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CASE REPORT

Cutaneous metastasis of papillary thyroid carcinoma ten years after thyroidectomy, without evidence of other sites: a case report and literature review

Metástase cutânea de carcinoma papilífero da tireoide dez anos após tireoidectomia, sem evidências de outros sítios: relato de caso e revisão de literatura

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ABSTRACT

The annual incidence of thyroid tumors in Brazil from 2023 to 2025 is estimated at 16,660 cases, with Papillary Thyroid Carcinoma (PTC) being the most common histological type. PTC typically metastasizes to lymph nodes, but cutaneous metastasis is rare. We present a case of cutaneous metastasis occurring ten years after initial treatment for PTC. A 50-year-old male, diagnosed with multinodular goiter in 2014, underwent total thyroidectomy and neck dissection after fine-needle aspiration (FNA) consistent with Papillary Thyroid Carcinoma (Bethesda system, 2022). Pathology confirmed multicentric PTC without extrathyroidal extension. Subsequently, the patient received radioiodine therapy. In 2015, the patient developed lymph node metastasis and underwent further surgery. In 2024, at age 60, he presented with a cutaneous nodule on his neck. Excision confirmed PTC metastasis, with immunohistochemistry showing positivity for markers CK-7, TTF-1, PAX-8, and Tg, and molecular analysis revealing a $BRAF^{V600E}$ mutation. Postoperative evaluation showed no other metastases. Cutaneous metastasis of PTC can present in various forms, making diagnosis challenging. Elevated thyroglobulin levels often correlate with metastasis, but our patient had consistently low levels. The $BRAF^{V600E}$ mutation is associated with more aggressive PTC. Histological and molecular analyses are essential for diagnosis, and prolonged surveillance is necessary due to the possibility of late recurrence.

Keywords: Skin neoplasms; Thyroid neoplasms; Prognosis.

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RESUMO

A incidência anual de tumores de tireoide no Brasil entre 2023 e 2025 é estimada em 16.660 casos, com o Carcinoma Papilífero da Tireoide (CPT) sendo o tipo histológico mais comum. O CPT geralmente apresenta disseminação para os linfonodos, porém metástases cutâneas são raras. Apresentamos um caso de metástase cutânea ocorrido dez anos após o tratamento inicial para CPT. Um homem de 50 anos, diagnosticado com bócio multinodular em 2014, foi submetido à tireoidectomia total e esvaziamento cervical após punção aspirativa por agulha fina (PAAF) sugerir Carcinoma Papilífero da Tireoide (Sistema Bethesda, 2022). Análise histopatológica confirmou CPT multicêntrico sem extensão extratireoidiana. Posteriormente o paciente recebeu terapia com iodo radioativo. Em 2015, o paciente desenvolveu metástase linfonodal e passou por nova cirurgia. Em 2024, aos 60 anos, apresentou um nódulo cutâneo no pescoço. Após a exérese confirmou-se metástase de CPT, com imuno-histoquímica mostrando positividade para os marcadores CK-7, TTF-1, PAX-8 e Tg e análise molecular revelando uma mutação $BRAF^{V600E}$. A avaliação pós-operatória não mostrou outras metástases. A metástase cutânea de CPT pode se apresentar de várias formas, tornando o diagnóstico desafiador. Níveis elevados de tireoglobulina frequentemente correlacionam-se com metástase, mas nosso paciente manteve níveis consistentemente baixos. A mutação $BRAF^{V600E}$ está associada a um CPT mais agressivo. As análises histológicas e moleculares são essenciais para o diagnóstico, e a vigilância prolongada é necessária devido à possibilidade de recidiva tardia.

Palavras-chave: Neoplasias cutâneas; Neoplasias da glândula tireoide; Prognóstico.

Introduction

The estimated incidence of thyroid tumors in Brazil for each year of the three years from 2023 to 2025 is 16,660 cases, corresponding to a risk of 7.68 per 100,000 inhabitants[1]. Well-differentiated carcinomas represent approximately 85% of malignancies of the thyroid gland. Papillary thyroid carcinoma (PTC) is the most common histological type and tends to spread predominantly to lymph nodes[2]. We present the case of a patient with cutaneous metastasis ten years after initial treatment for PTC.

Case report

This case report was approved by the local Research Ethics Committee under protocol number 02839212.4.0000.5149. The patient authorized the publication of their medical history.

A 50-year-old man with a multinodular goiter discovered during a routine appointment was seen at a Head and Neck Surgery Service in December 2014. Thyroid ultrasound (US) at this time showed a hypoechoic nodule (2.2 x 1.4 x 1.7 cm) with exuberant central and peripheral vascularization, continuous with the upper left pole of the gland, another solid hypoechoic nodule (1.3 x 0.9 x 0.9 cm) with microcalcifications on left lobe, and a third isoechoic nodule (3.0 x 2.0 x 2.4 cm) with regular contours, in the same lobe. Laboratory tests showed thyroid-stimulating hormone (TSH) 1.37 mUI/L (Normal range 0.3-5.0 mIU/mL), free T4 (FT4) 0.75 ng/dL (Normal range 0.75-1.80 ng/dL), and cytopathological diagnosis of the fine-needle aspiration (FNA) sample was positive for malignancy, consistent with Papillary Thyroid Carcinoma (Bethesda System, 2022).

Total thyroidectomy with neck dissection of left and right level VI and level VII was performed. The pathological examination revealed multicentric PTC with the larger lesion measuring 1.6 cm, follicular infiltrative subtype, without extrathyroidal extension, and no metastasis in nine cervical and mediastinal lymph nodes, T1 N0 M0 (TNM, 8 ed). Subsequently, radioactive iodine therapy (100 mCi) was administered.

During the follow-up in October 2015, an atypical lymph node in the left level III (1.8 x 0.7 cm) was seen in the US. FNAB was performed and revealed thyroglobulin (Tg) levels of 2367 ng/mL (Normal range 2-35 ng/mL). Cytology confirmed metastasis of PTC. The patient underwent a neck dissection of the left levels II-IV with the removal of 27 lymph nodes. Of these, two lymph nodes were positive for PTC metastasis, in level III (1.4 cm) and level IV (0.5 cm), without extranodal extension.

Regular follow-up in the subsequent years had no intercurrence and the patient had undetectable thyroglobulin levels. He returned to the clinic in July 2024 at the age of 60 complaining of a violet-colored, pedunculated, and painless nodule on the right paramedian cervical region, approximately five centimeters above the surgical scar, and therefore unrelated to it (Figure 1). Laboratory tests showed levels of anti-thyroglobulin (anti-Tg) 1.3 IU/mL (Normal range < 40 IU/mL), Tg 0.10 ng/mL, and TSH 4.35 mIU/L. The lesion was excised and the pathological examination revealed a 0.5 x 0.4 cm lesion consistent with PTC neoplasm infiltrating the dermis, without angiolymphatic invasion. Immunohistochemical (IHC) analysis was positive for markers cytokeratin-7 (CK-7), thyroid transcription factor-1 (TTF-1), PAX-8, Tg (staining), and negative for calcitonin. Molecular analysis revealed a somatic mutation in the $BRAF^{V600E}$ gene (next-generation sequencing) with a variant allele frequency (VAF) of 14%. Postoperative laboratory tests showed TSH 3.84 mIU/L; FT4 1 ng/dL; Tg < 0.14 ng/mL and anti-Tg < 1 IU/mL. A new investigation with neck US and chest and abdominal computed tomography (CT) showed no signs of other metastatic sites.

Figure 1. Violet-colored, pedunculated, painless nodule in the right paramedian cervical region.

Discussion

Cutaneous metastases of PTCs are rare[3,4]. Two large studies have demonstrated a risk of less than 1.0%[3,4]. Høie et al. (1988)[4] identified six cases among 731 patients and Dinneen et al. (1995)[3] reported one case among 1,800. The diagnosis of these lesions can be challenging due to the varied clinical presentation. They may appear as plaques, single or multiple nodules, painful or painless, flesh-colored or pigmented[5]. From a histological analysis, the presence of psammoma bodies is a typical feature, and with the aid of IHC, reactivity to TTF-1 and Tg (staining) generally is observed[5,6]. However, markers such as CK-7 and PAX-8 have also been added in other analyses[7,8], including our patient.

A search was conducted in the PubMed and Embase databases using the following strategy: ("Papillary thyroid cancer" OR "thyroid cancer" OR "thyroid carcinoma") AND ("skin metastasis" OR "skin metastases" OR "cutaneous metastases" OR "dermal metastases") resulting in a total of 358 articles. Duplicates, non-English language studies, reviews, or studies not focused on cutaneous metastasis of PTC were excluded. From this search, a table (Table 1) was created with 16 case reports of patients who presented cutaneous metastases of PTC without evidence of other distant metastases[7-21].

Monitoring thyroglobulin levels can be particularly useful for the diagnosis and follow-up of metastases. Among the reports included in our study, thyroglobulin or anti-thyroglobulin levels were elevated in six of seven cases that reported them[11,13-15,18,21], and in a large review of 238 studies up to 2013 on metastases of well-differentiated thyroid carcinomas, thyroglobulin levels were elevated in 93% of the cases that reported them[22]. Despite this, our patient consistently presented low levels of both markers over the years, with no other clinically or radiologically detectable metastatic foci.

Molecular biology plays a promising role in understanding the profile of neoplasms and in providing individualized therapeutic approaches. The $BRAF^{V600E}$ mutation appears to be the main one associated with classic subtype PTC (51.00%) and the follicular infiltrative subtype PTC (24.10%)[23]. The literature has shown that this genetic alteration may indicate a more aggressive disease[24], with larger rates of recurrence and disease persistence[23,24]. Other alterations have also been described in the literature, such as RET gene rearrangement[25,26] and RAS point mutations[26]. In our patient, a somatic mutation in the $BRAF^{V600E}$ was identified, with a VAF of 14%.

There is some divergence regarding which subtype of well-differentiated thyroid carcinoma is most commonly associated with cutaneous metastases. Some studies have mentioned a higher overall prevalence of distant metastases caused by PTC, but among metastatic cases, follicular thyroid carcinomas (FTC) showed disproportionately higher rates of spread to the skin, 42%[22,27], which may

Table 1. Patients who presented cutaneous metastases of PTC without evidence of other distant metastases.

Author	Age/Sex	Histology/ Primary tumor staging	Site of cutaneous metastasis	Interval	Other metastases	Thyroglobulin	IHC/Molecular biology	Previous treatments	Approach to metastasis	Outcomes	Follow-up
Reusser et al.[7]	95/M	NM	Neck	6 years	No	NM	TTF-1 and CK-7 positive PSA negative (past of prostate cancer)	Partial thyroidectomy	Biopsy (NS)	NM	NM
Soylu et al.[8]	65/F	PTC	Neck	5 years after initial treatment	No	NM	Tg positive (staining) PAX-8 positive TTF-1 positive	TT/ Neck dissection/ Iodine therapy (NS)	Excision	NM	NM
Soylu et al.[8]	83/F	PTC	Neck (on thyroidectomy scar)	3 years after initial treatment	No	NM	Tg positive (staining) PAX-8 positive TTF-1 positive	TT/ Iodine therapy (NS)/ Levothyroxine at suppressive doses (NS)	Excision	NM	NM
Shinohara et al.[9]	71/M	PTC Extracapsular invasion	Neck (near the thyroidectomy scar)	3 years after thyroidectomy	No	NM	NM	TT/ Sacrifice of the right recurrent laryngeal nerve/ Regional neck dissection/ Iodine therapy (NS)	Excision	No evidence of recurrence during the follow-up	About 3 years
Mahalingam et al.[10]	75/M	PTC	Scalp	4 years	No	NM	Tg positive (staining) TTF-1 positive	Thyroidectomy/ Iodine therapy (NS)	Biopsy (punch)	Mass extending into the superior mediastinum indicative of mediastinal involvement during the follow up. The patient was being evaluated for suitability for iodine therapy.	NM

Ronga et al.[11]	59/F	PTC	Neck (on thyroidectomy scar)	19 years	No	After initial treatment: Tg 0.2 ng/mL, anti-tg negative 19 years later: Tg 17.8 ng/mL, anti-Tg negative 3 months after excision of the lesion: Tg 0.76 ng/mL, anti-Tg negative	NM	TT/ Levothyroxine at suppressive doses (100 µg/day)/ Iodine therapy (100 mCi)	Excision	No distant metastases	NM
Chakraborty et al.[12]	40/F	PTC Follicular variant	Scalp	At diagnosis	No	NM	NM	Total thyroidectomy	NM	NM	NM
Ward et al.[13]	76/M	PTC T3N1M0	Neck	5 years	LN	During the treatment, Tg ranged from 186 ng/mL to 401 ng/mL	Tg positive (staining) NIS positive	Thyroidectomy/Neck dissection/Levothyroxine at suppressive doses (NS)/ Iodine therapy (200 mCi + 300 mCi)	Biopsy (NS)/ Iodine therapy (400 mCi = total dose of 900 mCi during the treatment/ Recombinant TSH	The patient developed progressive respiratory distress due to tracheal invasion. Death 3 months after discovery of the skin lesions. The authors suggest that a positive NIS indicates a poorer response to iodine.	3 months
Onoda et al.[14]	74/F	PTC LN involvement	Neck	24 months	LN	At primary diagnosis: Tg 4,340 ng/ml	Tg positive (staining)	TT/ Neck dissection/ Partial resection of the superior vena cava and the esophageal wall, and shaving of the left recurrent laryngeal nerve	Docetaxel 25 mg/m2 (once a week)	The skin lesion disappeared after the 14th course had been completed. The chemotherapy was terminated because of an adverse effect of grade 3 peripheral neuropathy. No recurrent disease had been identified with TSH suppression at 45 months after the initial operation. The patient died because of an accident of causes unrelated to the disease itself or the adverse effects of chemotherapy.	7 weeks after the last course of chemotherapy

Kwon et al.[15]	55/F	PTC pT3N0M0	Neck	3 years (first cutaneous metastasis)	No	After thyroidectomy: Tg 0.08 mcg/L, anti-Tg 93.9 UI/L During the follow-up: Tg 0.08 mcg/L After the diagnosis of the first metastasis: Tg 0.08 mcg/L, anti-Tg 74.6 UI/L	Tg positive (staining) TTF-1 positive	TT/ Central neck dissection/ Iodine therapy (5.5 GBq)	Excision	No evidence of recurrence during the follow-up	4 months
Nguyen et al.[16]	70/F	PTC	Abdomen	Not mentioned	No	NM	Tg positive (staining) TTF-1 positive	Hemithyroidectomy/ Iodine therapy (NS)	Biopsy (punch)	NM	NM
Rodríguez-Lomba et al.[17]	58/F	PTC pT3N1Mx	Neck (near the thyroidectomy scar)	About 5 years	LN	NM	Tg positive (staining) TTF-1 positive	TT/ Percutaneous ethanol injection (PEI)/ Iodine therapy (NS)	Biopsy (punch)	The metastasis was most likely secondary to the previous PEI	NM
Iñiguez-Ariza et al.[18]	48/M	PTC pT1aN1b	Neck	12 years (first cutaneous metastasis)	LN	Tg ranged from 2 to 42 ng/mL during 15 years of treatment	NM	Near-total thyroidectomy/ Neck dissection/ Ethanol ablation/ Iodine therapy (150 mCi + 188 mCi = total dose of 338 mCi)	Excision/ Mohs Surgery (MS)	No evidence of recurrence during the follow-up	20 months
Tiao et al.[19]	72/F	PTC No LN involvement	Neck (on thyroidectomy scar)	About 15 years	No	NM	Tg positive (staining) TTF-1 positive	TT/ Iodine therapy (NS)	Excision	CT of the neck and chest showed no local recurrence at the original site of PTC. A left parotid gland mass measuring 1.4 cm was noted on the CT, which was concerning for possible nodal metastasis (FNAB was indeterminate). The patient opted to monitor the mass.	NM

Choi et al.[20]	44/F	PTC	Neck (on thyroidectomy scar)	10 years	No	At the discovery of the metastasis: Tg: 1.00 ng/ml, anti-Tg: < 20 U/ml	$BRAF^{V600E}$ and TERT promoter C228T mutations	TT/ Levothyroxine (150 mcg/day)/ Iodine therapy (120 mCi)	Biopsy (punch)/ Excision/ Iodine therapy (100 mCi = total dose of 220 mCi during whole treatment)	NM	NM
Thewjitcharoen et al.[21]	60/M	PTC Lymphatic invasion No LN involvement	Neck	3 years	No	At the discovery of the metastasis: Tg increased from 17.2 ng/mL to 62.8 ng/mL	Tg positive (staining)	TT/ Levothyroxine at suppressive doses (NS)/ Iodine therapy (NS)	Neck reoperation (NS)	The patient was in stable condition with persistent biochemical incomplete response at the last follow-up. Cutaneous implantation PTC metastasis following the FNA was diagnosed.	NM
Our case	60/M	PTC Follicular variant pT1m, pN0	Neck (near the thyroidectomy scar)	10 years	LN	Tg was undetectable after thyroidectomy. At the discovery of the cutaneous metastasis: Anti-Tg: 1,3 UI/mL e Tg 0,10 ng/mL After the metastasis excision: Tg < 0,14 ng/mL e anti-Tg < 1 UI/mL	Tg positive (staining) TTF-1 positive PAX-8 positive Calcitonin negative $BRAF^{V600E}$ mutation (VAF 14%)	TT/ Neck dissection/ Iodine therapy (100 mCi)	Excision	No radiological or biochemical signs of recurrence or involvement of other sites.	6 months

Caption: Anti-Tg = Anti-thyroglobulin; CK-7 = Cytokeratin 7; CT = Computerized tomography; F = Female; FNAB = Fine-needle aspiration biopsy; IHC = Immunohistochemical; LN = Lymph node; M = Male; NIS = Sodium iodide symporter; NM = Not mentioned; NS = Not specified; PAX-8 = Paired box 8; PEI = Percutaneous ethanol injection; PSA = Prostate-specific antigen; PTC = Papillary thyroid carcinoma; Tg = Thyroglobulin; TT = Total thyroidectomy; TTF-1 = Thyroid transcription factor-1; VAF = Variant allele frequency. *Interval: Interval between primary tumor and cutaneous metastasis

be related to the greater tendency for hematogenous dissemination of this subtype[22]. However, other studies identified PTC as the main cause of cutaneous metastases, followed by the follicular carcinoma, 47.79% *vs*. 30.15%[28] and 41.00% *vs.* 28.00%[6]. The main poor prognostic factors for these patients seem to be follicular histology, older age, and distant metastases. Age is directly related to tumor differentiation and low avidity for radioiodine therapy[29]. A poor response to this treatment impacts both overall survival and disease-specific survival[30]. The TNM/AJCC staging system does not adequately predict the risk of recurrence in differentiated thyroid carcinomas. The 2015 American Thyroid Association (ATA) guideline proposed a correlation between recurrence risk and primary tumor characteristics, classifying patients into low, intermediate, or high-risk categories. However, individual risk varies within these groups and depends on histology, multifocality, genotype, and extrathyroidal extension. Our patient can be considered low-risk, with an estimated recurrence risk of 4% to 6%[31].

The scalp appears to be the main region of the skin affected by metastases, according to descriptions by some authors[5,6,27,28], in contrast to our review, in which the neck was affected in 81.25% of the cases. The average age at diagnosis of metastasis in 136 patients with cutaneous dissemination of thyroid tumors was 63.13 years, with a mean interval of 48.27 months after the primary diagnosis according to Sciscent[28]. In our review, the average age at diagnosis of metastasis was 65.31 years, with a mean interval of 76 months after the discovery of the primary cancer. This difference may be related to the less aggressive behavior of the neoplasms included in our study, which mostly had no lymph node metastases at the time of the primary diagnosis and did not develop other distant metastases beyond the skin. Despite the indolent behavior, there are reported cases of cutaneous metastases presenting decades after initial treatment[20], indicating the need for prolonged surveillance.

A limitation of this study is the inability to access the primary tumor specimen, as the patient underwent surgery more than ten years ago.

Conclusion

Cutaneous spread of PTC is rare. The differential diagnosis of the lesions is challenging; however, it can be aided by histological and immunohistochemical analysis. Development of molecular biology is promising and useful for understanding the neoplasm profile and for an individualized therapeutic approach, but high cost remains a significant limitation for its widespread use. In our case and for the majority of patients, PTC behaves indolently, but it can present with skin metastases many years after the primary diagnosis.

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Author's Contributions:

We describe contributions to the papers using the taxanomy (CRediT) provided above: *Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing*: A de A Sousa; LFM da Rocha; BFR Teixeira; CA Ribeiro. *Project administration, Supervision & Writing – original draft*: A de A Sousa; LFM da Rocha; BFR Teixeira; CA Ribeiro. Validation & Software: A A de A Sousa; LFM da Rocha. *Resources & Funding acquisition*: None. *Data curation & Formal Analysis*: A de A Sousa; BFR Teixeira.

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