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Analysis of thyroid carcinomas with immunohistochemical panel application: retrospectively study of 52 cases

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Abstract

Aim: The aim of this study was to share our cases of thyroid carcinoma with the literature and to emphasize the importance of evaluation with an immunohistochemical panel in cases with difficulty in the differential diagnosis.

Background: Thyroid carcinomas are the most common malignant endocrine tumors. Its incidence is 1% among all cancer. They constitute 0.2% of cancer-related deaths. The papillary carcinoma is the most common group with 70-90%. It has the best prognosis. It is diagnosed by the presence of nuclear features such as the appearance of clarification in the core, the inclusion body, and the core like a groove. Follicular carcinoma is the second most common thyroid tumor with 10-15%. In the differential diagnosis of follicular carcinoma, the capsular invasion and vascular invasion are important. Medullary carcinoma constitutes 3-5% of all thyroid carcinomas. Immunohistochemical stains such as calcitonin, CEA, CK7, chromogranin, synaptophysin, and Congo-Red were applied to confirm the diagnosis of medullary carcinoma. Anaplastic thyroid carcinoma constitutes 1-2% of all thyroid carcinomas. Cellular pleomorphism in the anaplastic carcinoma is higher than that of other thyroid carcinomas.

Results: In this retrospective study, of the 52 thyroid carcinoma cases, 45 (86.6%) were papillary carcinoma, 4 (7.7%) were follicular carcinoma, 2 (3.8%) were anaplastic carcinoma, and 1 (1.9%) was medullary carcinoma.

Conclusion: In the diagnosis of thyroid pathologies, mainly cellular properties are determinative. The evaluation with the immunohistochemical panel will reduce the risk of diagnostic error when the cases that difficultly diagnosed with cellular properties.

Key words: thyroid, carcinoma, immunohistochemistry

ИММУНДЫҚ ГИСТОХИМИЯЛЫҚ ТӘСІЛДІ ҚОЛДАНА ОТЫРЫП ҚАЛҚАНША БЕЗІ КАРЦИНОМАСЫН ТАЛДАУ: 52 ЖАҒДАЙДЫ РЕТРОСПЕКТИВТІ ЗЕРТТЕУ

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ТҰЖЫРЫМДАМА

Мақсаты: Осы зерттеудің мақсаты қалқанша безінің карциномасы жағдайларымызбен әдебиетте бөлісу және саралап диагностикалау күрделігі жағдайында иммундық гистохимиялық тәсіл көмегімен бағалау маңыздылығын атап өту болып табылады.

Кіріспе: Қалқанша безінің карциномасы анағұрлым кең таралған қатерлі эндокриндік ісік болып табылады. Ауру коэффициенті обырдың барлық түрлері арасында 1% құрайды. Ол онкологиялық аурудан келетін өлімнің 0.2% құрайды. Күретамырлық карцинома ең көп таралған топ (70-90%) болып табылады және ең жақсы болжамға ие. Ол ядрода жарықтанудың пайда болу, вирустық қосылыс секілді ядролық ерекшеліктердің және жырашық түріндегі ядроның болуымен диагностикаланады. Фолликулдық карцинома қалқанша безінің таралуы дағынан екінші орында тұрған ісігі болып табылады (10-15%). Фолликулдық карциномалардың саралау диагностикасында күретамырлық және тамырлы инвазия маңызды. Сүйек кеміктік карцинома қалқанша безі ісігінің барлық типтерінің 3-5% құрайды. Тиреокальцитонин, КЭА, СК7, хромогранин, синаптофизин, және конго-рот секілді иммундық гистохимиялық бояулар сүйек кеміктік карцинома диагнозын растау үшін қолданылды. Қалқанша безінің анапластикалық карциномасы қалқанша безі ісіктерінің 1-2% құрайды. Анапластикалық карцинома кезіндегі жасушалық плеоморфизм қалқанша безінің басқа ісіктері кезіндегіге қарағанда жоғары.

Нәтижелері: Осы қалқанша безі карциномасының 52 жағдайын ретроспективті зерттеу күретамырлы карциноманың 45 (86.6%) жағдайын, фолликулдық карциноманың 4 (7.7%) жағдайын, анапластикалық карциноманың 2 (3.8%) жағдайын және сүйек кеміктік карциноманың 1 (1.9%) жағдайын қамтиды.

Қорытынды: Қалқанша безінің патологиясын диагностикалауда, көп жағдайда, жасушалық қасиеттер шешуші рөл атқарады. Иммундық гистохимиялық тәсілді қолдана отырып, бағалау жасушалық қасиеттердің көмегімен күрделі диагностикаланатын жағдайлардағы қателердің қауіпін төмендетеді.

Негізгі сөздер: қалқанша безі, карцинома, иммундық гистохимия

АНАЛИЗ КАРЦИНОМЫ ЩИТОВИДНОЙ ЖЕЛЕЗЫ С ПРИМЕНЕНИЕМ ИММУНОГИСТОХИМИЧЕСКОГО МЕТОДА: РЕТРОСПЕКТИВНОЕ ИССЛЕДОВАНИЕ 52 СЛУЧАЕВ

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РЕЗЮМЕ

Цель: Цель настоящего исследования состояла в том, чтобы поделиться нашими случаями карциномы щитовидной железы в литературе и подчеркнуть важность оценки с помощью иммуногистохимического метода в случаях со сложностью дифференцированной диагностики.

Введение: Карцинома щитовидной железы является наиболее распространенной злокачественной эндокринной опухолью. Коэффициент заболеваемости составляет 1% среди всех видов рака. Он составляет 0.2% смертности от онкозаболеваний. Папиллярная карцинома является наиболее распространенной группой (70-90%) и имеет наилучший прогноз. Она диагностируется наличием ядерных особенностей, таких как появление просветления в ядре, вирусное включение, и ядро в виде бороздки. Фолликулярная карцинома является второй наиболее распространенной опухолью щитовидной железы (10-15%). В дифференцированной диагностике фолликулярной карциномы важны капсулярная и васкулярная инвазия. Медуллярная карцинома составляет 3-5% всех типов рака щитовидной железы. Иммуногистохимические окрашивания, такие как тиреокальцитонин, КЭА, CK7, хромогранин, синаптофизин, и конго-рот применялись для подтверждения диагноза медуллярная карцинома. Анапластическая карцинома щитовидной железы составляет 1-2% всех опухолей щитовидной железы. Клеточный плеоморфизм при анапластической карциноме выше, чем при других опухолях щитовидной железы.

Результаты: Настоящее ретроспективное исследование 52 случаев карциномы щитовидной железы состояло из 45 (86.6%) случаев папиллярной карциномы, 4 (7.7%) случаев фолликулярной карциномы, 2 (3.8%) случаев анапластической карциномы, и 1 (1.9%) случая медуллярной карциномы.

Заключение: В диагностике патологий щитовидной железы, в большинстве случаев, решающими факторами являются клеточные свойства. Оценка с применением иммуногистохимического метода снизит риск диагностической ошибки в случаях трудно диагностируемых с помощью клеточных свойств.

Ключевые слова: щитовидная железа, карцинома, иммуногистохимия

Introduction

Thyroid carcinomas are the most common malignant endocrine tumors [1]. Its incidence is 1% among all cancer but thyroid carcinoma incidence has increased in the world [2,3]. The recent incidence in the USA has risen to 3% [4]. Thyroid carcinomas are seen predominantly Caucasian, female, and an elderly person [4,5]. The rate of female/male reaches 70-90%, particularly in the papillary carcinomas [6,7].

The incidence of thyroid carcinoma has high variability due to genetic factors and a variety of environmental effects [3]. They predominantly develop from nodules. While thyroid nodules are extremely common thyroid carcinomas are relatively rare. Thyroid nodules, like carcinomas, are the most common in women and older populations [5,8]. In 70% of normal thyroid glands, there are available nodules of less than 1 cm by ultrasonographically [9]. The palpable thyroid nodules are seen in 8% of the adult population [10]. Thyroid carcinomas are responsible for 0.2% of cancer-related deaths [2].

Thyroid carcinomas are divided into differentiated thyroid carcinoma and undifferentiated thyroid carcinoma. Differentiated thyroid carcinoma includes papillary carcinoma and follicular carcinoma. Undifferentiated thyroid carcinoma includes medullary carcinoma and anaplastic carcinoma [11,12]. Papillary carcinomas are the most common group with a rate of 70-90% among the thyroid carcinomas [2,11,13-15]. Papillary carcinoma has the best prognosis among thyroid carcinomas [6]. The 10-year overall survival rate is 97%, 15-year overall survival rates are 95%, and 20-year overall survival rates are 90% [6]. Therefore, the differential diagnosis of papillary carcinoma from other thyroid carcinomas is very important. The diagnosis of papillary carcinoma is made by the presence of nuclear features such as the abundant nuclear grooves, intranuclear inclusions, psammoma bodies, the appearance of clarification in the core. In this study, nuclear clarification was present in all cases. In some cases, significant papillary structures were present (Figure 1) [16-17]. In the differential diagnosis, immunohistochemical methods such as HBME-1, CK19, galectin-3, and molecular studies are also used [18].

Follicular carcinoma is the second most common thyroid tumor after papillary carcinoma with a rate of 10-15% [19]. The 20-year overall survival rate of it is 65% [20]. The pattern of micro or macrofollicular structures is dominant. The

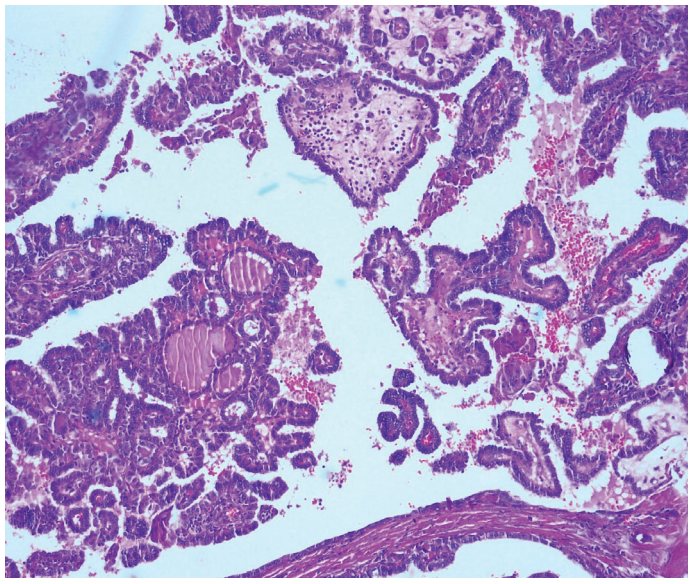


Figure 1 A - The papillary carcinoma.(HEx100)

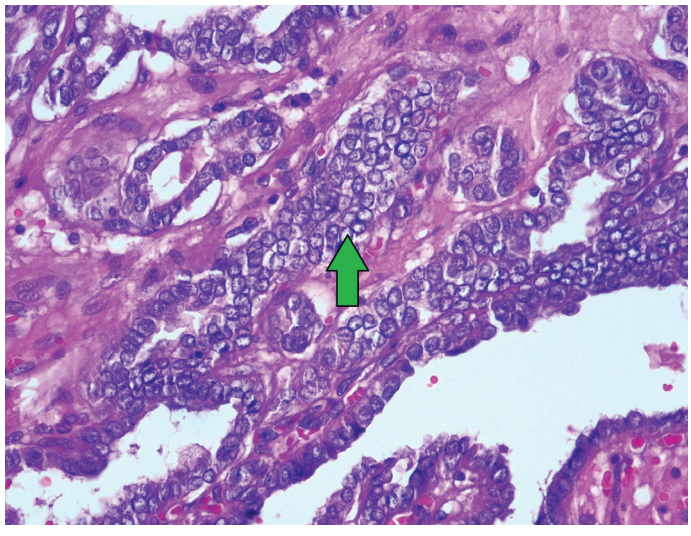


Figure 1 B - The nuclear clarification (green arrow) in the papillary carcinoma.(HEx400)

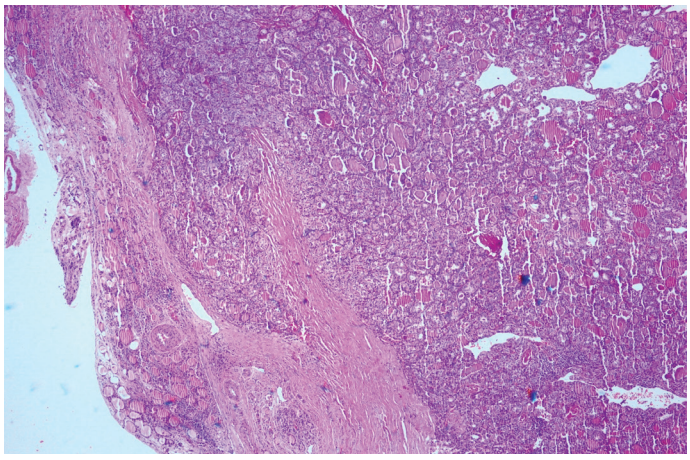


Figure 2 A - The follicular carcinoma.(HEx40)

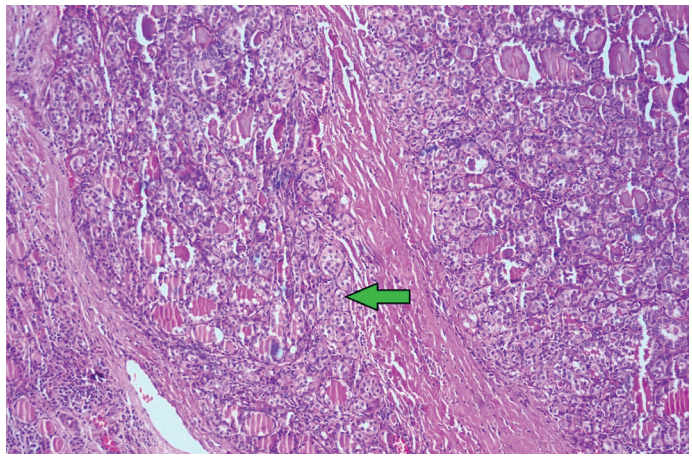


Figure 2 B - The capsular invasion (green arrow) in the follicular carcinoma.(HEx100)

presence of vascular and capsular invasion is important for the differentiation of follicular adenoma and papillary carcinoma with the follicular variant. There should be vascular and/or capsular invasion for cancer diagnosis [21]. In this study, there were nodules composed of follicular structures surrounded by conspicious a capsule. Follicular carcinoma was diagnosed with capsular invasion (Figure 2).

Medullary carcinoma is a rare type of thyroid carcinoma. It constitutes 3-5% of all thyroid carcinomas [22]. It originates from parafollicular C cells. The C-cells secrete several hormones. Of these, calcitonin and CEA are valuable tumor markers [23]. Medullary carcinoma has an aggressive clinical course. It has a poor prognosis [24]. Histochemical and immunohistochemical studies are important in the differential diagnosis. The amyloid material present in the medullary carcinoma. Amyloid accumulation seen as eosinophilic hyalinized structures can be detected by histochemical dyes [25]. Calcitonin, CEA, chromogranin positivity, and thyroglobulin negativity as immunohistochemically are important in the differential diagnosis (Figure 3) [23].

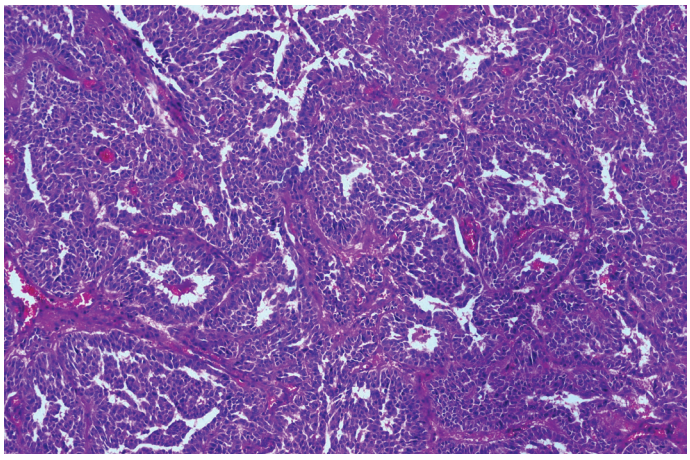


Figure 3 A - The medullary carcinoma.(HEx200)

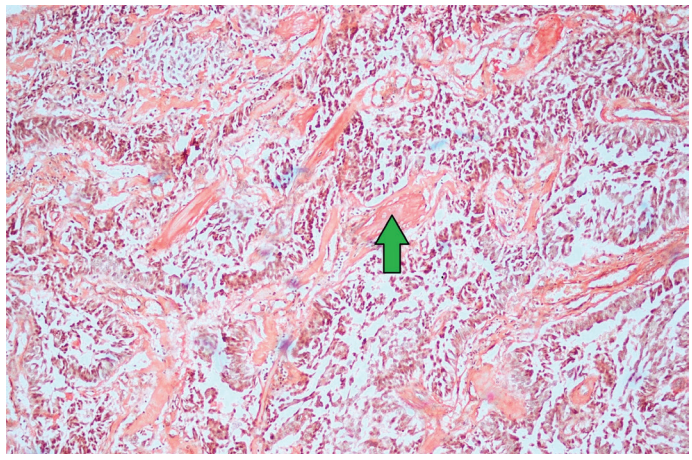


Figure 3 B - Amyloid (green arrow) seen as reddish with Congo-Red stain in the medullary carcinoma.(x200)

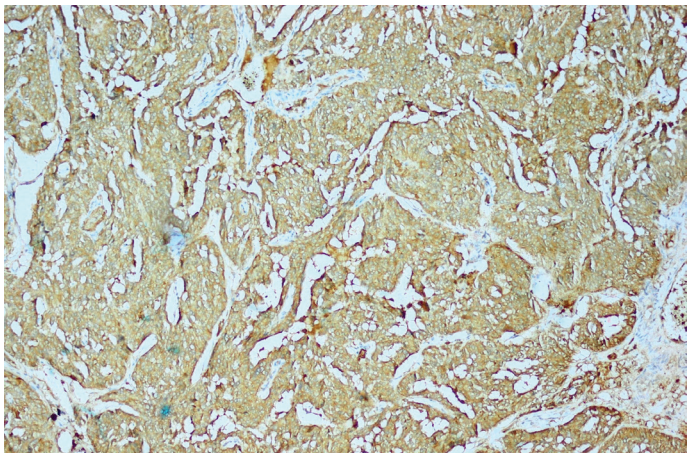


Figure 3 C - Calcitonin stain in the medullary carcinoma. (x200)

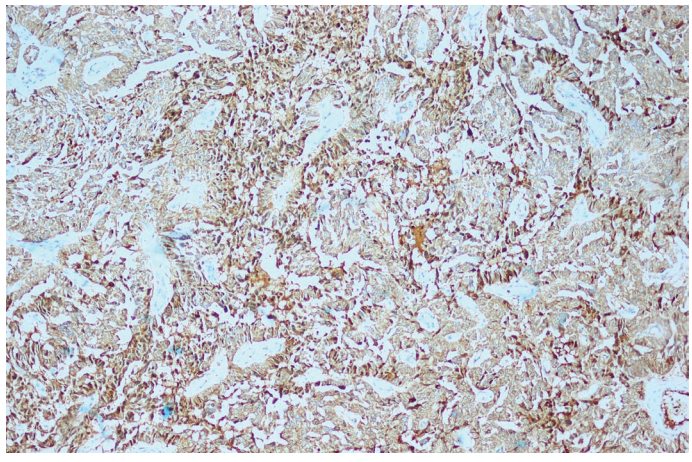


Figure 3 D - Chromogranin stain in the medullary carcinoma. (x200)

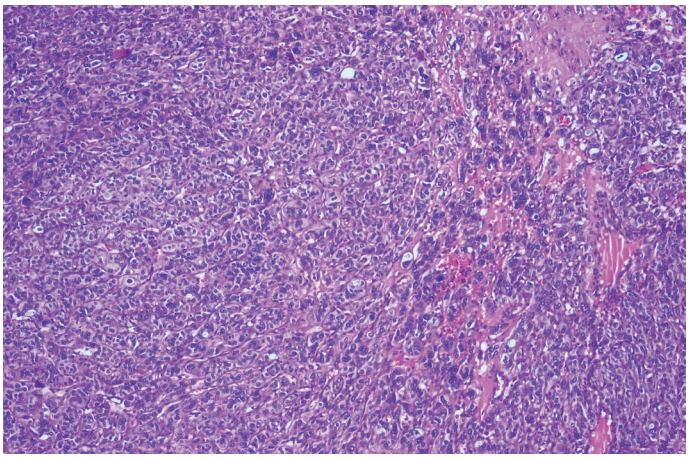


Figure 4 A - The anaplastic carcinoma.(HEx100)

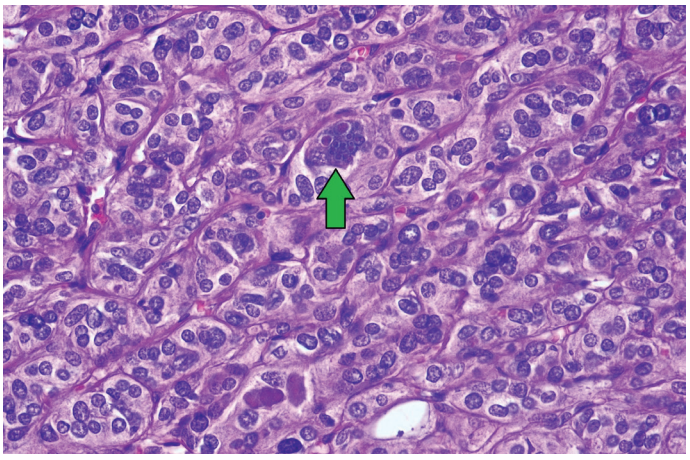


Figure 4 B - A giant bizarre nuclues (green arrow) including conspicious nucleoli in the anaplastic carcinoma.(HEx400)

Anaplastic thyroid carcinomas are very rare. Anaplastic thyroid carcinoma constitutes 1-2% of all thyroid carcinomas and their prognosis is worse than other types [11,26]. It often originates in a pre-existing thyroid cancer lesion, as suggested by the simultaneous presence of areas of differentiated or low differentiated thyroid carcinoma. Significant pleomorphism, neutrophilic infiltrate and necrosis are common. Cellular pleomorphism is higher than that of other thyroid tumors (Figure 4). No nuclear grooves, colloid or well-differentiated component not identify [27].

When there are diagnostic difficulties with cellular features, evaluation with an extensive immunohistochemical panel is helpful in the diagnosis.

The aim of this study was to share our cases of thyroid carcinoma with the literature and to emphasize the importance of evaluation with an immunohistochemical panel in cases with difficulty in the differential diagnosis.

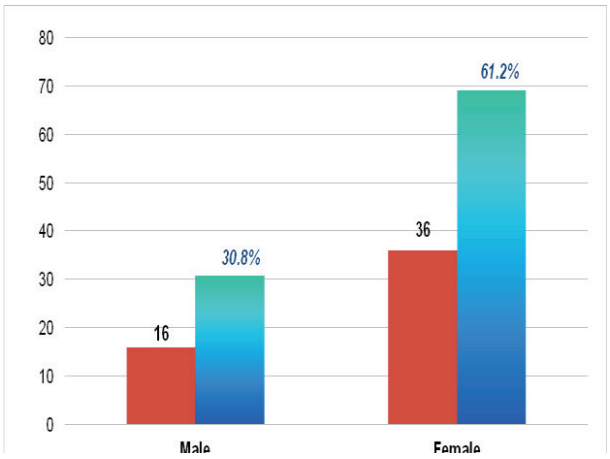
Material and methods

Ethics committee approval was received with the decision dated 25/06/2019 and numbered 07/02. 52 thyroidectomy specimens diagnosed as thyroid carcinoma in the archives of the Pathology Department at Faculty of Medicine, Erzincan University between 2011-2017 were re-examined. Paraffin blocks of thyroid carcinomas were supplied from the pathology archive and 4-micron-thick sections were taken from these blocks. After deparaffinization, the sections were stained with Hematoxylin-Eosin stain. 4 µm thick sections were taken from the blocks of tumor suspected preparations on positively charged slides. The immunohistochemical staining such as thyroglobulin, HBME1, CK19, galectin-3 with positive control was performed to confirm the diagnosis of papillary carcinoma. Calcitonin, CEA, CK7, chromogranin, synaptophysin, Congo-Red with positive control performed to confirm the medullary carcinoma. Differential diagnosis of anaplastic carcinoma was performed according to cellular characteristics. The wide immunohistochemical panel was performed when the cases that difficultly diagnosed with cellular properties. Follicular carcinoma was diagnosed according to capsular invasion and vascular invasion. Data were evaluated by simple statistical method. Results were expressed as percentages.

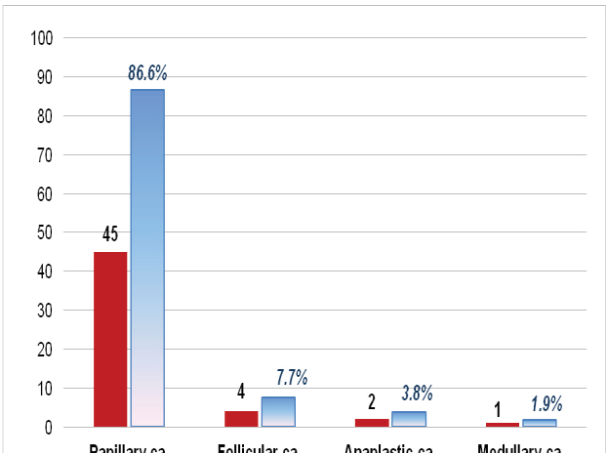
Results

In this study, the distribution of patients by gender was 36 (69.2%) female and 16 (30.8%) male (Graphic 1). The age range of the patients was 18-76 and the mean age was 51.2. The most common age group was between 40-50 years. In the study, it was revealed that the prevalence of thyroid cancer was higher in women (69.2%).

The distribution of cases according to tumor types was as follows: of the 52 cases, 45 (86.6%) were papillary carcinoma, 4 (7.7%) were follicular carcinoma, 2 (3.8%) were anaplastic carcinoma, and 1 (1.9%) was medullary carcinoma (Graphic 2).



Graphic 1. - Gender distribution in thyroid carcinomas.



Graphic 1. - Distribution of thyroid carcinomas according to tumor types.

Discussion

Thyroid diseases predominantly affect female; their incidence is 5-20 times higher in the female than in the male [28-30]. Similarly, the incidence of thyroid carcinomas is higher in the female than in the male. Thyroid carcinomas are seen predominantly female [4,5]. The rate of female/male reaches 70-90%, particularly in the papillary carcinomas [6,7].

Thyroid carcinomas are seen predominantly in the female [4,5,28]. In the study of Olson et al. the rate of the female was 56.4%. In the study of Shah et al. the rate of the female was 57.5%. In the study of Robertson et al. the rate of the female was 82%. In this study, there was an available predominance of the female with 61.2%. This rate was compatible with the literature [4,31,32].

Thyroid carcinomas are seen in the elderly population [4,5,8,28,30]. In the study of Shah et al. the mean age was 49.3 [31]. In the study including papillary carcinomas of Marques et al. the mean age was 47 [13]. In the study of Robertson et al. the mean age was 44 [32]. In this study, the mean age was 51.2 years. The mean age in this study was compatible with the literature.

Papillary carcinomas are the most common group with a rate of 70-90% among the thyroid carcinomas [2,11,13-15]. In the study of Shah et al. the rate of papillary carcinomas among thyroid carcinomas was 67.8 % [31]. In the study of Robertson et al. this rate was 60.6% [32]. In the study of Olson et al. this rate was 49.4% [4]. In this study, of 52 cases, 45 (86.6%) were papillary carcinoma. This rate was compatible with the literature.

Follicular carcinoma is the second most common thyroid tumor after papillary carcinoma with a rate of 10-15%. Follicular carcinoma and papillary carcinoma with a follicular variant should be differentiated. The presence of vascular and capsular invasion is important for the differentiation of follicular adenoma and papillary carcinoma with the follicular variant [21]. In this study, of 52 cases, 4 (7.7%) were follicular carcinoma. This rate was compatible with the literature.

Medullary carcinoma is a rare type of thyroid carcinoma. It constitutes 3-5% of all thyroid carcinomas [22]. In this study, of 52 cases, 1 (1.9%) was medullary carcinoma. In this case with a diagnosis of medullary carcinoma, there was papillary structures and nuclear clarification with suspicion of papillary carcinoma. In the immunohistochemical study, there were no staining of tumor cells with thyroglobulin, HBME1, CK19, galectin-3. The case was reported as medullary carcinoma in the tumor cells due to the presence of calcitonin, CEA, CK7, chromogranin, synaptophysin positivity, and amyloid deposition in Congo-Red staining (Figure 3).

Anaplastic carcinoma constitutes 1-2% of total thyroid carcinomas. In this study, in an anaplastic carcinoma case, there was a giant bizarre nucleus including conspicious nucleoli (Figure 4). It has a low survival rate and a high mortality rate of 86% [11,26]. In this study, of 52 cases, 2 (3.8%) were anaplastic carcinoma. This rate was compatible with the literature.

As a result, in the diagnosis of thyroid carcinomas, mainly cellular properties are determinative.

The evaluation with the immunohistochemical panel will reduce the risk of diagnostic error when the cases that difficultly diagnosed with cellular properties.

Disclosures: There is no conflict of interest for all authors.

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