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Anaplastic Thyroid Carcinoma, Evaluation of Clinical, Histopathological, and Immunohistochemical Features

Anaplastik Tiroid Karsinomlarının Klinik, Histopatolojik ve İmmünohistokimyasal Açıdan Değerlendirilmesi

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ABSTRACT

Background: Anaplastic thyroid carcinoma (ATC) is the most lethal but also the rarest thyroid cancer. Pathologic diagnosis can be challenging in this clinically and morphologically aggressive tumor. The main objective of this study is to evaluate the contribution of immunohistochemical (IHC) markers, especially epithelial markers, commonly used in the diagnosis of ATC. We also aimed to uncover ATC-related demographic data and determine its frequency among thyroid carcinomas.

Materials and Methods: A retrospective analysis was used to identify 13 cases of ATC in the pathology department of our institution. In addition to demographic data, all cases were evaluated for a history of multinodular goiter (MNG), the predominant pattern, the presence of concomitant differentiated/poorly differentiated thyroid carcinoma, invasion of surrounding structures, lymph node metastasis (LNM), and distant metastasis. The intensity of staining and percentage of tumor cells with TTF-1, thyroglobulin, PAX8, CAM5.2, vimentin, p53, Ki-67, CEA, and calcitonin antibodies were interpreted by IHC studies.

Results: The incidence of ATC was 0.77% (13/1.678). MNG was present in 46% of cases. LNM was observed in 62% and distant metastases in 46% of cases. Sixty-nine percent of patients died of the disease and the median survival was 5.7 months. An associated component of differentiated/poorly differentiated thyroid carcinoma was noted in 62% of the cases. The epithelioid pattern was the most common histologic subtype. On IHC analysis, the positivity rate was 54% for CAM5.2, 38% for TTF-1 and PAX8, and 31% for thyroglobulin.

Conclusion: In this study, we have shown demographic, clinical and histopathological data related to ATC. Because this tumor can have different morphologies, IHC studies are crucial for diagnosis, especially in small biopsies. We recommend the use of TTF-1, thyroglobulin, and CAM 5.2 in addition to PAX8 to confirm the diagnosis of ATC.

Keywords: Anaplastic thyroid carcinoma, immunohistochemistry, TTF-1, PAX8, thyroglobulin

ÖZ

Amaç: Anaplastik tiroid karsinomu (ATK) oldukça ölümcül ancak aynı zamanda en nadir görülen tiroid kanseridir. Klinik ve morfolojik açıdan agresif olan bu tümör patolojik açıdan tanı güçlüğü oluşturabilmektedir. Bu çalışmada amacımız ATK tanısında sık kullanılan başta epitelyal olmak üzere immünohistokimyasal (İHK) belirleyicilerin tanı üzerine olan katkısını değerlendirmektir. Ayrıca ATK ilişkili demografik verileri ortaya koymak ve tiroid kanserleri içinde görülme sıklığını belirlemeyi de hedefledik.

Gereç ve Yöntemler: Retrospektif özellikteki çalışmamızda kurumumuz patoloji bölümünde ATK tanısı konulan 13 olgu saptandı. Olgular demografik verileri yanı sıra multinodüler guatr öyküsü, tümörün baskın paterni, eşlik eden iyi/az diferansiye tiroid karsinomu varlığı, çevre yapılara invazyon, lenf nodu metastazı ve uzak metastaz açısından değerlendirildi. İHK çalışması ile TTF-1, tiroglobulin, PAX8, CAM5.2, vimentin, p53, Ki-67, CEA ve kalsitonin antikorlarının boyanma yaygınlığı ve yoğunluğu araştırıldı.

Bulgular: ATK'nın sıklığı %0,77 (13/1,678) olarak saptandı. Olguların %46'sında multinodüler guatr mevcuttu. %62'sinde lenf nodu metastazı, %46'sında uzak metastaz gözlendi. %69 olguda hastalığa bağlı ölüm geliştiği izlenmiş olup ortalama yaşam süresi 5,7 ay olarak bulundu. Eşlik eden diferansiye/az diferansiye tiroid kanseri %62 oranında saptandı. Histolojik alt tipler içinde en sık epiteloid patern izlendi. İHK çalışmalarda CAM5.2 ile %54, TTF-1 ve PAX8 ile %38, tiroglobulin ile %31 oranında pozitiflik saptandı.

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ÖZ

Sonuç: Çalışmamızda ATK ile ilişkili demografik, klinik ve histopatolojik veriler sunuldu. Bu tümör farklı morfolojiler gösterebileceği için İHK'sal çalışmalar özellikle küçük biyopsilerde tanıyı destelemekte oldukça faydalıdır. ATK tanısında PAX8 yanı sıra TTF-1, tiroglobulin ve CAM 5.2 kullanılmasını öneriyoruz.

Anahtar Kelimeler: Anaplastik tiroid karsinomu, immünohistokimya, TTF-1, PAX8, tiroglobulin

Introduction

Anaplastic thyroid carcinoma (ATC) is a rare but very aggressive tumor of the thyroid. It accounts for approximately 1-2% of all thyroid cancers. It is more common in older ages and demonstrates female predominance. ATC often arises in the setting of an abnormal thyroid gland (1,2). Although the etiology is unknown, the frequent coexistence of differentiated thyroid carcinoma (DTC)/poorly differentiated thyroid carcinoma (PDTC) areas in ATC suggests that high-grade/anaplastic transformation is involved in the etiology of these tumors. There are also publications showing that de novo development is also in question (2,3). Consistent with its aggressive behavior, ATC has a significantly higher mutation load than papillary thyroid carcinoma (PTC) and PDTC (2). TP53 and CTNNB1 mutations are detected at a high rate in ATC, which are 70-80% and 60-70% respectively. RAS (40-50%) and BRAF (10-15%) mutations may be also detected in ATC (4). Clinically, it presents with a rapidly growing mass in the neck. Other common symptoms are hoarseness, dysphagia, and vocal cord paralysis. In a majority of the cases, lymph node involvement and distant organ metastases are present at the time of diagnosis. The prognosis is dismal, with a mortality rate of more than 90% (1,2,5,6).

ATC is composed of undifferentiated cells that can be recognized as thyroid follicle cell origin by immunohistochemically (IHC) or ultrastructurally. According to the World Health Organization Classification of Endocrine Organ Tumors, it contains three main histological patterns: Sarcomatoid, giant cell, and epithelioid. Less frequently, paucicellular, angiomatoid, rhabdoid, lymphoepithelioma-like, and small cell variants have also been described (1,6).

IHC studies have an important role in the diagnosis of ATC and are commonly used to establish thyroid cell origin, especially in small biopsy materials. TTF-1, thyroglobulin, and PAX8 antibodies are frequently used for this purpose. The immunoreactivity of TTF-1 and thyroglobulin in ATC is controversial and generally not detected in most cases (2,7). PAX8 expression is maintained in approximately half of the ATC cases (6). Positive staining of cytokeratins, which is frequently used to support epithelial origin, supports the diagnosis of ATC, but negative staining does not exclude this diagnosis. The use of IHC is valuable in differentiating from other undifferentiated/anaplastic tumors such as metastatic carcinoma, lymphoma, malignant melanoma, and sarcoma (5,6).

In this study, we aimed to i) determine the frequency of ATC among thyroid carcinomas, ii) identify demographic data associated with this tumor, iii) evaluate the contribution of IHC markers to the diagnosis, iv) reveal possible different staining patterns of IHC markers in various histological patterns, and v) determine the presence of other thyroid tumors that may accompany.

Material and Methods

A total of 1.678 resected thyroid carcinomas were identified between January 2014 and April 2020 at the pathology clinic of our hospital. In the retrospective analysis, 13 ATC cases were found. Clinical, radiological, surgical, and pathology data were obtained using the electronic medical information system of our hospital. Resection materials were fixed in 10% buffered formaldehyde, 3.5 µ-thick sections were obtained after routine tissue processing and were stained with hematoxylin-eosin.

This retrospective study was approved by the Ethics Committee of University of Health Sciences Türkiye, Dışkapı Yıldırım Beyazıt Training and Research Hospital (88/11, 20.05.2020), and was carried out by the principles of the Declaration of Helsinki. In addition to demographic data such as age and gender, the patients were evaluated in terms of multinodular goiter (MNG) history, histological subtype, presence of accompanying DTC/PDTC, invasion of surrounding structures, lymph node metastasis, distant metastasis, and presence of BRAF mutation.

IHC staining was performed using a fully automated immunostaining device (Ventana Benchmark XT, Roche Diagnostics, USA). To block endogenous biotin activity, Ultraview Universal DAB Detection kit (Ventana Medical Systems, Roche Diagnostics, USA) was used. The antibodies applied in the study were TTF-1 [Ventana, 8G7G3/1, monoclonal, ready-to-use (RTU)], thyroglobulin (Cellmarque, 2H11+6E1, RTU), PAX8 (Cellmarque, MRQ-50, RTU), Cam 5.2 (Ventana, RTU), vimentin (Ventana, RTU), p53 (Ventana, Bp53-11, RTU), Ki-67 (Ventana, 30-8, RTU), CEA

(Cellmarque, monoclonal, RTU), and calcitonin (Cellmarque, SP17, RTU). Staining intensity (0: None staining, +1: Weak staining, +2: Moderate staining, +3: Strong staining) and percentage of positive cells for IHC markers were evaluated considering different components in the tumor. The immunohistochemical studies were not financially supported by any institution or organization.

BRAF mutation analysis was conducted in 4 cases from formalin-fixed paraffin-embedded tissue blocks, which were collected from our pathology medical database. Mutational status for BRAF was done by direct sequencing method. Exon 15 was checked for V600E, V600A, V600D, and V600K mutations.

Statistical Analysis

Statistical analysis was performed with the SPSS 25.0 package programme (SPSS Inc, Chicago, IL, USA). Only descriptive statistics were used to analyse the data. Mean, standard deviation, and range were used for continuous data analysis, whereas frequency and percentages were used for categorical variables.

Results

Clinico-pathological Features

The frequency of ATC in total thyroid cancers was 0.77% (13/1678). Among 13 cases, 5 were total thyroidectomy, 3 were excisional biopsy, 1 was lobectomy, and 4 were incisional biopsies. The mean age was 66.15 (range 47-78, standard deviation 11,39), and the female to male ratio was 1.17. Clinical and descriptive characteristics are shown in the table (Table 1).

Clinical examination revealed MNG in 46% (6/13) of cases. One case, who had MNG, was diagnosed with PTC 4 years ago and treated with radioactive iodine. At presentation, 62% (8/13) of cases had lymph node metastases, and 46% (6/13) had distant metastases. All patients with distant metastases had lung metastases. Follow-up data were available for all patients. Sixty-nine percent (9/13) of patients died of disease (DOD). Median overall survival was 5.7 months (range, 1 month-23 month). A history of DTC/PDTC and/or concurrent DTC/PDTC was found in 62% (8/13) of patients, including PTC (6/13), PDTC (1/13), and PTC+PDTC (1/13).

On histologic examination, more than one histologic subtype was found in 92% (12/13) of cases. Epithelioid subtype was the most common pattern, followed by sarcomatoid/spindle cell and giant cell patterns, respectively (Figure 1). In 38% (5/13) of cases, accompanying giant cell areas were detected as a minor component (<5%). Focal or diffuse necrosis, marked pleomorphism, and high mitotic rate (typical and atypical) were observed in all cases. Vascular invasion was observed in 69% (9/13) of cases, perineural invasion in 54% (7/13), and invasion into the surrounding muscle tissue in 38% (5/13) (Figure 2). Skin invasion was noted in 15% (2/13) and invasion of the submandibular gland in 7.7% (1/13) of all cases. In four cases, with the clinical request, BRAF status was evaluated by Sanger sequencing. No BRAF mutation was detected.

Table 1. Demographics and clinicopathological features of anaplastic thyroid carcinoma

Case	Age	Sex	History of MNG	Procedure type	Distant metastasis	Lymph node metastasis	Survival, months	Predominant pattern	ATC associated with DTC/PDTC
1	54	F	-	L	-	-	DOD, 3 months	Epithelioid	PTC
2	71	M	+	EB	-	+	DOD, 4 months	Sarcomatoid	PTC
3	75	F	-	IB	-	-	DOD, 11 months	Epithelioid	-
4	76	F	+	IB	Lung	-	DOD, 4 months	Sarcomatoid	-
5	66	F	+	EB	Lung, liver, surrenal	-	DOD, 1 month	Sarcomatoid	PDTC
6	76	F	-	TT	-	+	Alive, 13 months	Sarcomatoid	-
7	56	M	+	TT	-	+	DOD, 14 months	Epithelioid	PTC+PDTC
8	48	M	+	TT	-	+	Alive, 11 months	Sarcomatoid	PTC
9	63	M	-	TT	Lung	-	DOD, 3 months	Rhabdoid	PTC
10	47	M	-	IB	Lung	+	Alive, 12 months	Epithelioid	-
11	78	F	-	IB	Lung, liver	+	DOD, 1 month	Epithelioid	-
12	73	M	+	EB	-	+	DOD, 23 months	Epithelioid	PTC
13	77	F	-	TT	Lung	+	DOD, 1 month	Epithelioid	PTC

M: Male, F: Female, MNG: Multinodular goiter, L: Lobectomy, EB: Excisional biopsy, IB: Incisional biopsy, TT: Total thyroidectomy, DOD: Death of disease, ATC: Anaplastic thyroid carcinoma, DTC: Differentiated thyroid carcinoma, PTC: Papillary thyroid carcinoma, PDTC: Poorly differentiated thyroid carcinoma

Immunohistochemical Findings

Of the antibodies used to support thyroid cell origin, 38% (5/13) were positive for TTF-1 and 31% (4/13) for thyroglobulin. Staining with TTF-1 was often higher than 10% and staining intensity was weak to moderate. In all cases where immunoreactivity with thyroglobulin was detected, the percentage of staining was less than 5% and weak. PAX8 was positive in 38% (5/13) of cases. In PAX8 positive cases, all showed more than 10% and usually more than half of the tumor cells were stained. Fifty-four % (7/13) of cases were positive with CAM5.2. An epithelioid component was present in cases that positive staining with TTF-1, PAX8, and CAM5.2 was detected (Figure 3). The results of immunostaining with epithelial markers are shown in the table (Table 2).

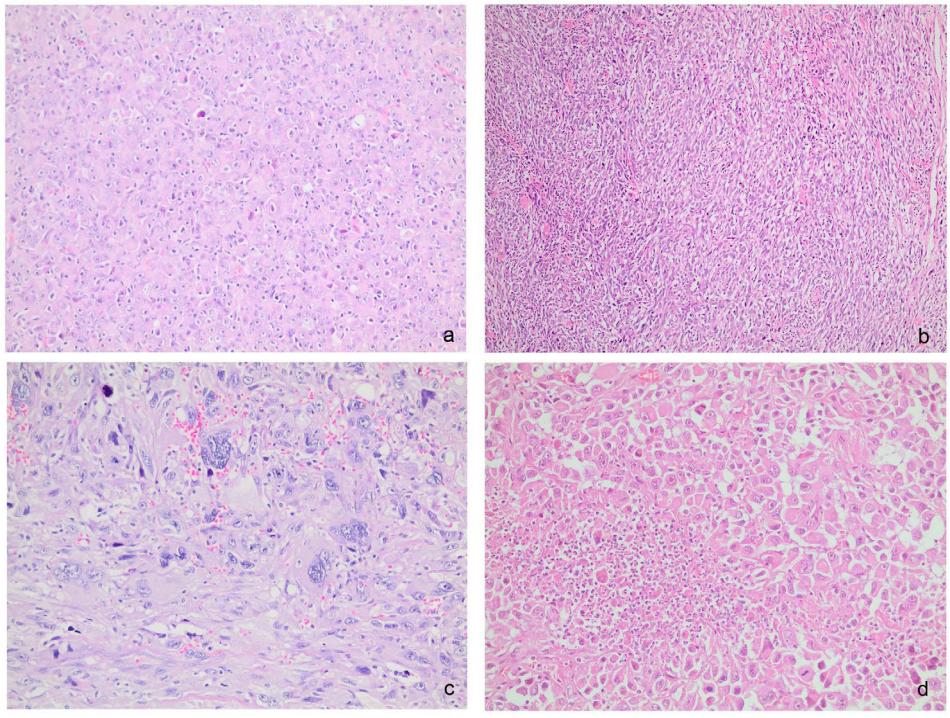

Figure 1. Histologic features of anaplastic thyroid carcinoma. Anaplastic thyroid carcinoma may show **a)** epithelioid, **b)** sarcomatoid, **c)** giant cell-rich, **d)** rhabdoid features (hematoxylin and eosin, X100, a-d)

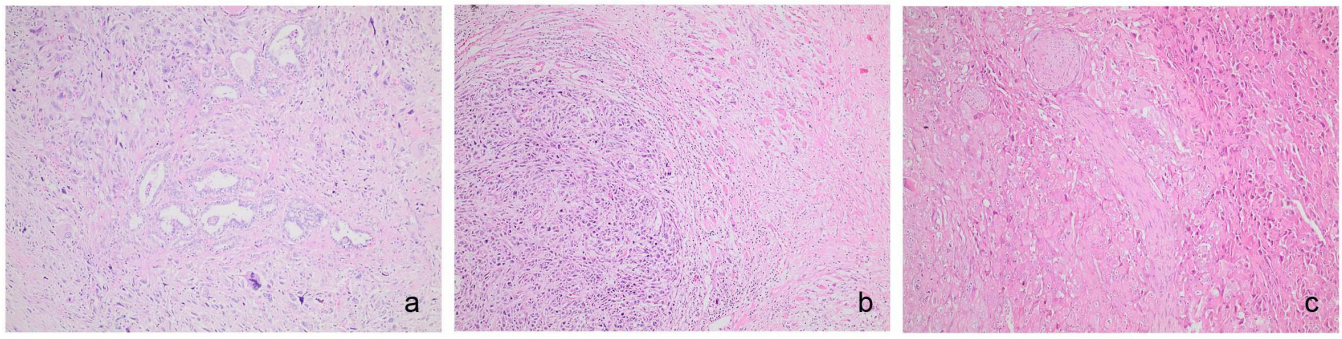

Figure 2. Anaplastic thyroid carcinoma having areas of **a)** concurrent papillary thyroid carcinoma, **b)** striated muscle invasion, **c)** extensive perineural invasion (hematoxylin and eosin, X100, a-c)

Strong immunostaining with p53, which varied between 35-100%, and diffuse strong immunostaining with vimentin were observed in all (100%) cases. The Ki-67 proliferation index was high, ranging from 20% to 90%. No immunoreaction was detected with calcitonin. In 7.7% of cases (1/13), CEA showed weak and patchy/focal immunostaining. Immunohistochemical staining features of vimentin, p53, CEA, calcitonin, and Ki-67 are provided in the table (Table 3).

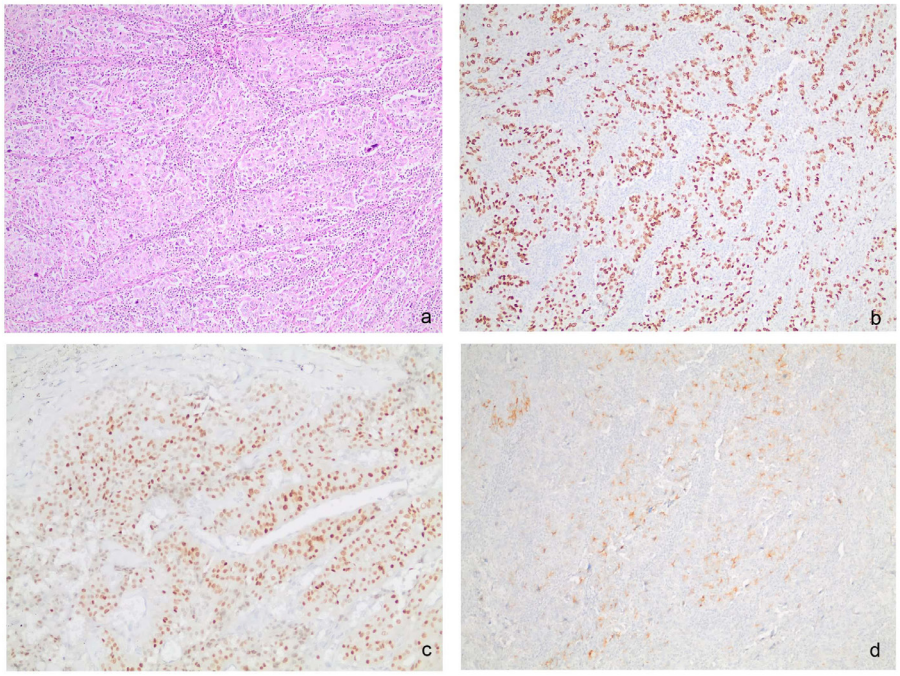

Figure 3. a) Immunprofile of epithelioid anaplastic carcinoma, **b)** PAX8 positivity, diffuse and strong, **c)** TTF-1 positivity, less pronounced and moderate, **d)** Thyroglobulin, focal and weak staining (X200 a, c, d; X100 b)

Table 2. Immunohistochemical profile of anaplastic thyroid carcinoma with TTF-1, PAX8, thyroglobulin, and CAM5.2

Case number	1	2	3	4	5	6	7	8	9	10	11	12	13
TTF-1	+2	0	0	0	0	0	+1	0	0	+3	0	+2	+3
PAX8	+2	0	+3	0	0	0	+2	0	0	0	0	+3	+3
Thyroglobulin	0	0	0	0	0	0	+1	+1	+1	0	+1	+1	0
CAM 5.2	+2	0	+2	0	0	+1	+2	0	+1	0	+2	+3	0

0: Negative staining, +1: Immunostaining in 10%≤ of tumor cells, +2: Immunostaining in 11-50% tumor cells, +3: Immunostaining in 50%> tumor cells

Table 3. Immunohistochemical profile of anaplastic thyroid carcinoma with vimentin, p53, CEA, calcitonin and Ki-67 antibodies

Case number	1	2	3	4	5	6	7	8	9	10	11	12	13
Vimentin	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3
p53	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3
CEA	0	0	0	0	0	0	+1	0	0	0	0	0	0
Calcitonin	0	0	0	0	0	0	0	0	0	0	0	0	0
Ki-67	55%	50%	20%	80%	75%	80%	35%	25%	50%	20%	85%	90%	70%

For vimentin, p53, CEA, and calcitonin staining intensity; for Ki-67 percentage of tumor cells are provided. 0: Negative staining, +1: Immunostaining in 10%≤ of tumor cells, +2: Immunostaining in 11-50% tumor cells, +3: Immunostaining in 50%> tumor cells

Discussion

ATC is a rare thyroid carcinoma that has a very aggressive clinical course and high mortality. The incidence of ATC varies from 0.5% to 5% (1,5,8). In our retrospective study, we found the incidence of ATC among thyroid carcinomas to be 0.77% (13/1.678).

The morphologic spectrum varies from case to case and may show different morphologies even within the same tumor. There are three main histologic patterns: epithelioid, sarcomatoid/spindle-shaped, and giant cell. These patterns usually coexist (1,7,9,10,11,12). Rarely, rhabdoid, paucicellular, lymphoepithelioma-like, angiomatoid, and small cell variants may also be observed. Common features of ATC include marked nuclear pleomorphism, necrosis, high proliferation rate, and invasiveness. In the present study, we observed at least two histological subtypes together in 12 of 13 (92%) cases. The predominant pattern was epithelioid, followed by sarcomatoid and giant cell patterns. One case had a purely epithelioid morphology. Focal or diffuse necrosis, marked pleomorphism, and high mitotic activity were present in all cases, also vascular invasion was a common finding.

ATC may be associated with or have a history of DTC and PDTC (3,7,12,13). This may suggest dedifferentiation of the existing differentiated/poorly differentiated tumor component. It has been postulated that it may arise de novo, and this situation is more common in younger patients (<50 years) (1). In our series, accompanying PTC was observed in 6 (46%) cases, PDTC in 1 case (7.7%), and coexistence of PTC and PDTC in 1 case (7.7%).

The differential diagnosis of ATC can be quite broad, as there are different morphological appearances even within the same tumor. To support the diagnosis of ATC, it is very important to demonstrate the differentiation of the follicular cells of the thyroid gland. In the absence of evidence of thyroid differentiation, the presence of an accompanying DTC component, localization of the tumor primarily within the thyroid gland, and exclusion of metastasis or direct invasion of the thyroid gland from elsewhere are critical to the diagnosis of ATC (14). IHC can be helpful in differentiating ATC from other aggressive/high-grade malignancies, such as sarcomas, melanomas, lymphomas, and carcinomas which may be difficult to distinguish on a morphologic basis alone, especially in small biopsies where the surrounding thyroid tissue cannot be observed.

The tumor cells of ATC have lost the biological properties or functions of follicular thyroid cells (1). The immunohistochemical antibodies TTF-1, thyroglobulin, and PAX8 are commonly used to demonstrate thyroid origin. PAX8 is a transcription factor expressed early in thyroid development and is a very specific marker for primitive thyroidal differentiation (5). It has been reported to be the most sensitive IHC marker for the diagnosis of ATC (7,9,12). PAX8 is also expressed in kidney and Müllerian epithelium (7,14,15). TTF-1 is a transcription factor and plays a very important role in thyroid organogenesis (16). In addition to the thyroid, it is also expressed in the lung and diencephalon (1). Thyroglobulin serves as a substrate for T4 and T3 synthesis and is produced and secreted only by thyroid cells.

TTF-1, thyroglobulin, and PAX8 antibodies are commonly used to detect the thyroid origin of the tumor in ATC. TTF-1 expression in ATC has been reported to be 0-41% (8,12,15,16,17). PAX8 expression is observed more frequently than TTF-1, and immunostaining with PAX8 ranges from 36-79% (7,8,11,12,14,16). The expression of thyroglobulin in ATC is controversial, and among the other IHC markers of thyroid lineage, the lowest expression is observed with thyroglobulin (1,5,7,8,11,12,18). Although thyroglobulin positivity ranges from 0-50%, it has been reported that staining is often weak (1). In our study, we found 38% positivity for PAX8 and TTF-1 and 31% for thyroglobulin, but the staining for thyroglobulin was focal (less than 5%) and weak. We observed higher positivity for TTF-1 and especially for thyroglobulin compared with the literature. This result may be attributed to the relatively frequent presence of an epithelioid component in the ATC cases in our study. In the study of Nonaka et al. (16), 3 of 5 TTF-1 positive cases of ATC were squamoid, 1 case and epithelioid, 2 cases. It is also suggested that PAX8 expression was positively correlated with the presence of an epithelial pattern, also lower PAX8 expression rates were observed in tumors with a sarcomatoid pattern (7). The presence of a DTC component was positively correlated with PAX8 expression (7). Similarly, Bishop et al. (14) described that ATC cases with a well-differentiated component were more likely associated with PAX8 expression.

In three cases, we could not detect positive immunostaining with PAX8, TTF-1, CAM5.2, and thyroglobulin. In these cases, radiological localization of the tumor in the epicenter of the thyroid, presence of PTC and PDTC in two cases, detection of higher uptake values with positron emission tomography at the thyroid mass compared to distant metastases in two cases were the facts that led us to the ATC diagnosis, despite negative immunostaining with epithelial and thyroid lineage markers. In a multicenter study of 360 ATC cases by Xu et al. (12), no immunostaining was observed in 25% of 225 cases in which immunohistochemical studies of cytokeratin were performed. This result suggests that epithelial markers may not be found in a proportion of ATC cases.

Female to male ratio in ATC varies from 1.2:1 to 3.83:1 (12,16,17,19). In our series, we found female to male ratio as 1.16:1, which is consistent with the previous studies. The mean age of patients was 66.15 in our study; this also supports the literature (12,16,17,19). We found the median survival of patients 5.7 months. Only for 3 patients the survival was over 12 months; which were 13 months alive, 14 months DOD, and 23 months DOD. In the series of Deeken-Draisey et al. (8) only 20% of affected patients survived for 1 year after initial diagnosis.

Regional lymph node metastases are common, and it is estimated that more than half of the patients have distant metastases at the time of diagnosis (1,5,19). Distant metastases to the lung, bone, and brain are most common (1,2,16). We observed regional lymph node and distant metastases in 62% of our cases, with lung being the most common site for distant metastases.

Although some studies claim that the histological subtype of ATC does not alter prognosis (11,13), others reported that epithelioid morphology and the presence of differentiated thyroid cancer are associated with a better outcome, whereas rhabdoid morphology is associated with a poor prognosis (10). Hirokowa et al. (10) suggested that the incidence of epithelial growth was higher in long term survival patients (longer than 1 year) than short-term survival patients (survival of less than 3 months), which they suggested this finding may be associated with more indolent course. They also stated that ATC cases with papillary carcinomas showing squamous cell carcinoma component may have long-term survival. Of our cases with longer survival (≥12 months), 3 had more than one histologic pattern, and only one had pure epithelioid morphology. Of the two patients with rhabdoid morphology, one died within three months and the other was alive for 12 months with lung metastases. Although our results suggest that the predominant pattern in the tumor does not influence survival, we do not have a sufficient number of cases to determine the impact of histologic subtype on survival.

Study Limitations

The major limitations of this study were the relatively few sample number and for some cases type of procedure being incisional biopsy. For particularly small biopsy samples, we could not exclude the possibility of heterogeneous immunostaining, especially when all epithelial markers were negative. Another limitation is that we could only test BRAF mutation status in four cases

Conclusion

ATC is a rare but very aggressive tumor originating from the follicular epithelial cells of the thyroid gland. In our tertiary care and treatment center, we found that the incidence of ATC among thyroid cancers 0.77%. A history of differentiated/PDTC and/or concurrent differentiated/PDTC may support the diagnosis of ATC. The diagnostic process is sometimes challenging, especially with small biopsies, and may require the use of a broad immunohistochemical panel, as morphology may vary, immune profile is variable, and a large number of malignancies are part of the differential diagnosis. Previous studies claim that PAX8 is the most useful immunohistochemical marker for detecting the origin of thyroid cell origin in ATC. Although the positivity of TTF-1 and thyroglobulin are reported to be low in the literature, we found similar positivity for PAX8 and TTF-1, and lower positivity for thyroglobulin. We observed that TTF-1 and thyroglobulin staining was more common with tumors with a predominant epithelioid component. Our results suggest that in addition to PAX8; TTF-1, thyroglobulin, and CAM 5.2 may be useful in supporting ATC diagnosis.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Ethics Committee of University of Health Sciences Türkiye, Dışkapı Yıldırım Beyazıt Training and Research Hospital (88/11, 20.05.2020), and was carried out by the principles of the Declaration of Helsinki.

Informed Consent: Informed consent is not required because this is a retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.T.T., D.Y., Concept: T.T.T., D.Y., Design: T.T.T., D.Y., Data Collection or Processing: T.T.T., D.Y., Analysis or Interpretation: T.T.T., D.Y., Literature Search: T.T.T., D.Y., Writing: T.T.T., D.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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