.uk

Roberto Dina[2] (MD, FIAC, FRCPath) roberto.dina@imperial.nhs.uk

Dorothy J Gujral [3] (MBChB MRCP MSc FRCR PhD) dorothy.gujral@imperial.nhs.uk

F. Fausto Palazzo[1] (MS, FRCS (Eng), FRCS (Gen)) f.palazzo@imperial.ac.uk

[1] Department of Thyroid & Endocrine Surgery, Hammersmith Hospital, Imperial College Hospitals NHS Trust, London, W12 0HS, UK

[2]Department of Histopathology, Hammersmith Hospital, Imperial College Hospitals NHS Trust, London, W12 0HS, UK

[3]Department of Oncology, Charing Cross Hospital, Imperial College Hospitals NHS Trust, London, W6 8RF

Address for correspondence: Agata Plonczak, Flat 26 Cranston Court, W127FE London, email: agata.plonczak@gmail.com, phone: 0044 7534378695

Abstract

Background

Metastases to the thyroid are rare. The most common primary cancer to metastasize to the thyroid is renal cell carcinoma, followed by malignancies of the gastrointestinal tract, lung and skin, with breast cancer metastases to the thyroid being rare. Overall, the outcomes in malignancies that have metastasised to the thyroid are poor. There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Isolated thyroidectomy has been proposed as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway. Here, we present a case of a patient with breast cancer metastases to the thyroid gland and discuss the role of thyroidectomy in the context of the current literature.

Case description

A 62 year old Afro-Caribbean female was diagnosed with bilateral breast carcinoma in 2004, for which she underwent bilateral mastectomy. The pathology revealed multifocal disease on the right: T2N0 (0/20)M0 Gr1+2 invasive ductal carcinoma (IDC) and T3N1(2/18)M0 Gr 1 IDC on the left side. Surgery was followed by adjuvant chemotherapy and regional radiotherapy. The disease was under control on hormonal therapy until 2016, when the patient developed cervical lymphadenopathy. The fine needle aspiration cytology (FNAC) of the thyroid was reported as papillary thyroid cancer; and the fine needle biopsy of the left lateral nodal disease was more suggestive of breast malignancy. The patient underwent a total thyroidectomy and a clearance of the central compartment lymph nodes and a biopsy of the lateral nodal disease. The histopathological analysis was consistent with metastatic breast cancer in the thyroid and lymph nodes with no evidence of a primary thyroid malignancy.

Conclusion

A past history of a malignancy elsewhere should raise the index of suspicion of metastatic disease in patients presenting with a thyroid lumps with or without cervical lymphadenopathy. Detection of metastases to the thyroid generally indicates poor prognosis, obviating the need of surgery in an already compromised patient. The empirical thyroidectomy should be considered in select patients for local disease control.

Keywords: thyroid disorders, breast cancer, clinical oncology, endocrine surgery

Background

Breast cancer is the most commonly diagnosed cancer amongst women [1]. The common sites for metastatic spread are bone, lung and liver [2]. Metastases to the thyroid gland from a non-thyroid primary are uncommon and are mostly from the kidney, followed by gastrointestinal tract, lung, skin and rarely breast [3-7]. It is usually associated with poor prognosis. There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Isolated thyroidectomy has been proposed as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway. Here, we present a rare case of a patient with breast cancer metastases to the thyroid gland, and review the evidence for the role of thyroidectomy in the context of the current literature.

Case description

A 62 year old Afro-Caribbean female was diagnosed with bilateral carcinoma of the breast in 2004. Her past medical history included hypertension, controlled by Amlodipine and Losartan in addition to diabetes, on treatment with Metformin. The patient underwent bilateral mastectomy and axillary node clearance with immediate implant-based reconstruction. The pathology revealed multifocal disease on the right: T2N0 (0/20)M0 Gr1+2 invasive ductal carcinoma (IDC) and T3N1(2/18)M0 Gr 1 IDC on the left side. The disease was estrogen receptor (ER) positive, weak progesterone receptor (PR) positive and Her2 negative. Surgery was followed by adjuvant chemotherapy, consisting of the 5-fluorouracil, Epirubicin and Cyclophosphamide (FEC) regimen and regional radiotherapy. Hormonal therapy initially consisted of 20mgs daily of Tamoxifen. After three years this was switched to an Aromatase inhibitor (Anastrazole 1mg daily) until 2009 when she completed 5 years of adjuvant endocrine therapy. The patient then subsequently relapsed with metastatic disease with lung nodules in 2008 and bone metastases were noted on bone scan four years later. She was commenced on 25 mgs once a day of Exemestane and 4mg intravenous monthly injections of Zoledronic acid in early 2014. Due to disease progression Capecitabine (1250 mg/m^2 (based on total

body surface area) twice daily) was commenced until after 6 cycles when it was discontinued due to Capecitabine-related toxicity and the patient was started on 2.5 mgs once a day of Letrozole and 150 mgs once a day of Ibandronic acid. In February 2016 the patient presented with neck swelling with intermittent neck discomfort without airway pressure symptoms. On clinical examination she was found to have cervical lymphadenopathy. Laboratory findings revealed a white cell count of 5.2 $x10^9$/L, haemoglobin of 115 g/L, and normal liver and renal function with an estimated glomerular filtration rate of 67ml/min/1.73m^2. The neck swelling was investigated with an ultrasound and confirmed both lateral cervical nodal disease in levels II to IV and a goitre with left-sided dominance. The fine needle aspiration cytology (FNAC) of the thyroid was reported as in keeping with a papillary thyroid cancer; however, the cytology of the left lateral nodal disease was described as more suggestive of a breast malignancy. The patient had no personal or familial risk factors for thyroid malignancy. Staging investigations including magnetic resonance imaging (MRI) of the spine demonstrated stable deposits involving C2, C5, T4 and L1 without neural compromise [Figure 1] and computer tomography (CT) of the thorax demonstrated no change in the lung nodules [Figure 2]. Since the diagnosis was not clear following the Multidisciplinary Team discussion the decision was made to proceed with a total thyroidectomy and a clearance of the central compartment lymph nodes coupled with an excision biopsy of the laterocervical lymph nodes. The histopathological analysis of the specimen demonstrated an ill-circumscribed white tumour at the posterior margin of the left lobe measuring 1.2x0.9x1.5cm. On immunocytochemistry the tumour cells were positive for CEA, synaptophysin, GATA3 and ER (5/8), focally positive for CK7 and GCDFP-15 and negative for TTF-1, calcitonin, thyroglobulin, CK20, PgR and HER-2. The overall appearances were consistent with metastatic breast cancer [Figures 3-4] with no evidence of a primary thyroid malignancy. The level IV and level VI lymph nodes contained metastatic breast cancer. The patient was discharged on daily 125mcgs of Levothyroxine. The chemotherapy was switched to 500mg intramuscular monthly injections of Fulvestrant and she continues to take the Ibandronic acid. Currently, 14 months following the thyroidectomy, the patient remains clinically stable. She developed local recurrences in

the level II-IV lymph nodes in her neck and her recent MRI of the spine show stable spinal metastatic disease.

Discussion

Metastatic deposits have a predilection for highly vascularised organs but despite one of the highest blood supplies per weight of tissue (4 to 6 mL/minute/g) [8] the thyroid is rarely the site for metastatic deposits. It is difficult to establish the true rate of metastases from breast cancer to the thyroid gland with a quoted range of prevalence from 3%, of all thyroid metastases [4] to 34% (Table 1) [2, 3, 6, 7, 9-27]. Metastases to the thyroid gland represent the indication for surgery in under 1 in a 1000 thyroidectomies [24, 28] of which almost half are from a renal cell carcinoma primary [7,29]. Other primary tumours that have been documented to metastasise to the thyroid include colorectal, lung and malignant melanoma [3-7] and gastrointestinal tract tumours [10].

Table 1: Clinical studies (case reports and case series) of breast metastases to the thyroid gland published so far.

Author	Study Years	Number of patients	Percentage of thyroid metastases from breast
Harcourt-Webster [9]	-	2	18%
Lam et al [10]	-	7	9%
Mayo and Schlicke [11]	-	2	11%
Elliott and Frantz [12]	1947-1958	4	29%
Wychulis et al [13]	1907-1962	4	29%
Pillay et al [14]	1974-1976	1	10%
Lin et al [15]	1977-1995	1	7%
Chacho et al [16]	1978-1985	1	13%
Rosen et al [17]	1978- 1993	1	9%
Hegerova et al [7]	1980-2010	11	11%
De Ridder et al [18]	1982-2002	1	17%
Russell et al [19]	1983-2013	2	12%
Cichon et al [20]	1984-2003	1	6%
Nakhajavani et al [21]	1985-1994	7	16%
Wood et al [22]	1985-2002	1	7%
HooKim et al [6]	1986 – 2013	3	11%
Saito et al [23]	1987 -2008	3	34%

Papi et al [24]	1993-2003	5	14%
Moghaddam et al [3]	1993-2013	1	10%
Calzolari et al [25]	1995-2005	1	4%
Kim et al [26]	1997-2004	5	23%
Surov et al [4]	1997- 2013	1	3%
Choi et al [27]	2001-2013	7	15%

Breast cancer is the most common malignant tumour among women [1], whilst being uncommon, thyroid cancers are the most common endocrine malignancies and the incidence is rising [30]. It has been suggested that possibly due to some common risk factors (genetic, lifestyle, diet habits, hormonal, menstrual and reproductive factors) individuals with breast cancer are more likely to develop primary thyroid cancer [31, 32]. Therefore, an individual presenting with both thyroid and breast malignancy is more likely to have primary cancer of thyroid and breast, rather than breast metastases to the thyroid.

Up to 80% of thyroid metastases are metachronous [29] with mean intervals from as little as 2.3 years in head and neck cancer [7, 21] to as long as 21 years in the case of foregut neuroendocrine tumours [33]. Other metachronous tumours present varying levels of delay with a mean of 9.4 years in renal cell carcinoma primaries [34] and 48.2 months [29] in breast primary malignancies. Longer delays in metachronous tumours probably reflect a less aggressive biology and indeed the rarer synchronous metastases to the thyroid is associated with much poorer prognosis with a mean 5-year survival rate of 7.9% [35].

Most reports of metastases to the thyroid are solitary with Surov and colleagues [4] reporting that thyroid metastases are to be solitary in 76% of patients in their study. However; Hegerova et al [7] report 79% of their patients have evidence of other metastases at the time of diagnosis of thyroid metastases, that may suggest that the extent of investigations plays a part in determining the other disease identified.

Fine needle aspiration cytology is the investigation of choice in the work-up of thyroid nodules. It has been shown to achieve an accuracy of over 90% in the diagnosis of secondary tumors of the thyroid [36]. Unfortunately as in the case presented metastatic ductal breast carcinoma involving the thyroid may morphologically mimic primary thyroid malignancy on FNA and secondary malignancies of the thyroid may be misdiagnosed.

Outcomes in metastatic thyroid disease tend to be poor since it is a reflection of the aggression and advanced stage of the primary disease [5, 15]. The Mayo clinic series demonstrate that the mean survival post diagnosis of metastases to the thyroid is 3 years and 6 years from the original diagnosis of a primary malignancy [7].

There are no prospective studies addressing the role of surgery in metastatic disease of the thyroid. Our patient with breast metastasis to the thyroid and co-existing lung and bone metastatic deposits, was managed with a total thyroidectomy with a good outcome. Isolated thyroidectomy has been proposed in previous studies [20, 37] as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway [37]. It has been also suggested that this may be beneficial for a selected group of patients with clinically significant and relatively isolated metastatic disease of the thyroid especially from a renal primary [25]; however, in the absence of prospective trials this is at best speculative.

Conclusion

A past history of a malignancy elsewhere should raise the index of suspicion of metastatic disease in patients presenting with a thyroid lumps with or without cervical lymphadenopathy. Detection of metastases to the thyroid generally indicates poor prognosis, obviating the need of surgery in an already compromised patient. The empirical thyroidectomy should be considered in select patients for local disease control.

Declarations:

•Ethics approval and consent to participate- Not applicable

• Consent for publication- Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

•Availability of data and material- Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

•Competing interests- The authors declare that they have no competing interests.

•Funding – Not applicable

•Authors' contributions- AP drafted the manuscript. AD contributed to the literature searc, wrote parts and revised the first draft of the manuscript. DG is the oncologist of the patient, who provided wrote the information regarding medical management. RD provided the histopathological images and analysis. FP is the consultant of the patient, who carried out the thyroidectomy and revised the draft of the manuscript. All authors read and approved the final manuscript.

•Acknowledgements- Not applicable

References:

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. Ca Cancer J Clin. 2016;66:7-30
2. Weigelt B, Peterse JL, van't Veer LJ. Breast cancer metastasis: markers and models. Nature Rev. Cancer. 2005;5:591-602.
3. 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.
4. Surov A, Machens A, Holzhausen HJ, Spielmann RP, Dralle H. Radiological features of metastases to the thyroid. Acta Radiol. 2016,57:444-50.
5. Mirallié E, Rigaud J, Mathonnet M, Gibelin H, Regenet N, Hamy A, Bretagnol F, de Calan L, Le Néel JC, Kraimps JL. Management and prognosis of metastases to the thyroid gland. J Am Coll Surg. 2005;200:203-7.
6. HooKim K, Gaitor J, Lin O, Reid MD. Secondary tumors involving the thyroid gland: A multi-institutional analysis of 28 cases diagnosed on fine-needle aspiration. Diag Cytopathol. 2015; 43:904-11.
7. Hegerova L, Griebeler ML, Reynolds JP, Henry MR, Gharib H. Metastasis to the thyroid gland: report of a large series from the Mayo Clinic. Am J Clin Oncol. 2015;38:338-42.
8. Salvatore D, Davies, T, Schlumberger, MJ, Hay, ID, Larsen, RP. Thyroid Physiology and Diagnostic Evaluation of Patients with Thyroid Disorders. In: Melmed, S, Polonsky, KS, Larsen RP. et al. editors. Williams Textbook of Endocrinology. Philadelphia: Elsevier; 2016. p. 334-368.
9. Harcourt-Webster JN. Secondary neoplasm of the thyroid presenting as a goitre. J Clin Pathol. 1965;18:282–7.
10. Lam KY, Lo CY. Metastatic tumors of the thyroid gland: a study of 79 cases in Chinese patients. Arch Pathol Lab Med. 1998;122:37–41.
11. Mayo CW, Schlicke CP. Exogenous tumors of the thyroid gland. Am J Pathol. 1941;17:283–8.

12. Elliott RH Jr, Frantz VK. Metastatic carcinoma masquerading as primary thyroid cancer: a report of authors' 14 cases. Ann Surg. 1960;151:551–61.
13. Wychulis AR, Beahrs OH, Woolner LB. Metastasis of carcinoma to the thyroid gland. Ann Surg. 1964;160:169–77.
14. Pillay SP, Angorn IB, Baker LW. Tumour metastasis to the thyroid gland. S Afr Med J. 1977;51:509–12.
15. Lin JD, Weng HF, Ho YS. Clinical and pathological characteristics of secondary thyroid cancer. Thyroid. 1998;8:149-53.
16. Chacho MS, Greenebaum E, Moussouris HF, Schreiber K, Koss LG. Value of aspiration cytology of the thyroid in metastatic disease. Acta Cytol. 1987;31:705–12.
17. Rosen IB, Walfish PG, Bain J, Bedard YC. Secondary malignancy of the thyroid gland and its management. Ann Surg Oncol. 1995;2:252–6.
18. De Ridder M, Sermeus AB, Urbain D, Storme GA. Metastases to the thyroid gland—a report of six cases. Eur J Intern Med. 2003;14:377–9.
19. Russell JO, Yan K, Burkey B, Scharpf J. Nonthyroid metastasis to the thyroid gland: case series and review with observations by primary pathology. Otolaryngol Head Neck Surg. 2016;155:961-8.
20. Cichon S, Anielski R, Konturek A, Barczyński M, Cichon W. Metastases to the thyroid gland: seventeen cases operated on in a single clinical center. Langenbecks Arch Surg. 2006;391:581-7.
21. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA. Metastasis to the thyroid gland. A report of 43 cases. Cancer. 1997;79:574-8.
22. Wood K, Vini L, Harmer C. Metastases to the thyroid gland: the Royal Marsden experience. Eur J Surg Oncol. 2004;30:583–8.

23. Saito Y, Sugitani I, Toda K, Yamada K, Fujimoto Y. Metastatic thyroid tumors: ultrasonographic features, prognostic factors and outcomes in 29 cases. Surg Today. 2014;44:55-61.

24. Papi G, Fadda G, Corsello SM, Corrado S, Rossi ED, Radighieri E, Miraglia A, Carani C, Pontecorvi A. Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. Clin Endocrinol (Oxf). 2007;66:565-71.

25. Calzolari F, Sartori PV, Talarico C, Parmeggiani D, Beretta E, Pezzullo L, Bovo G, Sperlongano P, Monacelli M, Lucchini R, Misso C, Gurrado A, D'Ajello M, Uggeri F, Puxeddu E, Nasi P, Testini M, Rosato L, Barbarisio A, Avenia N. Surgical treatment of intrathyroid metastases: preliminary results of a multicentric study. Anticancer Res. 2008;28:2885-8.

26. 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

27. Choi SH, Baek JH, Ha EJ, et al. Diagnosis of metastasis to the thyroid gland: comparison of core-needle biopsy and fine-needle aspiration. Otolaryngol Head Neck Surg. 2016;154:618–25.

28. Diaconescu MR, Costea I, Glod M, Grigorovici M, Diaconescu S. Unusual malignant tumors of the thyroid gland. Chirurgia. 2013;108:482-9.

29. Chung AY, Tran TB, Brumund KT, Weisman RA, Bouvet M. Metastases to the thyroid: a review of the literature from the last decade. Thyroid. 2012;22:258-68.

30. Zamora-Ros R. et al. Reproductive and menstrual factors and risk of differentiated thyroid carcinoma: The EPIC study. Int J Cancer. 2015;136:1218–27.

31. Joseph KR, Edirimanne S, Eslick GD. The association between breast cancer and thyroid cancer: a meta-analysis. Breast Cancer Res Tr. 2015;152:173–81.

32. Fei X, Christakos G, Lou Z, Ren Y, Liu Q, Wu J. Spatiotemporal Co-existence of Female Thyroid and Breast Cancers in Hangzhou, China. Sci Rep. 2016;6:2-11.

33. Mattavelli F, Collini P, Pizzi N, Gervasoni C, Pennacchioli E, Mazzaferro V. Thyroid as a target of metastases. A case of foregut neuroendocrine carcinoma with multiple abdominal metastases and a thyroid localization after 21 years. Tumori. 2008;94:110-3.
34. Heffess CS, Wenig BM et Thompson LD. Metastatic renal cell carcinoma to the thyroid gland: a clinicopathologic study of 36 cases. Cancer. 2002; 95:1869–78.
35. Chen JY, Chen IW, Hsueh C, Chao TC, Gao BR, Lin JD. Synchronous diagnosis of metastatic cancer to the thyroid is associated with poor prognosis. Endocr Pathol. 2015;26:80-6.
36. 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.
37. Chen H, Nicol TL et Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland. World J Surg. 1999;23:177-80.

Figure legends:

Figure 1: T2-weighted sagittal magnetic resonance image demonstrating the deposits in C5 and T4. They appeared confined to the vertebral body with no evidence of vertebral body collapse.

Figure 2: Computer tomography of the thorax demonstrating a small (5mm in diameter) subpleural nodule within the anterior left upper lobe, which remained unchanged since the previous scan.

Figure 3: Haematoxylin and eosin stain at x100 magnification demonstrating solid nests of atypical epithelial cells among normal colloid-filled thyroid follicles.

Figure 4: Immunoperoxidase for thyroglobulin showing the solid nests, which are negative while the follicles are positive, including a small trapped microffolicle within the larger nest of metastatic cells. TTF-1, calcitonin, were equally negative; however, Ck7 was negative and synaptophysin was expressed by the majority of cells. This raises the possibility of a carcinoma with neuroendocrine features.

Figure

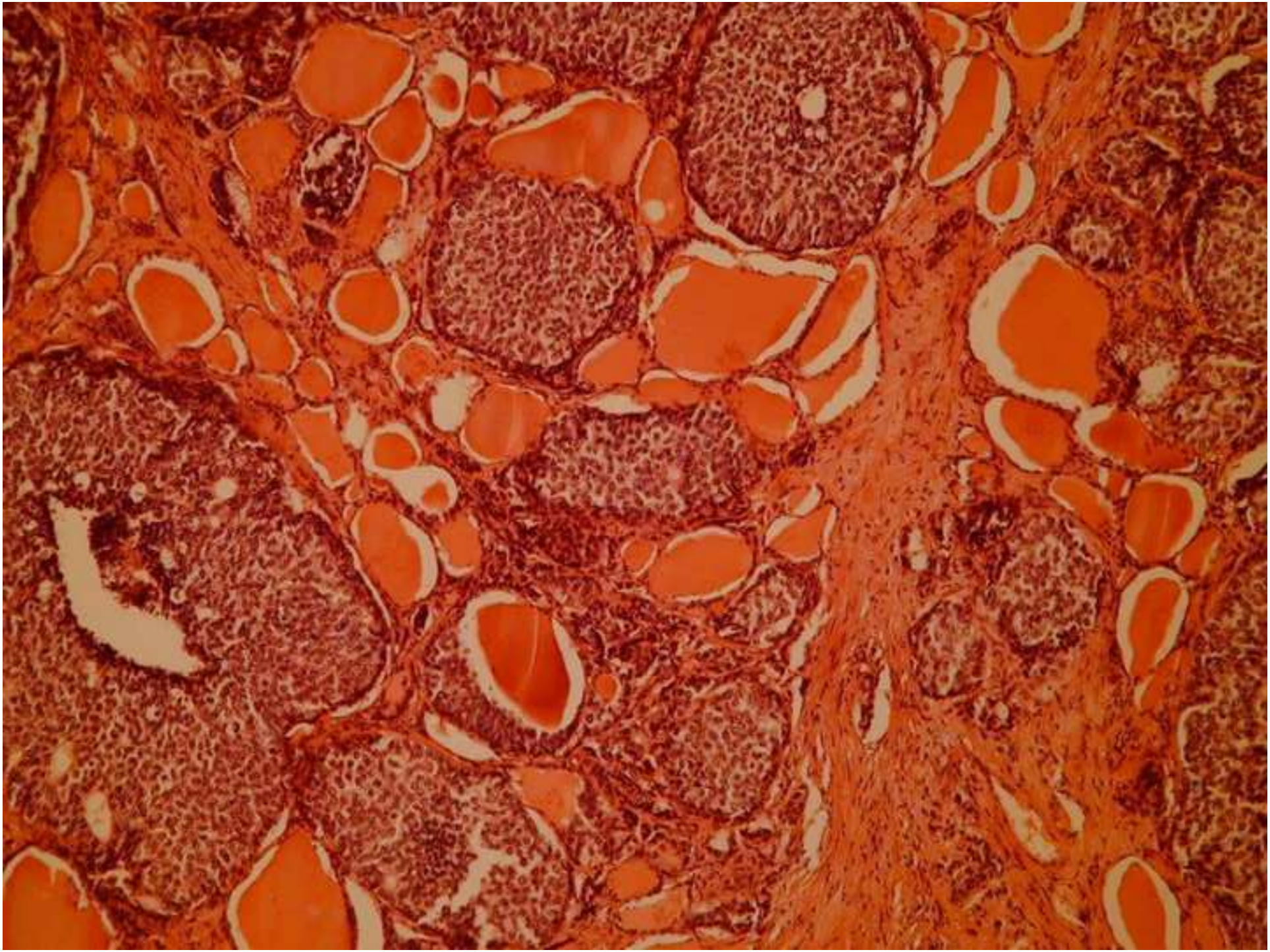
Click here to download Figure Figure 1.png

Figure

Click here to download Figure Figure 2.png

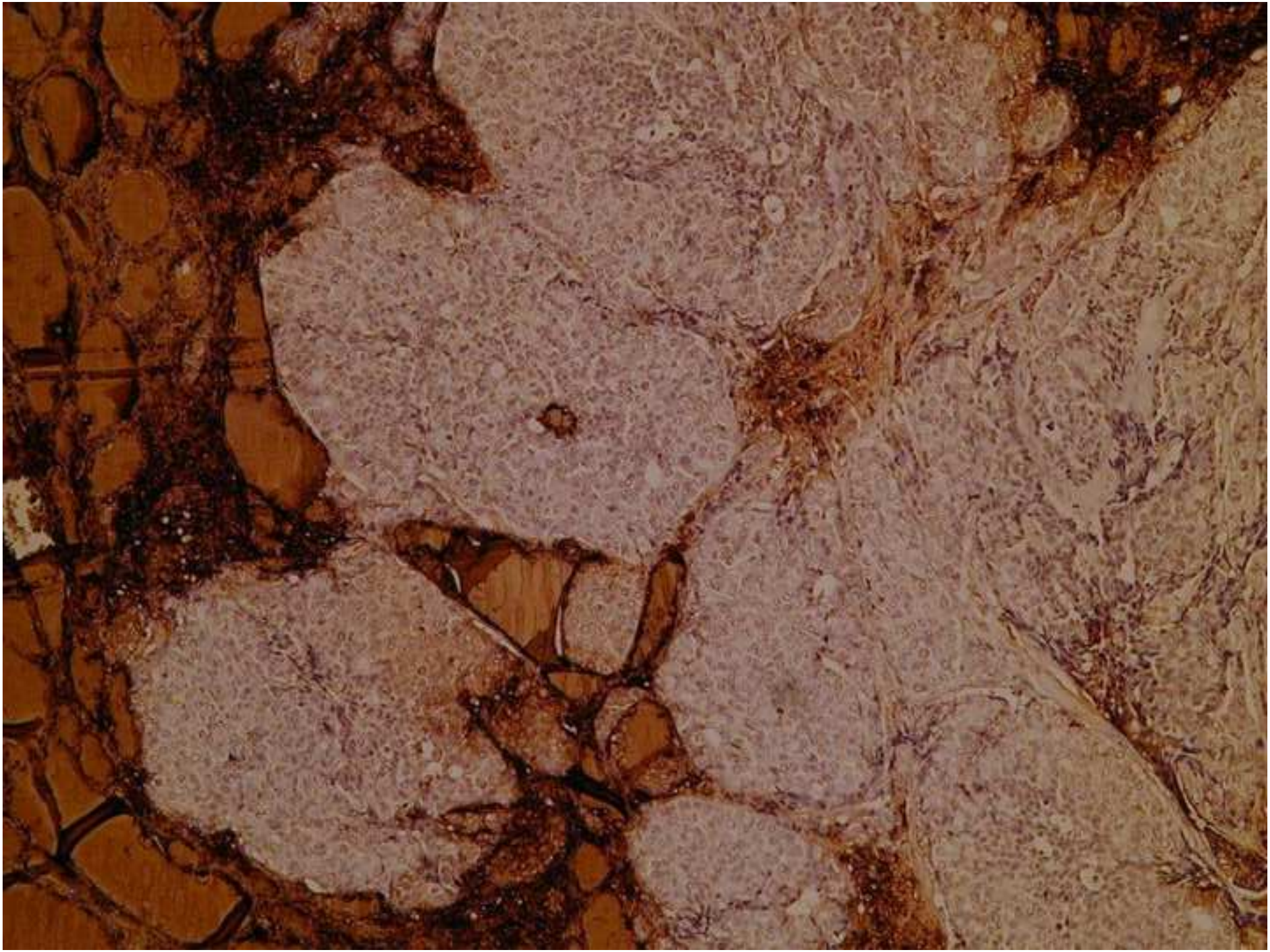
Figure

Click here to download Figure Figure 3.jpg



Figure

Click here to download Figure Figure 4.jpg



Click here to access/download

Supplementary Material

CAREchecklist-English-AP.pdf