Aberrant Intrathyroid Tissue: a Report of Intrathyroid Lymph Node Metastasis and a Review of Literature

Michael S Shawky¹ · Win Meyer-Rochow^{1,2}

Received: 16 March 2016 / Accepted: 13 January 2017 / Published online: 20 January 2017
© Association of Surgeons of India 2017

Abstract Aberrant histological elements have been infrequently reported to exist within the intact thyroid gland. In addition to distant metastases to the thyroid, a number of ectopic tissue rests and unusual cysts have been described within the thyroid gland. In this article, we report the presence of a true intrathyroid lymph node and describe the first reported case of intrathyroid lymph node metastasis of papillary thyroid cancer. Other reported aberrant intrathyroid tissues, possible pathophysiology, diagnostic features and surgical implications are also discussed.

Keywords Thyroid nodule · Thyroid neoplasms · Papillary carcinoma · Metastatic lymph node · Hurthle cell

Introduction

Histologically, the thyroid gland is composed of functional units known as follicles which contain colloid and are surrounded by follicular cells, the calcitonin producing parafollicular cells also known as C-cells, a delicate connective tissue stroma and vascular elements [1]. Any other histological elements detected inside the thyroid gland are unusual and are considered aberrant. Such aberrant intrathyroid tissue

may be classified into either non-metastatic or metastatic. Non-metastatic intrathyroid tissue may be either ectopic rests of non-thyroid tissue or unusual cysts; both are thought to result from dysembryogenesis. Existence of intrathyroid metastasis however always indicates dissemination from a distant primary malignancy. In this article, we aim to review unusual non-thyroidal components that have been described in the thyroid gland and discuss their surgical importance. The index case which prompted this review will be described as a case report and—to the best of our knowledge—appears to be the first published case of an intrathyroid lymph node metastasis.

Case Presentation

A 63-year-old female patient presented with a slowly enlarging thyroid mass over the preceding 5 years. She complained of mild dyspnoea without any other symptoms or signs of compressive effects from her thyroid. On examination, the mass was firm, and mobile with deglutition. There were no palpable cervical lymph nodes (LNs). Biochemically, she was euthyroid. Sonography showed multiple thyroid nodules, the largest was replacing the right lobe, measuring $4 \times 3.4 \times 4.6$ cm, containing solid and more cystic areas with some internal vascularity and an incomplete capsule. Another two smaller nodules were also seen in the right lobe; inferiorly and close to the isthmus. Sonographically, there were no pathologically enlarged LNs. Fine needle aspiration cytology (FNAC) showed a population of Hurthle cells with occasional nuclear grooves and inclusions and concluded a thyroid aspirate of Bethesda 4 category ‘suspicious for Hurthle cell neoplasm versus oncocyctic variant of papillary thyroid cancer (PTC)’. After discussing risks and benefits of the surgery, a routine diagnostic right hemithyroidectomy was performed. The final

✉ Michael S Shawky
michael.s.shawky@gmail.com; michael.shawky@alexmed.edu.eg

¹ Department of Surgery, Waikato Hospital, Hamilton, New Zealand

² Waikato Clinical Campus, Faculty of Medical and Health Science, University of Auckland, Auckland, New Zealand

histopathology reported triple pathology—Hurthle cell adenoma (HCA) in the main nodule, Hashimoto's thyroiditis and a 5-mm focus of PTC (Fig. 1). In addition, a well-circumscribed lesion was detected at the periphery of the main nodule, between the adenomatous part (HCA) on the one side and the normal colloid filled follicles on the other side; confirming its intrathyroid location. The latter lesion showed an intact fibrous capsule and subcapsular lymphocytic areas with multiple germinal centres, conforming to lymph node histology. Intracellularly, there were also papillae and nests of atypical polyhedral cells with vesicular nuclei, inclusions and grooves, indicating PTC metastasis, however, without evidence of extra capsular extension (Fig. 2). Based on these data, the patient was diagnosed with stage III PTC on account of her age and regional metastatic lymphadenopathy.

Literature Review

Several different aberrant intrathyroid tissue elements have been previously described in the literature including intrathyroid lymph nodes, salivary tissue, parathyroid tissue, thymic tissue, congenital cysts and metastasis from another tissue of origin.

Ectopic Intrathyroid Tissue Rests

Intrathyroid Lymph Node

While the presence of LN tissue inside the parotid gland is a normal and usual finding [2], a similar finding within the thyroid seems to be exceedingly rare and has been reported only once in a 40-year-old Egyptian female with multinodular goiter [3]. To the best of our knowledge, our case represents the first reported case of a metastatic intrathyroid LN. The findings here

Fig. 1 Mid power H&E stained section, showing normal thyroid follicle (Thy) and focus of micro papillary thyroid cancer (mPTC)

Fig. 2 Low power H&E stained section, showing Hurthle cell adenoma (Hu) on the left side, colloid filled follicles (Co) on the right side and a lymph node (LN) in the middle; showing an intact fibrous capsule (Ca), lymphocytes with germinal centres (black arrows) and papillary thyroid cancer metastasis (white arrow)

do not represent lymphocytic infiltration of the thyroid parenchyma; rather, a true LN demonstrating germinal centres and an intact capsule, lying entirely within thyroid tissue and showing features of papillary thyroid carcinoma metastasis. A possible explanation to such finding would be a deviation from the normal developmental process [4]; possibly, aberrant extension of the juglo-axillary lymph sacs or aberrant sprouting of the lymphatic primordials in the cervical region during the 8–9th weeks of gestation. The existence of an intrathyroid LN could potentially cause the FNAC to contain lymphocytes and be justifiably misinterpreted as Hashimoto's disease or lymphoma, hence, the importance of routine sonographic guidance for all FNACs, even for well palpable nodules. Furthermore, the presence of a metastatic intrathyroid LN, with a small differentiated thyroid cancer as in our case, should be regarded as N1a if the neck is node negative. This would otherwise up-stage the disease to stage III in patients older than 45 years with a potential impact on the prognosis and management plan according to the revised American Thyroid Association 2009 guidelines [5].

Intrathyroid Salivary Tissue

While there have been several reports of 'Warthin-like' tumour of the thyroid gland which histologically mimic salivary Warthin tumours [6], only one report of intrathyroid ectopic benign salivary tissue exists [7]. The thyroid gland may also be a potential implantation site for migrating cells from a salivary malignancy [8]. Thus, an extreme caution should be exercised when interpreting a cytological aspirate containing salivary or salivary-like components from a thyroid nodule, in

order to distinguish between the aforementioned three pathologies which have varying strategies of management.

Intrathyroid Parathyroid Tissue

Ectopic parathyroid adenomas have been detected in 1.4–22% of the hyperparathyroidism (HPT) patients; of which 0.7–18% have been reported to be intrathyroid [9–12]. Occasionally, intrathyroid parathyroid tissues (ITPs) have been identified as the cause of persistent or recurrent HPT [13]. High resolution neck ultrasound has been reported to have 80% positive predicting value for detecting ITP adenomas [14], and nuclear medical imaging is able to help guiding the side for hemithyroidectomy in HPT patients after failed neck exploration [15]. Though blind thyroid lobectomy after negative neck exploration has also been successfully practised and recommended by some surgeons [16], its value has been questioned by others on the account of the generally low incidence of ITPs [10]. There have also been ten reports of intrathyroid parathyroid carcinoma (IT-PC) [17]. An IT-PC may represent a diagnostic pitfall while assessing a patient with a thyroid nodule without clinical or biochemical evidence of HPT, as it is not usually diagnosed preoperatively by routine FNA cytology and neck US [18].

Intrathyroid Thymic Tissue

In a large autopsy study, the frequency of ectopic thymic tissue has been found to be only 1% [19]. True occurrence of thymic tissue within the thyroid gland is exceedingly rare with very few cases reported to date [20, 21]. Although Segni et al. [22] has described the sonographic pattern of ITTT, preoperative diagnosis is usually difficult especially as the FNAC is usually unhelpful, and the diagnosis may only be correctly reached on histopathological examination of the excised specimen [23]. In their report, Megremis et al. [24] mentioned that the ITTT was often inappropriately addressed as a true thyroid nodule and recommended a cervical magnetic resonance imaging in suspected cases. If the diagnosis is made preoperatively, management is controversial. Some recommend surgical resection for fear of neoplastic transformation [24, 25]. However, on the account of its role in immunity development and regulation and the benign course observed in some studies, a more conservative approach has also been argued [22, 26].

Unusual Intrathyroid Cysts

Simple, haemorrhagic, colloid and degenerative cysts have been well-recognised as common types of intrathyroid cysts. However, other unusual types of intrathyroid cysts have also been reported in the literature. We have identified 23 cases of intrathyroid branchial cleft cysts (BCC), ten cases of

intrathyroid thyroglossal duct cyst (TGC), eight cases of intrathyroid epidemoid cysts (EDC) and three cases of intrathyroid dermoid cyst [27–30]. These unusual pathologies should be always kept in mind when evaluating a patient with thyroid nodule for several reasons. First, identification of squamous epithelial cells or mucoid material in FNAC from the thyroid gland should raise a suspicion about the possibility of intrathyroid BCC, TGC or EDC and prompt further workup. Differentiation may be helped by the history or presentation, as infection of the cyst occurs more commonly in BCC and by clinical examination, as TGC tend to be in a midline position while BCC tend to be lateral. Pathological examination, however, is more helpful; presence of ciliated columnar cells or abundant inflammatory infiltrate suggests TGC; detection of subepithelial lymphoid tissue points to BCC, while a cellular smear composed entirely of nucleated and anucleated squamous cells is in favour of EDC [27, 31, 32]. Secondly, these intrathyroid lesions should be surgically addressed, not only as a part of thyroid nodule management but also because these lesions are recognised to have a risk of malignancy [33–35]. Furthermore, if the diagnosis of intrathyroid TGC is confirmed or highly suspected, a TGT should be thoroughly searched intraoperatively as its presence necessitates a sistrunk operation along with lobectomy [36]. Likewise, surgery is the treatment of choice for intrathyroid dermoid cysts because of infection risk associated with them in general [37].

Metastasis to Thyroid

Metastasis to the thyroid seems to be rare with a frequency of 2.2% among patients who underwent thyroidectomy for malignancy [38]. Autopsy studies, however, have reported a considerably variable prevalence ranging from 1.25% in random patient autopsies to as high as 24% in those with metastatic neoplasms [39]. In addition, Mayo clinic experience may suggest a rising incidence of metastasis to the thyroid, detecting 19 and 43 cases in the years 1980–1985 and 1985–1994, respectively [40, 41]. It is uncertain whether such figures are due to an increased detection rate, selection bias or actual increase in incidence. Renal cell carcinoma has been reported in most series to be the commonest primary [42]. However, breast and lung cancer were reported in other series to be more common primary cancers [43, 44]. Metastasis to the thyroid may represent both diagnostic and therapeutic challenges. The metastatic focus may be very small and clinically undetectable. In one series, 8 out of the 22 patients were incidentalomas [43]. Even when clinically detectable, diagnosis may not be reached on cytological grounds. In their series, Wood et al. [42] reported that FNAC confirmed the diagnosis only in 5 out of the 12 patients presenting with thyroid mass. This may be due to the inability to distinguish anaplastic or clear cell thyroid cancer from metastatic poorly differentiated malignancy [42, 43]. In addition, the interval between detection of the primary

malignancy and its thyroid secondary has been reported to be variably long, as long as 26 years [40]. Prognostically, the appearance of metastatic lesions in the thyroid gland is an ominous sign with death of the patients often occurring soon after the diagnosis of thyroid gland metastasis has been made [45]. Hence, any thyroid nodule in a patient with a history of malignancy should be viewed with suspicion and must be thoroughly investigated with FNA, preferably in conjunction with immunohistochemistry and sonography [46, 47].

Conclusions and Recommendations

Aberrant non-metastatic histological elements, although rare, may exist in the thyroid gland. This should be considered when evaluating a thyroid nodule with atypical radiological and cytological features. A true lymph nodal structure can exist inside the thyroid gland and may be affected by metastasis from papillary thyroid cancer. Given their rarity, the pathophysiology of some of these aberrant tissues is not completely understood and requires further research. The fact that metastasis to the thyroid may occur even decades after detection of the primary malignancy calls for a thorough and meticulous investigation of any thyroid nodule in a patient with a past history of malignancy.

Acknowledgements We would like to acknowledge Dr. Dushy Samarasinghe for helping us with the pathology photos.

Compliance with Ethical Standards

Conflict of Interest Authors declare that they have no conflict of interest.

References

- Ritchie JE, Balasubramanian SP (2014) Anatomy of the pituitary, thyroid, parathyroid and adrenal glands. *Surgery (Oxford)* 32(10):499–503
- Bialek EJ, Jakubowski W, Zajkowski P, Szopinski KT, Osmolski A (2006) US of the major salivary glands: anatomy and spatial relationships, pathologic conditions, and pitfalls. *Radiographics* 26(3):745–763
- Abdou AG, Aiad HA (2009) Intrathyroid lymph node tissue in multinodular goiter in an Egyptian female. *Saudi Med J* 30(4):558–560
- Zadvinskis DP, Benson MT, Kerr HH, Mancuso AA, Cacciarelli AA, Madrazo BL et al (1992) Congenital malformations of the cervicothoracic lymphatic system: embryology and pathogenesis. *Radiographics* 12(6):1175–1189
- Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ et al (2009) Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 19(11):1167–1214
- Ludviková M, Ryška A, Korabečná M, Rydlová M, Michal M (2001) Oncocytic papillary carcinoma with lymphoid stroma (Warthin-like tumour) of the thyroid: a distinct entity with favourable prognosis. *Histopathology* 39(1):17–24
- Cameselle-Teijeiro J, Varela-Durán J (1994) Intrathyroid salivary gland-type tissue in multinodular goiter. *Virchows Arch* 425(3):331–334
- Chen H, Nicol TL, Udelsman R (1999) Clinically significant, isolated metastatic disease to the thyroid gland. *World J Surg* 23(2):177–181
- Roy M, Mazeh H, Chen H, Sippel RS (2013) Incidence and localization of ectopic parathyroid adenomas in previously unexplored patients. *World J Surg* 37(1):102–106
- Goodman A, Politz D, Lopez J, Norman J (2011) Intrathyroid parathyroid adenoma: incidence and location—the case against thyroid lobectomy. *Otolaryngol Head Neck Surg* 144(6):867–871
- Zerizer I, Parsai A, Win Z, Al-Nahhas A (2011) Anatomical and functional localization of ectopic parathyroid adenomas: 6-year institutional experience. *Nucl Med Commun* 32(6):496–502
- Phitayakorn R, McHenry CR (2006) Incidence and location of ectopic abnormal parathyroid glands. *Am J Surg* 191(3):418–423
- Chen CL, Lin SH, Yu JC, Shih ML (2014) Persistent renal hyperparathyroidism caused by intrathyroidal parathyroid glands. *J Chin Med Assoc* 77(9):492–495
- Abboud B, Sleilaty G, Ayoub S, Hachem K, Smayra T, Ghorra C et al (2007) Intrathyroid parathyroid adenoma in primary hyperparathyroidism: can it be predicted preoperatively? *World J Surg* 31(4):817–823
- French R, Maitra RK, Kurup V Sesta-MIBI scans, can they predict intrathyroid parathyroid adenoma? *Int J Surg* 10(8):S32
- Papavramidis T, Polyzonis M, Pliakos I, Michalopoulos N, Goutzamanis G (2014) Intrathyroid parathyroid adenoma: should preoperative imaging tests help guiding scheduled operation. Report of Two Cases *Annals Thyroid Res* 1(2):23–26
- Vila Duckworth L, Winter WE, Vaysberg M, Moran CA, Al-Quran SZ (2013) Intrathyroidal parathyroid carcinoma: report of an unusual case and review of the literature. *Case Rep Pathol* 2013:198643
- Lee KM, Kim EJ, Choi WS, Park WS, Kim SW (2014) Intrathyroidal parathyroid carcinoma mimicking a thyroid nodule in a MEN type 1 patient. *J Clin Ultrasound* 42(4):212–214
- Lavini C (2009) In: Lavini C, Moran CA, Morandi U, Schoenhuber R (eds) *Thymus gland pathology: clinical, diagnostic and therapeutic features*. Springer, Milan
- Gimm O, Krause U, Wessel H, Finke R, Dralle H (1997) Ectopic intrathyroidal thymus diagnosed as a solid thyroid lesion: case report and review of the literature. *J Pediatr Surg* 32(8):1241–1243
- Huang Y, Zheng S, Xiao X (2013) Ectopic intrathyroidal thymus in children: two case reports and review of the literature. *J Pediatr Surg Case Rep* 1(11):386–390
- Segni M, di Nardo R, Pucarelli I, Biffoni M (2011) Ectopic intrathyroidal thymus in children: a long-term follow-up study. *Horm Res Paediatr* 75(4):258–263
- Lignitz S, Musholt TJ, Kreft A, Engel R, Brzezinska R, Pohlenz J (2008) Intrathyroidal thymic tissue surrounding an intrathyroidal parathyroid gland, the cause of a solitary thyroid nodule in a 6-year-old boy. *Thyroid* 18(10):1125–1130
- Megremis S, Stiakaki E, Tritou I, Bonapart IE, Tsilimigaki A (2008) Ectopic intrathyroidal thymus misdiagnosed as a thyroid nodule: sonographic appearance. *J Clin Ultrasound* 36(7):443–447
- Weigensberg C, Daisley H, Asa S, Bedard Y, Muilen JB (1990) Thyroid thymoma in childhood. *Endocr Pathol* 1(2):123–127
- Halnon NJ, Cooper P, Chen DYH, Boechat MI, Uittenbogaart CH (2011) Immune dysregulation after cardiothoracic surgery and incidental thymectomy: maintenance of regulatory T cells despite impaired thymopoiesis. *Clin Dev Immunol* 2011:11

27. Chung EJ, Baek SK, Youn SW, Kim CH, Lee JH, Jung KY (2010) A case of bilateral intrathyroidal branchial cleft cyst in a newborn. *J Pediatr Surg* 45(1):E1–E4
28. Perez-Martinez A, Bento-Bravo L, Martinez-Bermejo MA, Conde-Cortes J, de Miguel-Medina C (2005) An intra-thyroid thyroglossal duct cyst. *Eur J Pediatr Surg* 15(6):428–430
29. Palombini L, Cozzolino I, Luigi S, Pifano A (2015) Fine needle cytology of intrathyroid epidermoid cyst. *Diagn Cytopathol* 43(5):390–391
30. Raxith SR, Preethi SP, Kavitha PP (2014) A rare case of intra-thyroid dermoid cyst in a middle aged female. *IJAR* 4(8)
31. Johnston R, Wei JL, Maddalozzo J (2003) Intra-thyroid thyroglossal duct cyst as a differential diagnosis of thyroid nodule. *Int J Pediatr Otorhinolaryngol* 67(9):1027–1030
32. Chen KT (2007) Fine-needle aspiration cytology of epidermoid cyst of the thyroid: report of a case and review of seven cases. *Diagn Cytopathol* 35(2):123–124
33. Nakano A, Mishima K, Katase N, Ueyama Y (2015) A case of squamous cell carcinoma arising from branchial cleft cyst. *J Oral Maxillofac Surg* 73(4):781–785
34. Forest V-I, Murali R, Clark JR (2011) Thyroglossal duct cyst carcinoma: case series. *J Otolaryngol Head Neck Surgery* 40(2):151–156
35. Ge P, Luo Y, Fu S, Ling F (2009) Recurrent epidermoid cyst with malignant transformation into squamous cell carcinoma. *Neurol Med Chir (Tokyo)* 49(9):442–444
36. North JH Jr, Foley AM, Hamill RL (1998) Intrathyroid cysts of thyroglossal duct origin. *Am Surg* 64(9):886–888
37. Görür K, Talas D, Özcan C (2005) An unusual presentation of neck dermoid cyst. *Eur Arch Otorhinolaryngol* 262(4):353–355
38. Ménégau F, Chigot J eds (2001) Secondary malignant tumors of the thyroid gland. *Annales de Chirurgie*. Elsevier
39. Kim AY, Park SB, Choi HS, Hwang JC (2007) Isolated thyroid metastasis from renal cell carcinoma. *J Ultrasound Med* 26(12):1799–1802
40. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA (1997) Metastasis to the thyroid gland: a report of 43 cases. *Cancer* 79(3):574–578
41. Smith SA, Gharib H, Goellner JR (1987) Fine-needle aspiration: usefulness for diagnosis and management of metastatic carcinoma to the thyroid. *Arch Intern Med* 147(2):311–312
42. Wood K, Vini L, Harmer C (2004) Metastases to the thyroid gland: the Royal Marsden experience. *Eur J Surg Oncol* 30(6):583–588
43. Kim TY, Kim WB, Gong G, Hong SJ, Shong YK (2005) Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. *Clin Endocrinol* 62(2):236–241
44. Michelow PM, Leiman G (1995) Metastases to the thyroid gland: diagnosis by aspiration cytology. *Diagn Cytopathol* 13(3):209–213
45. Lam KY, Lo CY (1998) Metastatic tumors of the thyroid gland: a study of 79 cases in Chinese patients. *Arch Pathol Lab Med* 122(1):37–41
46. Porcell AI, Hitchcock CL, Keyhani-Rofagha S (2000) Use of immunohistochemistry in fine needle aspiration of thyroid nodules in patients with a history of malignancy: a report of two cases. *Acta Cytol* 44(3):393–398
47. Yoon JH, Kim E-K, Kwak JY, Moon HJ, Kim GR (2013) Sonographic features and ultrasonography-guided fine-needle aspiration of metastases to the thyroid gland. *Ultrasonography* 33(1):40–48