Synchondrous thyroid papillary and medullary carcinoma in a pregnant patient

Gebe hastada senkron tiroid papiller ve medüller karsinomu

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Abstract

Mixed thyroid carcinoma is a term to describe the carcinomas composed of papillary-medullary or follicular-medullary carcinomas and these carcinomas arise from the same thyroid gland and display morphological and immunophenotypical features of both origins within the same lesion. A few cases has been reported in the literature and recently there are some molecular studies searching the developmental mechanisms of these tumors.
Here in, we aimed to present a pregnant case with synchronous medullary and papillary thyroid carcinoma.
In the present case, the most remarkable features of this case was the patient's being pregnant at the time of the diagnosis and the presence of metastatic lymph node on the side of papillary tumor originating from the contralateral medullary carcinoma. The patient went to bilateral total thyroidectomy, central neck dissection of left side and right sided modified radical neck dissection.

Key words: Thyroid , medullary carcinoma, papillary carcinoma, mixed carcinoma

Özet

Tiroid bezinin mikst tip olarak adlandırılan karsinomları, papiller-medüller, foliküler- medüller olmak üzere aynı tiroid bezinde her iki tümörün immünfenotipik ve morfolojik özelliklerini gösteren tümörleri ifade etmek için kullanılan bir terimdir. Literatürde az sayıda olgu bildirilmekle beraber, bu tümörlerin nasıl geliştiğiyle ilgili moleküler düzeyde çalışmalar mevcuttur.
Bu olgumuzda tiroid bezinde senkron papiller ve medüller tiroid karsinomu bulunan 6 aylık gebe hastayı sunmayı amaçladık.
Hastanın gebe olması ve papiller karsinomun bulunduğu lobda medüller karsinom lenf metastazının bulunması dikkat çekici özelliğiydi. Hastaya bilateral total tiroidektomiye ek olarak sol santral boyun diseksiyonu, sağ modifiye radikal boyun diseksiyonu uygulandı.

Anahtar Kelimeler: Tiroid, medüller karsinom, papiller karsinom, mikst karsinom

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Başvuru tarihi | Submitted on: 27.10.2018
Kabul tarihi | Accepted on: 15.01.2019

Introduction

Papillary thyroid cancer is the most common subtype of thyroid carcinoma and accounts for approximately 80% of all thyroid carcinomas[1,2].

Papillary thyroid cancer is more common in females than in males by a 2:1 ratio in adults[3].

Peak onset ages are 30-40 years.

It originates from the follicular cells of thyroid gland and radiation exposure is the most important known- risk factor.

Metastases to lymph nodes are common in childhood and young patients.

Distant metastases occurs in 20% of all cases. The most common sites of metastases are lung, bone, brain and liver[4].

Fine needle aspiration biopsy (FNAB) is the gold standard in the diagnosis of thyroid carcinoma.

There are some characteristic diagnostic nuclear and cell features by pathologically.

Nucleus show groove pattern and include intranuclear cytoplasmic inclusions.

These inclusions are diagnostic in FNAB.

Mortality rates of papillary carcinoma are 2% in 5 years follow up, 4% in 10 years follow up and 5% in 20 years follow-up[5].

Medullary thyroid carcinoma accounts for the 5% of all thyroid malignancies[5].

It is a neuroendocrine tumor originating from the parafoliculary C cells of thyroid gland. It is more common in females than in males by a 1.5:1 ratio.

Nearly 20% of cases are familial (hereditary?).

The diagnosis is made by FNAB. The presence of amyloid is diagnostic by pathology, however immunohistochemistry is more commonly used for calcitonin.

These tumors are positively stained with CEA and calcitonin related peptide (CGRP).

The term of mixt type thyroid carcinoma is used to describe the synchronous carcinomas of the thyroid gland.

The coexistence of medullary, papillary and follicular carcinoma may be in the thyroid gland.

In this case report we aimed to present a case with synchronous medullary and papillary carcinomas.

Case Presentation

Thirty three years old female with a 6 months pregnancy admitted to a secondary hospital with a 6-month history of a lump in the neck. Thyroid ultrasonography revealed an isoechoic nodule within 14 mm diameter in the lower pole of the right thyroid lobe and an isoechoic nodule within 9mm diameter in the middle zone of the right thyroid lobe. Also, 16x30 mm lymphadenopathy including microcalcifications in level III was reported in the right side of the neck.

FNAB was performed to the nodule in the left lobe of the thyroid and the lymphadenopathy in the right side of the neck. The pathology report was suspicious for papillary carcinoma and insufficient for the lymphadenopathy.

Positron emission tomography using F-18 fluorodeoxyglucose (FDG) showed increased focal FDG uptake in the left lobe of the thyroid (SUV MAX: 6,78) and 22x23x35 mm enlarged lymphadenopathy in the neck (level IIB) .

Surgery was suggested and patient refused it. Then patient was referred to the department of general surgery at our hospital.

She did not have an exposure of radiation.

There were not any other disease except venous insufficinecy in the history of the patient.

Physical examination revealed a 2,5 cm x 1,5 cm immobile, fixed mass in the right neck.

Thyroid lobe was enlarged (palpable). No other mass was detected at the physical examination.

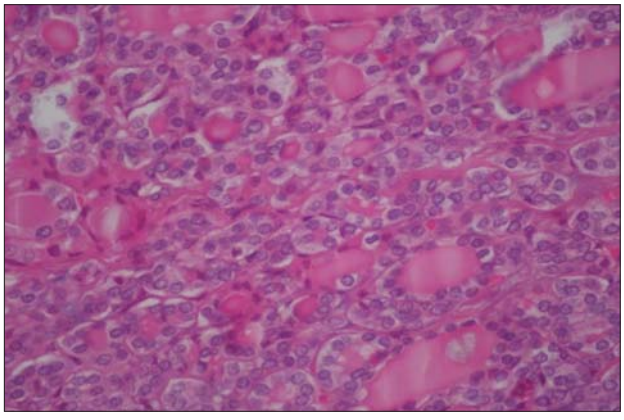

Figure 1. Left lobe Follicular Variant Papillary Carcinom; Large Nuckleus, Focal areas with frosted glass imaging (H&E, X 400)

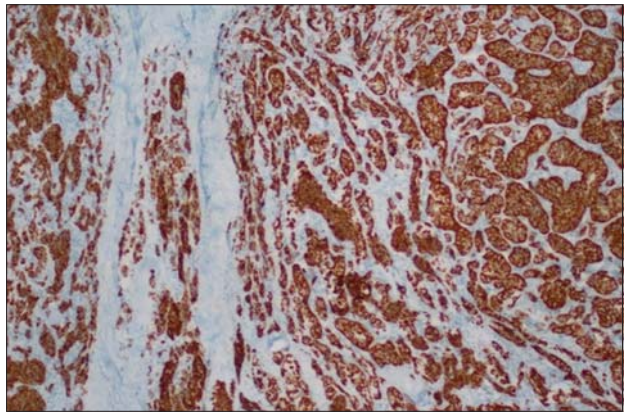

Figure 2. Left thyroid lobe, CK19 Pozitive Neoplastic Cells (IHC X 100)

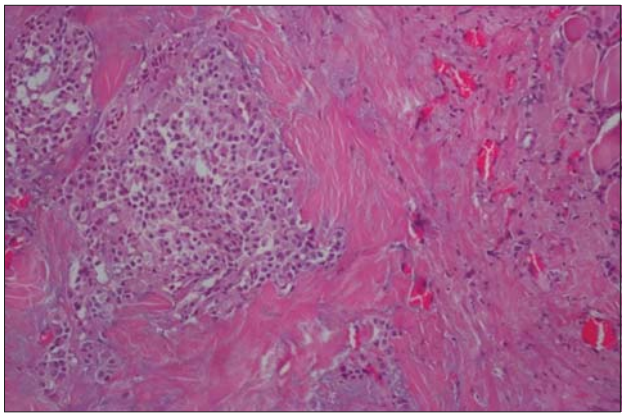

Figure 3. Right Lobe Medullary thyroid Carcinoma

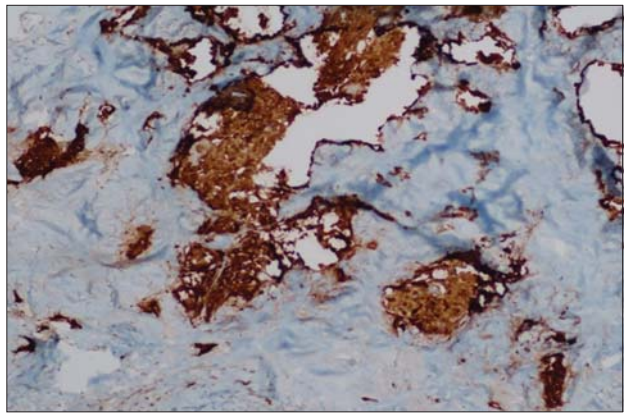

Figure 4. The positively stained neoplastic cells in right lobe by CEA (IHC X 100)

Preoperative hormone levels were as follows; TSH (0,006 uIU/ml), freeT_4 (1,25 ng/dl), freeT_3 (3,48 pg/ml), Anti TPO:negative, calcitonin: 464 pg/mL , PTH: 168 pg/mL. The patient with pressure symptoms and severe headache was consulted with the department of endocrinology preoperatively and accepted as subclinical hyperthyroidism.

US examination of the neck showed an isoechoic solid nodule located in the left thyroid lobe (1.5 cm of largest diameter), colloid nodules smaller than 0.5 cm in the right lobe. US also revealed a 4 cm x 2,5 cm lymph node in level V of right neck.

Then patient went to bilateral total thyroidectomy, left central neck dissection and right modified radical neck dissection. The patient is alive 12 months after surgery and taking thyroid hormone replacement.

Histopathological examination reports showed a 7mm diameter medullary carcinoma in the right thyroid lobe with the intact thyroid capsule. (***Figure 3-4***) The distance between the thyroid capsule and the nodüle was 0.2 cm. Both of the nodule in the right lobe and the lymphadenopathy in level II was stained positively by calcitonin, TTF-1, CEA, Amyloid A and chromogranin. They were negatively stained by Galectin 3, CK 19, HBME-1.

The nodule in the left lobe was positively stained by CK19, Galectin 3 and HBME-1 and negatively stained by Calcitonin, chromogranin and CEA. The final decision of the tumor was follicular variant type papillary carcinoma. (***Figure 1-2***) The tumor was presented as an encapsulated nodule and included diffuse oncocytic changes. The nodule was within 2 cm diameter and extending to the subcapsular area. The thyroid capsule was intact.

The metastatic lymp node in neck was positive for TTF-1, CEA, Amyloid A, Chromogranin and negative for Galectin 3, CK19 ve HBME-1. Despite the the papillery carcinoma in the left lobe, the origin of metastatic lymph node at the same side was contralateral medullary carcinoma (***Figure 5***).

Discussion and Conclusion

Thyroid carcinomas are classified in two different histopathologic types.

Differentiated thyroid carcinomas are papillary thyroid carcinomas and follicular carcinomas.

They originate from the foregut endoderm.

They tend to metastase by lymphatic and blood circulation.

Papillary carcinomas are the most comon type with an incidence of 80% among all thyroid carcinomas[7].

Approximately 30% of thyroid carcinomas have micro metastases at the time of the diagnosis. 29% of the cases show multifocal spread pattern[8].

Multifocality is common in papillary carcinomas. Multifocality is related with the increased risk of lymph node metastases. These tumors rarely invade the trachea, recurrent laryngeal nerve and esophagus.

10 year survival rate is more than 95%.

This protooncogen is responsible for the tyrosine kinase receptor coding and binding of many growth factor receptors[4].

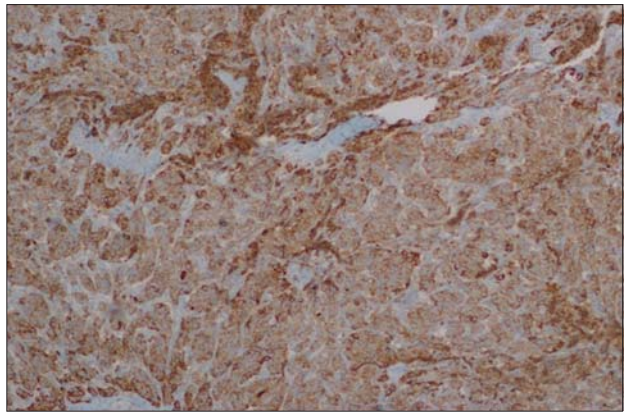

Figure 5. The metastases of the right sided medullary carcinoma to the lymph node in the lef thyroid lobe, the tumor was positive by chromogranin. The tumors were stained more prominent than the origin of the tumor

Medullary thyroid cancer is commonly presented with palpable neck mass and lymphadenopathy[4].

Diagnosis is made by FNAB with an accuracy rate of 50-80%. Nearly 25% of medullary thyroid cancers are hereditary and there is a pathology in RET proto oncogene.

There are three types of this disease which is named as multiple endocrine Neoplasia. Thyroid carcinoma, feochromacitomas and hyperpatahtroidism is seen in MEN IIa . In MEN IIb medullary thyroid carcinoma, pheochromocytoma and ganglioneuroma is seen.

Rarely calcification can be detected radiologically in neck.

Systemic symptoms may ocur due to the hormone secretion by tumor.

Calcitonin or calcitonin gene related peptide secretion can cause diarrhea and flushing. Corticotropin secretion may result with Cushing Syndrome.

Prognostic factors of medullary carcinoma are age, the extent of the disease (presence of metastatic lymph node or distant metastases), male sex, the diameter of the tumor, extra thyroid invasion, vascular invasion, immune reaction to calcitonin, the presence of amyloid in the tumor, postoperative residual tumor and high levels of calcitonin (5). In medullary carcinoma 5 and 10 years survival rates were 4 95% and 65% under 40 years old, more than 40 years old 75% ve 50% respectively.

The other prognostic factors are the presence of galectin in the thyroid tissue, high levels of CEA, and increase in the procalcitonin/calcitonin ratio[10].

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The presence of sencron or metachron tumor with different origins is a rare entity and nearly 50 cases have reported in the literature.

However some authors reported an incidence of 19% with the papillary microcarcinoma and medullary carcinoma[12-14].

Some hypothesis were suggested to explain the presence of syncron tumors

‘’The theory of Stem Cell’’ proposes that stem cells that are not transformed by neoplastic processes have the capacity to gain the ability of obtaining thyrocyte or C cell phenotypes.

Recent studies showed that RET protooncogene has a role in the oncogenesis of the both medullary and papillary carcinomas by activation of tyrosine kinase[15-17].

In the literature synchrone carcinomas has been reported previously. Machens et al. showed synchron thyroid papillary carcinoma among 727 thyroid medullary carcinomas. 6 of these cases were hereditary and 20 cases were sporadic.

Machens et al reported a synchronous thyroid papillary carcinoma in 26 of 727 medullary carcinoma patients. 6 of these 26 patients were hereditary.

They did not find a correlation with the sporadic or hereditary onset of these cases and the presence of synchronous thyroid tumor.

After a family scan we confirmed that our case is a sporadic case. Average diameter of medullary carcinoma has been reported 11 mm in patients with simultaneous medullary and papillary carcinoma[18].

The decision of the treatment plan was made base on the papillary carcinoma in these cases[18].

In this case different types of neck dissection was performed on both sides after total thyroidectomy.

Central neck dissection was performed on left lob due to the papillary carcinoma and radical neck dissection was performed on the right side for medullary carcinoma.

In conclusion, the most remarkable features of this case was the patient’s being pregnant at the time of the diagnosis and the presence of metastatic lymph node on the side of papillary tumor originating from the contralateral medullary carcinoma.

Compliance with ethical standarts

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.”

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