North Clin Istanb 2018;5(1):67-71
doi: 10.14744/nci.2017.27147

Case Report PATHOLOGY

Diagnosing between papillary carcinoma and reactive papillary changes in an infarcted thyroid nodule after fine needle aspiration and accompanied by a synchronous brain stem astrocytoma

Ceren Canbey Goret,[1] Nuri Emrah Goret,[2] Omer Faruk Ozkan,[3] Muammer Karaayvaz[3]

[1]Department of Surgical Pathology, Onsekiz Mart University Faculty of Medicine, Canakkale, Turkey
[2]Department of General Surgery, Canakkale State Hospital, Canakkale, Turkey
[3]Department of General Surgery, Onsekiz Mart University Faculty of Medicine, Canakkale, Turkey

ABSTRACT

A 22-year-old patient underwent fine needle aspiration of a nodule at the outer center of the right lobe of the thyroid, and it was reported to be Bethesda system category IV, Hurthle cell follicular neoplasia. The patient, who persented to Onsekiz Mart University Research and Application Hospital, underwent surgery. During right total thyroidectomy, an almost totally infarcted nodule and papillary structures around these infarcted areas were detected. Herein, we report on diagnostic challenges faced in confirming whether the infarcted nodule was a case of reactive papillary changes or an underdiagnosed papillary carcinoma and how the challenges were overcome using immunohistochemistry analysis and molecular genetic testing. In addition, we examined the case along with a literature review because an accompanying synchronous brain stem astrocytoma was detected in the patient after thyroidectomy.

Keywords: Infarction after biopsi; synchronous tumor; thyroid papillary carcinoma.

Thyroid nodules are very common in clinical practice and mostly benign. Although malignancy rates are low, it is absolutely necessary to cytologically exclude malignancy in nodules with some radiological features. In clinical practice, fine needle aspiration (FNA) has currently replaced radionuclide thyroid screening. FNA cytology is known to be a reliable method in terms of malignant and benign nodule differentiation before making a decision on surgical treatment of the thyroid [1, 2]. It was reported that sensitivity of FNA varies between 65% and 99%, and its specificity varies between 72% and 100% [1, 2].

Local pain and minor bleeding are among the most common post-FNA complications [4]. Serious post-FNA complications occur more rarely. Infarction in the thyroid nodule is one of the serious complications and a rare condition. Infarction is reported to occur more frequently in thyroid nodules of oncocytic morphology [9-10].

If cytologic findings by FNA are not correctly evaluated, it can be very difficult to correctly diagnose the resection episode in such cases because of the infarct.

In this case report, we aimed to present difficulties experienced in histopathologic evaluation of an almost totally infarcted thyroid nodule whose cytologic diagnoses was Hurthle cell follicular neoplasia and in deciding whether these papillary structures observed in the focal area were reactive or associated with a papillary carcinoma and to introduce it in the literature because an astrocytoma was detected in the 2nd synchronous primary brain stem.

Received: February 09, 2017 *Accepted:* June 18, 2017 *Online:* January 10, 2018

Correspondence: Dr. Ceren CANBEY GORET. Onsekiz Mart Universitesi Tip Fakultesi Cerrahi Patoloji Anabilim Dali, Canakkale, Turkey.
Tel: +90 507 950 02 12 e-mail: drcerencanbey@hotmail.com

© Copyright 2018 by Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

CASE REPORT

A 22-year-old patient underwent FNA as a nodule was detected on the outer center of the right lobe of the thyroid, and it was reported to be a Bethesda system [22] category IV, Hurthle cell follicular neoplasia.

A right total thyroidectomy was performed on the patient who presented to our hospital, and a frozen section was requested. In the right total, 3.5×2-cm thyroidectomy material section, a 1.7×1.2-cm nodule, including necrotic and focal hyalinized areas, located 0.3 cm from the thyroid capsule, was observed. The frozen section analysis was reported as "necrosis, focal papillary structures in some places around the hyalinized areas, malignant-benign differentiation was not clear, and paraffin sections were to be examined," and a total thyroidectomy was prevented.

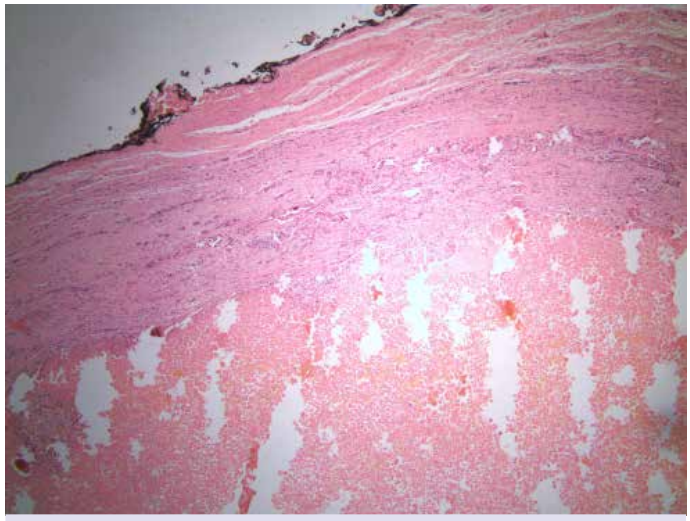

Figure 1. A nodule with large localized areas of necrosis under the thyroid capsule (H&E, ×40).

In the center of the paraffin sections, papillary structures composed of large oncocytic cytoplasmic thyrocytes in the focal area around intense infarct were noticed (Figs. 1, 2, 3).

These papillary structures were observed in the focal areas, and because of the previous FNA diagnosis of follicular neoplasia, these structures were initially considered to be "reactive papillary hyperplasia." However, when examined in detail, these papillary structures were found to be infiltrative in places in spite of being in a focal area, and their cytological evaluation suggested papillary carcinoma.

Immunohistochemical analysis of the papillary structures showed diffuse, strong positivity with cytokeratin 19 and focal, weak positivity with HBME-1, whereas the external control was positive with galectin-3 and no staining was observed in the case (Figs. 4, 5, 6).

On this basis, BRAF V600E was studied in terms of molecular genetics, and the patient was diagnosed with a "thyroid papillary carcinoma" because of a positive result.

FNA preparations of the patient that had been previously analyzed in the external center were made available for a re-evaluation to determine the extent to which the cytology would contribute in such cases, and FNA preparations were re-evaluated.

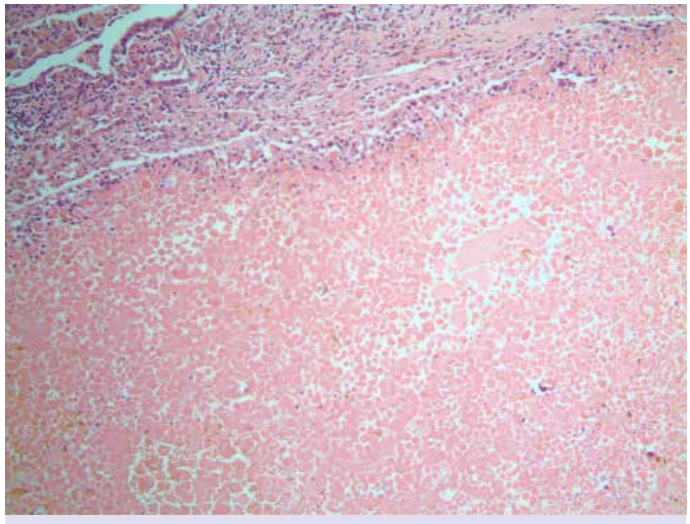

Figure 2. Focal papillary proliferations around large necrosis areas (H&E, ×100).

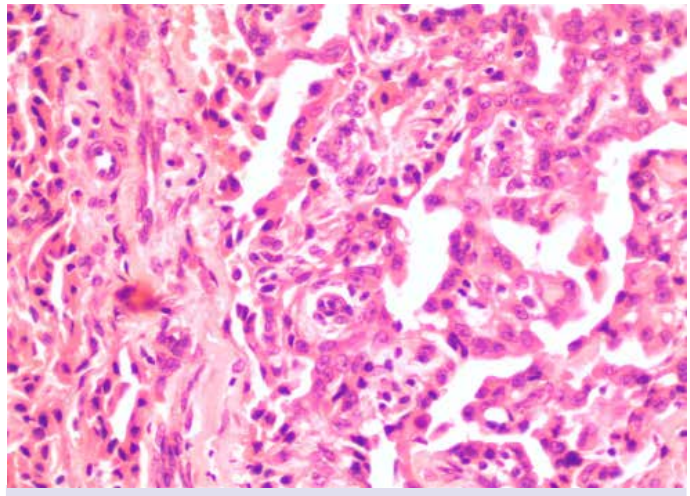

Figure 3. Thyrocytes of papillary carcinoma with a large oncocytic cytoplasm aligned around the fibrovascular core (H&E, ×400).

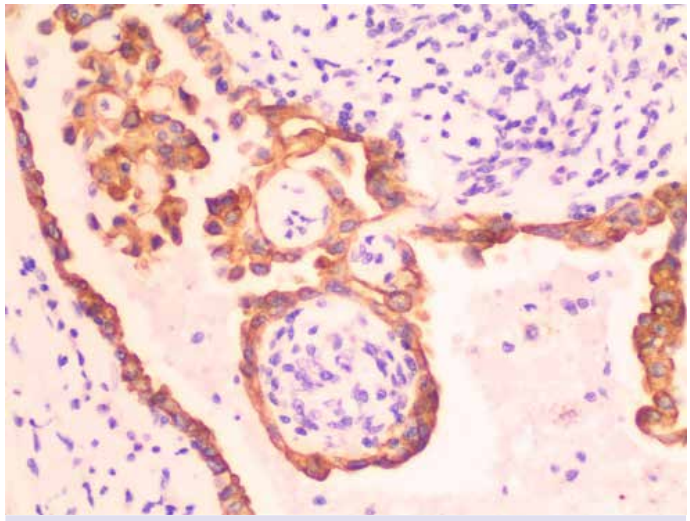

FIGURE 4. Extensive strong positivity with cytokeratin 19 and papillary structures (Immunohistochemistry, ×400).

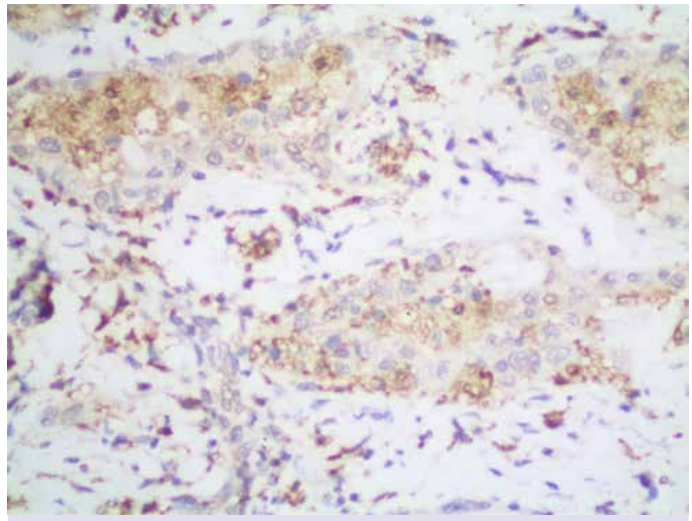

FIGURE 5. Focal weak positive staining with HBME 1 (Immunohistochemistry, ×400).

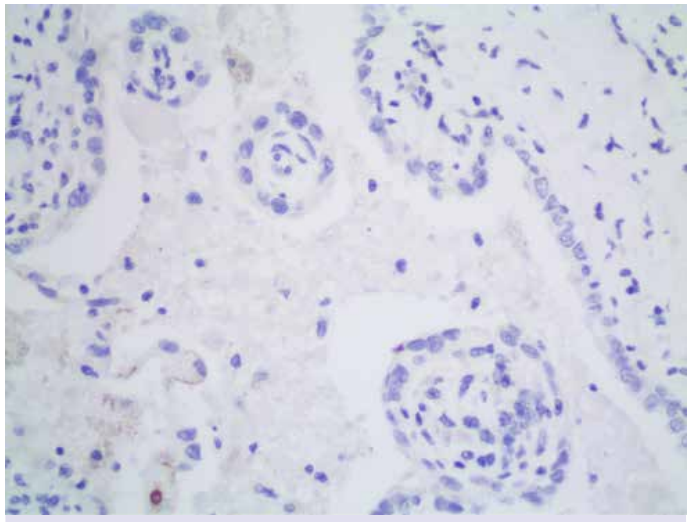

FIGURE 6. No staining with galectin-3 was observed (Immunohistochemistry, ×400).

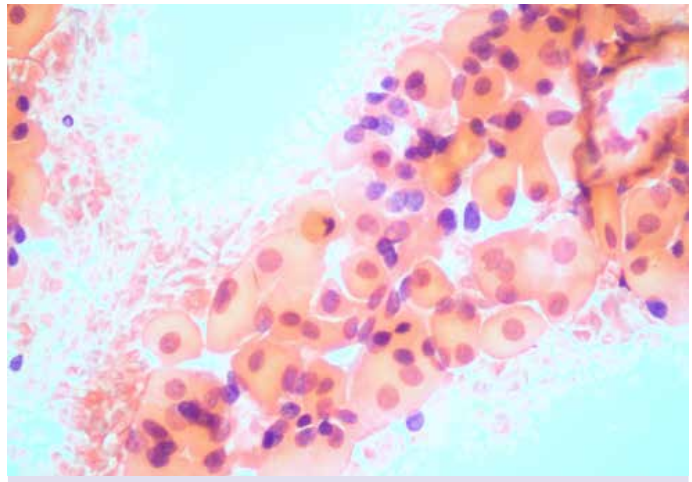

FIGURE 7. Cytologic examination revealed presence of mild hypochromia with large oncocytic morphology, focal overlapping, and infrequent intranuclear inclusion (PAP EA 50, ×400).

Cytological evaluation revealed focal groove structures with large oncocytic cytoplasm in hypercellular spreads, mostly in a microfollicular pattern; some of the structures were standing alone or in groups similar to focal papillary structures, overlapping in places, and also showed thyrocytes with intranuclear inclusion (Fig. 7).

It was considered that an underdiagnosis was made in the FNA analysis, and it could be evaluated as at least category V (suspicious for malignancy) or category VI (malign aspirate).

The patient presented to our hospital again with a complaint of dizziness and nausea after thyroidectomy. During MRI at our center (Fig. 8), a mass was detected in the brain stem. "Astrocytoma," as a 2nd synchronous primary tumor, was detected in the patient who underwent surgery at an external center at the patient's request.

DISCUSSION

Papillary carcinoma is the most common malignancy of the thyroid and has very good prognosis with early diagnosis. Thyroid FNA is a widely accepted and important method in terms of nodule evaluation and follow-up [2, 11].

The FNA procedure is easy, nominally invasive, and

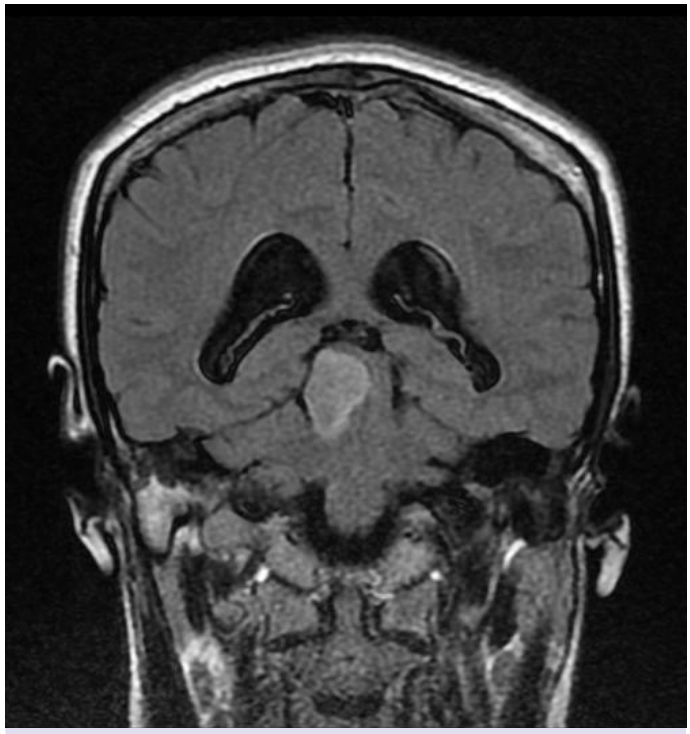

Figure 8. Magnetic Resonance Imaging (MRI) showed a 2.5×1.5-cm mass lesion in the right superior mesencephalon.

advantageous as it can be repeated several times. These repetitions may lead to a decrease in insufficiency rates. When an FNA procedure is performed, the preparation should be spread on the slide without waiting and should be fixed immediately. Otherwise, a fixation artifact may occur and cause problems in cytological evaluation. To avoid such problems, it may be preferable to have a pathologist accompanying the patient when performing FNA to ensure that the pathologist performs spreading and fixation procedures and confirms by staining the material immediately that the number of cells is sufficiently high to ensure lower insufficiency rates.

Local pain and minor bleeding are among the most common post-FNA complications [4]. Serious post-FNA complications occur rarely [2]. The literature contains a few studies on tissue changes post FNA.

According to Mukunyadzi et al., [12] the use of 23 gauge needles has been reported to cause less bleeding and tissue damage. In a report published by Pandit and Phulpagar, histopathological changes that may occur in the acute and chronic stages post FNA were discussed. Acute lesions were reported to include granulation tissue, siderophages, nuclear atypia, irregularly shaped granulomas, deterioration and infarct in the capsule, and thrombosis, and chronic lesions were reported to include bleeding, granulation tissue, linear fibrosis, nuclear atypia, vascular changes, papillary changes, thrombosis, capsular pseudoinvasion, infarction, necrosis, metaplasia, and calcification [13].

Diffuse infarcts and macrophages were noticed in our case. In addition, although existing papillary structures have been initially considered as post-FNA reactive changes, the case was interpreted as malignant because these papillary structures exhibited a focal invasive characteristic; their immunohistochemical analysis with cytokeratin 19 demonstrated diffuse, strong positivity; and the result of the BRAF V600E molecular genetic test was positive.

It has been reported that necrosis has been detected in various tumors and organs post FNA. Acinic cell carcinoma, pleomorphic adenoma, and Warthin's tumor in salivary glands; fibroadenoma in the breasts; and renal cell carcinoma in the kidneys are some of the cases reported in the literature [11, 14].

Infarctions of thyroid Hurthle cell neoplasms and papillary carcinomas post FNA have also been reported [3, 6]. Our patient had an oncocytic morphology.

Batsakis et al. classified post-FNA tissue effects into three categories: [1] micronecrosis and hemorrhage, where diagnostic properties can be recognized; [2] macronecrosis without diagnostic properties; and [3] reactive proliferative areas with macronecrosis and micronecrosis and stromal cells [15].

Us-Krasovec et al. reported that factors responsible for tissue damage post FNA included interruption of microvascular perfusion, traumatic venous thrombosis, and vascular leakage [16].

As stated in some publications, molecular genetic analyses are currently performed for thyroid malignancies. BRAF mutation exists in 29%–69% papillary thyroid carcinomas, most of which occurs at the V600E codon. In addition, it was detected in 13% differentiated thyroid carcinomas and 10% anaplastic carcinomas. These publications also reported that papillary thyroid carcinomas with a BRAF V600E mutation clinically follow a more aggressive course [5, 17-19].

In our patient, in addition to all of these, a second primary synchronous malignancy was detected in the brain stem and a diagnosis of "astrocytoma" was present. Similar to the case presented here, Pulivarthi et al. have reported a case where synchronous glioblastoma and associated thyroid papillary carcinoma are present [20].

Although two primary synchronous malignancies are rarely observed simultaneously, it is reported that the presence of multiple primary malignancies have been observed more frequently than before and the incidence of second primary cancer varies from 1% to 16% depending on the index primary cancer [21].

Numerous synchronous and metachronous tumors have been reported in the literature. These include many synchronous tumor cases, such as small cell lung carcinoma after surgery for lung carcinoid [23], synchronous pancreatic clear cell carcinoma and gastrointestinal stromal tumor [24], synchronous stomach and rectum adenocarcinoma [25], and synchronous papillary and medullary carcinoma in the thyroid [26].

As a conclusion, we should be aware of post-FNA tissue changes, and we should remember that such changes may lead pathologists to misdiagnosis. In addition, in cases with this type of diffuse necrosis, cytologic findings should certainly be correlated with histopathological findings, and even if a small area exists that can be evaluated histopathologically, further immunohistochemical analyses and molecular genetic examinations, if necessary, should be conducted.

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

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship contributions: Concept – C.C.G.; Design – N.E.G.; Supervision – N.E.G.; Materials – C.C.G., O.F.O.; Data collection &/or processing – C.C.G., O.F.O.; Analysis and/or interpretation – O.F.O., M.K.; Writing – C.C.G.; Critical review – O.F.O., M.K.

REFERENCES

1. Liu YF, Ahmed S, Bhuta S, Sercarz JA. Infarction of papillary thyroid carcinoma after fine-needle aspiration: case series and review of literature. JAMA Otolaryngol Head Neck Surg 2014;140:52–7.
2. Usha M, Rashmi K, Sridhar M, Aarathi RR. Infarcted papillary carcinoma of thyroid following fine needle aspiration. Thyroid Research and Practice 2014;11:124–6.
3. Das DK, Janardan C, Pathan SK, George SS, Sheikh ZA. Infarction in a thyroid nodule after fine needle aspiration: report of 2 cases with a discussion of the cause of pitfalls in the histopathologic diagnosis of papillary thyroid carcinoma. Acta Cytol 2009;53:571–5.
4. Polyzos SA, Anastasilakis AD. Clinical complications following thyroid fine-needle biopsy: a systematic review. Clin Endocrinol (Oxf) 2009;71:157–65.
5. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin 2007;57:43–66.
6. Pinto RG, Couto F, Mandreker S. Infarction after fine needle aspiration. A report of four cases. Acta Cytol 1996;40:739–41.
7. Akerman M, Tennvall J, Biörklund A, Mårtensson H, Möller T. Sensitivity and specificity of fine needle aspiration cytology in the diagnosis of tumors of the thyroid gland. Acta Cytol 1985;29:850–5.
8. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med 1993;118:282–9.
9. Ramp U, Pfitzer P, Gabbert HE. Fine needle aspiration (FNA)-induced necrosis of tumours of the thyroid. Cytopathology 1995;6:248–54.
10. Alejo M, Matias-Cruiu X, de las Heras Duran P. Infarction of a papillary thyroid carcinoma after fine needle aspiration. Acta Cytol 1991;35:478–9.
11. Cobanoglu U, Ersoz S, Adamhasan F, Ozoran Y. Infarction of parotid pleomorphic adenoma following fine needle aspiration biopsy. Aegean Path J 2005;54–7.
12. Mukunyadzi P, Bardales RH, Palmer HE, Stanley MW. Tissue effects of salivary gland fine-needle aspiration. Does this procedure preclude accurate histologic diagnosis? Am J Clin Pathol 2000;114:741–5.
13. Pandit AA, Phulpagar MD. Worrisome histologic alterations following fine needle aspiration of the thyroid. Acta Cytol 2001;45:173–9.
14. Rau AR, Pai RR, Nayak S. Infarction of acinic cell carcinoma in a patient infected with HIV: a complication of fine-needle aspiration cytology obscuring definitive diagnosis. Diagn Cytopathol 2003;29:222–4.
15. Batsakis JG, Sneige N, el-Naggar AK. Fine-needle aspiration of salivary glands: its utility and tissue effects. Ann Otol Rhinol Laryngol 1992;101:185–8.
16. Us-Krasovec M, Golouh R, Auesperg M, Pogacnik A. Tissue damage after fine needle aspiration biopsy. Acta Cytol 1992;36:456–7.
17. Xing M, Westra WH, Tufano RP, Cohen Y, Rosenbaum E, Rhoden KJ, et al. BRAF mutation predicts a poorer clinical prognosis for papillary thyroid cancer. J Clin Endocrinol Metab 2005;90:6373–9.
18. Cohen Y, Xing M, Mambo E, Guo Z, Wu G, Trink B, et al. BRAF mutation in papillary thyroid carcinoma. J Natl Cancer Inst 2003;95:625–7.
19. Fukushima T, Suzuki S, Mashiko M, Ohtake T, Endo Y, Takebayashi Y, et al. BRAF mutations in papillary carcinomas of the thyroid. Oncogene 2003;22:6455–7.
20. Pulivarthi S, Haglind E, McGary CT, Gurram MK. Glioblastoma multiforme and papillary thyroid carcinoma - A rare combination of multiple primary malignancies. J Neurosci Rural Pract 2015;6:241–4.
21. Hayat MJ, Howlader N, Reichman ME, Edwards BK. Cancer statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Results (SEER) Program. Oncologist 2007;12:20–37.
22. Cibas ES, Ali SZ; NCI Thyroid FNA State of the Science Conference. The Bethesda System For Reporting Thyroid Cytopathology. Am J Clin Pathol 2009;132:658–65.
23. Çeldir Emre J, Baysak A, Çok G, Nart D, Çağırıcı U. Second Primary Neuroendocrine Tumor in a Patient Operated Because of Lung Carcinoid Tumor: Small Cell Lung Cancer. J Clin Anal Med 2013;4:178–80.
24. Kilic MO, Turkan A, Bozer M, Arslan N, Koktener A. Synchronous tumors: clear cell carcinoma of pancreas and gastointestinal stromal tumor of stomach. J Turgut Ozal Med Cent 2016;1–3.
25. Tavusbay C, Sarı E, Kar H, Gür EÖ, Hacıyanlı M, Ekinci N. Synchronous Gastric and Rectal Cancer: Case Report. Kolon Rektum Hast Derg 2015;25:38–42.
26. Olgen U, Dilek G, Özaslan C. Concurrent Thyroid Papillary Carcinoma and Medullary Carcinoma in The Thyroid. Acta Oncologica Turcica 2015;39–42.