

Scalp metastases from thyroid carcinomas: review of clinical and pathological features*

Tiroid karsinomlarına bağlı skalp metastazları: Klinik ve patolojik özelliklerin incelenmesi

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Abstract

Thyroid carcinomas reported to metastasize to scalp were reviewed and discussed with histopathological, prognostic and diagnostic aspects. All cases of scalp metastasis from thyroid carcinomas published in PubMed and MedLine were reviewed and the data of all patients were analyzed to obtain information about the patient demographics, histologic type of thyroid carcinoma, additional cutaneous sites, time interval between the diagnosis of the primary tumor and the diagnosis of scalp metastasis. The literature review revealed 38 cases of scalp metastasis from thyroid carcinoma. The most common histologic type was follicular carcinoma (46%), followed by papillary (35%), medullary (16%) and anaplastic carcinomas (3%). Scalp as a distinct cutaneous area has a rich dermal vasculature and is a site of various primary and metastatic neoplasms. Metastases to scalp from thyroid carcinomas are extremely rare and demonstrate advanced disease and poor prognosis. A scalp nodule may be a diagnostic challenge if it is the presenting symptom of an occult neoplasm with low metastatic potential. Awareness of the histopathological characteristics, and cutaneous metastatic patterns of thyroid carcinomas can help us to overcome the difficulty in diagnosis of such lesions.

Keywords: Metastasis, scalp, thyroid carcinoma.

Özet

Bu derlemede literatürde skalp metastazı yaptığı bildirilen tiroid karsinom vakaları taranarak tanısız, histopatolojik ve prognostik özellikleri ile tartışıldı. PubMed ve MedLine servislerinde yayınlanan tüm tiroid karsinomlarına bağlı skalp metastazı vakaları araştırıldı ve hastaların yaş ve cinsiyetine, tiroid karsinomunun histolojik tipine, skalp dışında cilt alanlarına metastazlarına ve primer tümörün teşhisiyle metastaz teşhisi arasındaki süreye ilişkin verilere ulaşmak için hasta bilgileri incelendi. Literatürde günümüze kadar bildirilen 38 vaka bulundu. Bildirilen vakalarda en sık görülen histolojik tip foliküler karsinom (%46) idi. Papiller karsinom, medüller karsinom ve anaplastik karsinom vakalarının oranları ise sırasıyla %35, %16 ve %3 olarak bulundu. Özel bir cilt alanı olan skalp zengin bir damar ağına ve kanlanmaya sahip olup çeşitli primer veya metastatik tümörlerin odağı olabilir. Tiroid karsinomlarına bağlı skalp metastazları oldukça nadir olup ilerlemiş hastalığa ve kötü prognoza işaret eder. Düşük metastatik potansiyele sahip gizli bir neoplazmın ilk belirtisi olarak çıkabilen bir skalp nodülünün teşhisi oldukça güç olabilir. Tiroid karsinomlarının histopatolojik özelliklerinin ve cilt metastazı kalıplarının bilinmesiyle bu gibi lezyonların tanısına daha kolay ulaşılabilir.

Anahtar sözcükler: Metastaz, skalp, tiroid karsinomu.

Thyroid carcinoma represents 1% to 1.5% of all cancer cases reported annually and accounts for 57% of all deaths caused by endocrine malignancies.^[1] Well-differentiated thyroid carcinomas including papillary and follicular carcinoma are the most common thyroid malignancies comprising approximately 70% and 10% respectively, of all cases. Scalp as a distinct cutaneous area has a rich dermal vascula-

ture and is a site of various primary and metastatic neoplasms. Different visceral malignancies such as cancers of lung, breast, thyroid, colon, kidney, adrenal glands and larynx can metastasize to scalp. Metastases to scalp from thyroid carcinomas are extremely rare and demonstrate advanced disease and poor prognosis. Such lesions may indicate treatment failure or alternatively they may be the

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initial manifestation of an asymptomatic occult neoplasm of the thyroid gland.^[2] Metastatic scalp lesions can vary in appearance and might be misdiagnosed as benign or primary skin tumors. Therefore a high index of suspicion is necessary to reach the exact diagnosis. The diagnosis of the metastatic lesion and the primary tumor can be challenging particularly in the presence of occult disease. The histological appearance of scalp lesion is identical to the primary tumor but in some cases immunohistochemical studies are needed to differentiate the tissue of origin.

An extensive search of the literature was performed to reveal the reported cases of scalp metastases from thyroid carcinomas. Thirty-eight cases were found and classified according to histologic types. Patient demographics, time interval between the diagnosis of scalp lesion and the primary tumors and additional sites of cutaneous metastases were noted. Herein, thyroid carcinomas reported to metastasize to scalp were discussed with histopathologic, prognostic and diagnostic aspects.

Overview

Cutaneous metastases from internal malignancies are rare and often a marker for advanced disease with poor prognosis.^[2] Most commonly the neoplasms metastasizing to cutaneous areas are melanomas, cancers of colon, lungs and breast. Cutaneous metastasis from thyroid carcinoma is rare. Dahl et al.^[2] reported 43 cases of thyroid carcinoma with skin metastasis in their review of the literature between 1964 and 1997. Papillary thyroid carcinoma (PTC) was the most common histologic type representing 41% of cases. In contrast Koller et al.^[3] reported that follicular thyroid carcinoma (FTC) is more likely to have cutaneous metastases. Scalp was the most common site of cutaneous metastasis in both reports. In the literature review up to date we found 38 cases of scalp metastases from thyroid carcinoma (Table 1). Follicular thyroid carcinoma is the most common histologic type representing 46% of cases followed by PTC at 35%, with medullary thyroid carcinoma (MTC) contributing 16% of cases. Only 1 case of anaplastic carcinoma was reported contributing 3% of all cases of scalp metastasis from thyroid carcinomas. It can be inferred that FTC has a greater tendency than other thyroid carcinomas to metastasize to scalp as a distinct cutaneous area. The propensity of thyroid carcinoma skin metastases to localize to the head and neck region is documented in the majority of cases and may relate to local vascular factors essential for the highly complex nature of metastasis formation (initial tumor

recruitment of local vasculature, followed by angiogenic switch: the tumor establishes its own vascular network through the secretion of various angiogenic factors).^[4] The rich dermal capillary network of the scalp may facilitate the entrapment of the tumor cell emboli from the circulation and then provide the environment for successful formation of metastatic foci.^[4]

Metastatic thyroid carcinoma of scalp may be a diagnostic challenge. Scalp metastasis of thyroid carcinoma appears as solitary or multiple reddish nodules. Metastatic lesions display identical histological features with the primary tumors. Complex, branching papillary structures with fibrovascular cores and psammoma bodies typical for PTC can be recognized. Cuboidal cells that have nuclear grooves, inclusions and eosinophilic intranuclear inclusions are suggestive of follicular carcinoma. Immunohistochemical methods offer a unique opportunity to determine the tissue origin of scalp metastasis.

Immunohistochemical Methods

Identification of the primary origin of a scalp lesion suspected to be a metastatic focus is not always possible by histopathological examination. Various types of tumors can have similar morphology and architectural pattern with the presumed metastatic lesion. Immunohistochemical (IHC) methods evaluating expression of specific proteins are useful diagnostic tools to reveal the site of the primary tumor. Discrimination between carcinomas and melanomas is possible by analysis of cytokeratin-7, cytokeratin-20, and S-100 expression and evaluation of antibodies against p63, B72.3, calretinin, and CK5/6 could differentiate metastatic carcinoma from primary skin adnexal tumors. In the context of thyroid carcinoma metastases, immunoperoxidase staining for thyroglobulin, a 670 kd glycoprotein synthesized in the cytoplasm of follicular thyroid epithelium is an important method to determine the tissue of origin.^[2] Thyroglobulin has been demonstrated to be present in normal thyroid tissue, goiters, thyroiditis and thyroid carcinomas originating from follicular cells. Thyroglobulin expression is specific to carcinomas of thyroid follicular cell derivation, including both papillary and follicular types, but is not found in lung carcinomas. Therefore, IHC staining for thyroglobulin can be used to differentiate follicular thyroid carcinomas from MTC and to exclude lung carcinomas.^[5] Calcitonin expression can be identified by immunoperoxidase staining in the normal C cells of the thyroid and in 95% to 97% of medullary carcinomas. Additional neuroendocrine markers such as

Table 1. Details of 38 cases of scalp metastases from thyroid carcinomas reported in literature.

Author	Number of case	Age/Sex	Histotype	Interval*	Additional sites of cutaneous metastasis
Ibanez et al. ^[31]	1	67/M	Medullary	2	None
Auty ^[16]	1	41/M	Follicular	2	Face,neck,thorax
Horiguchi et al. ^[7]	2	62/M 70/F	Papillary Papillary	3 11	None Abdomen, shoulder, arm, thigh, cheek Abdomen, shoulder, arm, thigh, cheek
Ordenez & Saman ^[32]	1	51/F	Medullary	4	None
Doutre et al. ^[12]	1	59/F	Papillary	NA	None
Pavlidis et al. ^[17]	3	85/F 63/F 55/F	Follicular Papillary Follicular	0 3 0	None None Upper arm, pelvis
Elgart et al. ^[8]	1	62/M	Papillary	3	None
Tronnier et al. ^[23]	1	66/F	Follicular	-2 [†]	None
Vives et al. ^[24]	1	71/F	Follicular	9	None
Caron et al. ^[21]	1	66/M	Follicular	0	None
Ruiz de Erenchun et al. ^[25]	1	57/F	Follicular	6	None
Toyota et al. ^[26]	1	72/M	Follicular	1	None
Lissak et al. ^[20]	2	79/F 58/F	Fol.micro.ca Fol.micro.ca	0 0	None None
Dahl et al. ^[2]	3	63/M 47/M 51/F	Papillary Papillary Anaplastic	7 1.3 0.5	Chest Face None
Koller et al. ^[3]	1	81/F	Fol.micro.ca	0	None
Cariou et al. ^[27]	1	57/F	Follicular	9	None
Smit et al. ^[10]	1	79/F	Pap.fol.var	0	None
Rodrigues&Ghosh ^[18]	1	42/M	Follicular	0	Forearm
Avram et al. ^[4]	1	63/M	Papillary	17	Face
Alwaheeb et al. ^[6]	3	46/M 34/M 71/F	Medullary Medullary Pap.fol.var	0 0 6	None Chest None
Kumar et al. ^[28]	1	68/M	Follicular	13	None
Quinn et al. ^[29]	1	57/M	Follicular	8	None
Niederkoher et al. ^[13]	1	76/F	Papillary	NA	None
Agarwal et al. ^[19]	1	55/F	Follicular	0	Forehead, neck
Cupisti et al. ^[15]	1	76/F	Follicular	18	None
Chakraborty et al. ^[11]	1	40/F	Pap.fol.var	0	None
Santarpia et al. ^[30]	1	54/F	Medullary	3	None
Nashed et al. ^[5]	1	56/M	Medullary	1	None
Aghasi et al. ^[9]	1	64/F	Papillary	2	None
Karabekir et al. ^[22]	1	82/F	Follicular	0	None

*Time between diagnosis of primary tumor and diagnosis of scalp metastasis; Pap.fol.var: papillary follicular variant; Fol.micro.ca: follicular microcarcinoma; [†]Cutaneous metastases preceded diagnosis of thyroid cancer by 2 years. NA: not available

synaptophysin, chromogranin and CD 56 can be identified by IHC staining to diagnose MTC metastases.^[6] Thyroid transcription factor-1 (TTF-1) is a 38 kd DNA binding protein, originally detected in follicular cells of the thyroid, thyroid C cells and subsequently in pneumocytes.

Anti-TTF-1 antibodies may help distinguish thyroid and pulmonary carcinoma from other types of carcinomas. Pulmonary neuroendocrine neoplasms can also be differentiated by this IHC method from neuroendocrine tumors of other tissues such as intestines and pancreas.

Papillary Carcinoma

Papillary thyroid carcinoma is the most common type of thyroid malignancy, accounting for 50% to 89% of all cases. It is frequently seen between the ages of 30 to 40 years and is more common in women with a female/male ratio of 3:1. Papillary carcinoma has an indolent course and the mortality rate is low.

These lesions can be more commonly encountered in patients with Gardner's syndrome, Cowden's syndrome and familial poliposis. Only 6% of papillary carcinomas are associated with familial syndromes.

Three categories are defined based on size of primary lesion. The tumors up to 1 cm size with no evidence of invasiveness through the thyroid capsule or cervical lymph node metastasis are defined as minimal, occult or microcarcinoma. These lesions are non-palpable and incidentally diagnosed during investigation of thyroidectomy specimens or autopsy examination. Intrathyroid tumors are greater than 1cm size but are confined to thyroid gland. The third category comprises extrathyroid tumors extending through the thyroid capsule and invading the surrounding tissues.

Papillary carcinoma has typical papillary formation and characteristic nuclear features. The fibrovascular stroma is lined by epithelial cells that have crowded oval nuclei with folded and grooved nuclear margins. The characteristic "psammoma" bodies are remnants of necrotic neoplastic cells which are observed as laminated calcium densities in 25% of cases. Prominent nucleoli account for the "Orphan Annie eye" appearance. Histologically papillary carcinoma may exhibit follicular component but the presence of papillary features indicates that the tumor will behave clinically as papillary carcinoma. Thus mixed papillary follicular carcinoma and follicular variant of papillary carcinoma are cited as the subtypes of papillary carcinoma. The histologic variants of papillary carcinoma with a more unfavorable prognosis include diffuse sclerosing and tall-cell variants.

Papillary carcinoma is highly lymphotropic. Early spread to intrathyroidal and cervical lymph nodes is common leading to multifocal disease often present in patients. Local invasion to trachea, pharynx, larynx, esophagus and strap muscles can occur in 10% of cases. However, distant metastasis of PTC is rare. Lung, bone and central nervous system are the most common sites of distant metastasis. Metastasis of PTC to skin is a very rare condition. Scalp, face, neck, shoulder, chest, arm, abdomen and thigh are the reported cutaneous areas involved in metastatic PTC.^[7,8] Scalp is the most frequent cutaneous site of metastasis in PTC.^[9]

The literature reported 13 cases of scalp metastasis from PTC (Table 1). The primary tumor was papillary carcinoma in ten cases and follicular variant of papillary carcinoma in three cases. Scalp lesion was the only presenting symptom in three cases.^[6,10,11] Data relating to the interval between the diagnosis of the primary tumor and scalp metastasis is not available in two cases.^[12,13] Scalp lesions occurred 1.3 to 17 years after the diagnosis of PTC in the remaining 9 cases reported.

Follicular Carcinoma

Follicular thyroid carcinoma is the second most common differentiated thyroid malignancy arising from the follicular cells of the thyroid gland and represent 10% of thyroid malignancies. It has a more aggressive nature than papillary carcinoma and the mortality rate is higher when compared to PTC. The mean age of presentation is 50 years. The incidence is higher in iodine-deficient and endemic goiter areas with a female predominance (female/male ratio: 3:1). The usual presentation is a painless solitary nodule in the thyroid gland. History of long standing goiter and recent rapid enlargement of the gland may accompany the findings.

The histological analysis of FTC reveals follicular arrays or solid islets of cells. The degree of tumor differentiation affects the overall architectural pattern. Cytology alone is usually not enough to differentiate between follicular adenoma and follicular carcinoma in the preoperative assessment. The most important criterion for the diagnosis of FTC is the demonstration of thyroid capsule invasion or vascular invasion. Follicular thyroid carcinomas can be categorized into two major groups according to degree of invasion to tumor capsule. Minimally invasive tumors invade into but not through the capsule. Invasion through the tumor or vascular invasion is typical for widely invasive tumors. Vascular invasion indicates poorer prognosis when compared to capsule invasion and some authors concluded that the term "minimally invasive" is appropriate for tumors with capsule invasion alone.

The major histopathological variants of FTC are oncocytic follicular carcinoma (Hürthle cell carcinoma) and clear cell carcinoma.^[14] Hürthle cell carcinoma (HCC) is considered a subtype of FTC. Hürthle cells appear as large follicular cells which are polygonal and contain eosinophilic cytoplasm. It has a higher incidence of distant metastasis than both PTC and non-Hürthle cell FTC.

Follicular thyroid carcinoma has a more aggressive course than PTC and it has a propensity for vascular invasion and hematogenous spread.^[3] Distant metastasis is also

more common in follicular carcinoma than papillary cancers and is associated with worse prognosis. Hematogenous metastases are more likely to occur to bones and lungs. The other common sites are brain, liver and adrenal glands in decreasing order of frequency. The occurrence of skin metastasis from FTC is extremely rare and scalp is the most affected area of metastases.^[15] Face, neck, chest, arm and pelvis are the other cutaneous sites of metastasis affected with scalp.^[16-19]

Eighteen cases of FTC metastasis to scalp were reported in the literature^[3,15-29] (Table 1). Two cases reported by Lissak et al.^[20] were follicular microcarcinoma revealed by solitary scalp lesions. The thyroid lesions of 0.4 and 0.5 cm size in the cases were unrecognized by ultrasonography and they were only detected at serial histological examination of thyroid glands removed during surgery. Koller et al.^[3] reported another case of solitary scalp metastasis from follicular microcarcinoma of thyroid gland as the presenting symptom in an 81-year-old woman. Immunohistochemistry was positive for thyroglobulin and the histopathology was notable for atypical clear cell neoplasm. Interestingly, examination of the resected thyroid gland revealed separate foci (<1 cm) for both papillary and follicular carcinoma but the clear cell features found in the follicular focus in the thyroid gland confirmed that the primary was follicular thyroid carcinoma. The presenting symptom was a scalp lesion in 7 cases.^[3,17,20-22] Metastases to scalp 1 to 18 years after the diagnosis of the primary FTC were reported in the literature (Table 1).

Medullary Carcinoma

Medullary thyroid carcinoma (MTC) is a rare neoplasm originating from the calcitonin-producing parafollicular C cells of the thyroid. Parafollicular C cells may also secrete carcinoembryonic antigen (CEA), prostoglandins and serotonin. Medullary thyroid carcinoma accounts for approximately 5-10% of all thyroid cancers and there is no predilection for male or female gender.^[30] It is the most aggressive type of well-differentiated thyroid carcinomas with 10-year overall survival rates of 40-50%. Sporadic or hereditary forms of MTC are known, hereditary neoplasms being associated with multiple endocrine neoplasia (MEN) syndromes IIA (Sipple syndrome) and IIB.

Grossly, the tumor is solid, firm and well-circumscribed with a gray cut surface. Most lesions are located in the middle and upper posterior portion of the thyroid gland where the C cells are highly concentrated. The histopathologic examination reveals sheets of infiltrating neoplastic cells

separated by collagen, amyloid and dense irregular calcification. The amyloid deposits represent aggregated calcitonin gene products that are pathognomonic for MTC. Immunohistochemical staining for the presence of calcitonin is necessary to diagnose MTC in case the histopathologic appearance mimics the morphology of other thyroid neoplasms.^[14]

Medullary thyroid carcinoma has tendency to have early metastasis to locoregional lymph nodes but hematogenous spread to liver, lungs and bone may occur.^[5] Cutaneous metastases from MTC are extremely rare and scalp is the most common site.^[6] The lesions are in the form of solitary or multiple nodules or papules with pinkish or blue color. Thirteen cases of cutaneous metastases from MTC were reported to date.^[5] Chest and neck are the other cutaneous areas of metastasis with scalp being the most common site. Six cases of scalp metastasis from MTC were reported in the literature.^[5,6,30-32] In five cases scalp was the only cutaneous site of metastasis and in one case chest wall was also involved. Alwaheeb et al.^[6] reported 2 cases of MTC presenting initially with scalp nodules. In the other 4 cases scalp lesions were detected 1 to 4 years after the diagnosis of primary MTC.

Anaplastic Carcinoma

Anaplastic carcinomas are one of the most aggressive malignancies with few patients surviving 6 months beyond initial presentation.^[14] It represents 5% of all thyroid carcinomas. History of a rapidly enlarging mass is usual. Severely necrotic areas in the specimen and macroscopic invasion of the surrounding tissues can be demonstrated.

Only 1 case of scalp metastasis from thyroid anaplastic carcinoma was reported to date.^[2] The metastatic lesion appeared 5 months after the diagnosis of thyroid anaplastic carcinoma on the left temple as 4x3 cm flesh-colored mass. The patient died 4 months later of metastatic disease.

Conclusion

Various primary and metastatic neoplasms can develop from scalp. A scalp nodule may be a diagnostic challenge if it is the presenting symptom of an occult neoplasm with low metastatic potential. Awareness of the histopathologic characteristics, and cutaneous metastatic patterns of thyroid carcinomas can help us to overcome the difficulty in diagnosis of such lesions.

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