DOI: 10.4274/tjcd.galenos.2021.2021-9-4
Turk J Colorectal Dis 2022;32:157-159

CASE REPORT

A Rare Multiple Primary Cancer: A Case Report of Quadruple Primary Cancer

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ABSTRACT

Multiple primary tumors, especially quadruple primary cancers, are extremely rare with a reported incidence of 0.007%. In this study, a very rare case of quadruple primary cancer found and treated in a 74-year-old male patient over a 15-year period is presented.
Keywords: Multiple primary cancer, quadruple primary cancer, cancer

Introduction

Multiple primary cancer is the detection of two or more cancer types that are histologically unrelated to each other in the same or different organs of a patient. From this definition it is clear that metastasis must be excluded. Multiple primary cancers account for 2-6.3% of all cancers. With the development of diagnostic techniques and prolongation of life expectancy, patients with multiple primary cancers are being reported more frequently and the vast majority of these are patients in whom two different types of cancer have been described. As the number of primary cancer types included in multiple primary cancers increases, the incidence decreases. The incidence of quadruple primary cancer is less than 0.1%.[1] In this study, a patient with multiple primary cancer with four different types of malignancy, namely laryngeal, lung, prostate and colon cancer, is presented.

Case Report

In this study, a 74-year-old male patient with four types of primary cancer is presented. There was no history of cancer in the mother, father and children. Laryngopharyngectomy and adjuvant radiotherapy were performed with the diagnosis of squamous cell carcinoma located in the hypopharynx. Due to palpation of hard lymphadenopathy in the left neck during radiotherapy, the treatment was interrupted and left neck dissection was performed. Since no malignancy was detected in the pathological examination of the neck dissection material, the adjuvant radiotherapy program was continued and completed.

The patient was admitted to the urology clinic of our hospital with the complaint of inability to urinate in 2018 and was diagnosed as having prostate cancer by biopsy after further examination and treatment. On April 10, 2018, transurethral resection of the prostate (TUR-P) was performed. He was diagnosed as having prostatic acinar adenocarcinoma in TUR-P material. In the immunophenotypic examination of the material, positive staining was observed in the tumoral glands for prostate specific antigen (PSA) and alpha-methylacyl-CoA racemase. No positive staining was observed for p63 protein and high molecular weight cytokeratin.

The patient was admitted to the chest diseases outpatient clinic of our hospital with the complaint of cough in October 2018, and a mass lesion suspicious for cancer was observed on thorax tomography in the upper lobe of the right lung (Figure 1).

A diagnosis of pulmonary adenocarcinoma was made on October 16, 2018 by transthoracic biopsy. With staging suggesting locoregional early stage lung adenocarcinoma, chemoradiotherapy treatment was started. Colonoscopic evaluation was performed after detecting a hypermetabolic

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Received: 17.09.2021**Accepted:** 14.10.2021

area in the sigmoid colon on positron-emission tomography computed tomography during follow-up imaging. The colonoscopy revealed a tumor suspicious lesion in the sigmoid colon and a diagnosis of colonic type adenocarcinoma was made from the biopsies taken. In the immunophenotypic examination of the colon biopsy material, focal positive staining with cytokeratin 20, positive staining with CDX2, negative staining with PSA, negative staining with thyroid transcription factor 1 and NAPSIN A, used a double marker for lung adenocarcinoma, were observed. The patient, who was evaluated to be in the early stage both clinically and radiologically, underwent sigmoid colon resection on October 4, 2019, and the diagnosis of colonic adenocarcinoma was confirmed in the resection material.

Hematoxylin eosin and immunohistochemistry stained light microscopy images of prostate, colon, pericolonic lymph node and lung tumoral tissues are shown in Figure 2.

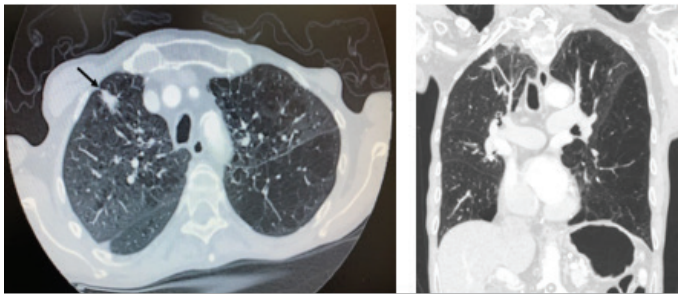

Figure 1. Mass detected in the upper lobe of the right lung on thorax CT
CT: Computed tomography

Discussion

More cases of multiple primary tumors have been identified due to advances in diagnostic techniques and prolongation of patient survival. However, among multiple primary cancers, quadruple cancers are still extremely rare with an incidence of 0.007%.[1]

Multiple primary cancer was first described by Billroth and von Winiwarter[2] in a case report. Diagnostic criteria for multiple primary cancer were defined by Warren and Gates[3] in 1932 and these criteria are still used today. Accordingly, each cancer should be histopathologically proven, cancer types should be histologically different, and the possibility of metastasis should be excluded. In the presented patient, four different primary cancer types, hypopharynx, prostate, lung and colon, were diagnosed histopathologically with typical immunophenotypic evidence.

According to the Warren and Gates[3] criteria, it is not always easy to distinguish multiple primary cancers from multicentric cancers. Therefore, Moertel et al.[4] created a new classification for multiple primary cancers. This classification is also widely used today. According to this classification, three groups are defined; Group 1 includes multiple primary cancers originating in organs with the same histology, while Group 2 includes multiple primary cancers originating from different tissues. Group 3, on the other hand, is the presence of primary cancer in different tissues or organs together with Group 1 in the presence of three or more primary cancers. Three subgroups are defined in Group 1, namely A, B and C. Group 1A includes primary cancer in the same tissues and organs, Group 1B includes primary cancer in the same tissue and different organs, and Group 1C includes primary cancer in bilateral organs. Our patient fits Group 3 in this classification.

Moertel et al.[5] classified multiple primary cancers into two groups as synchronous and metachronous according to the time between the occurrence of the malignancies included.

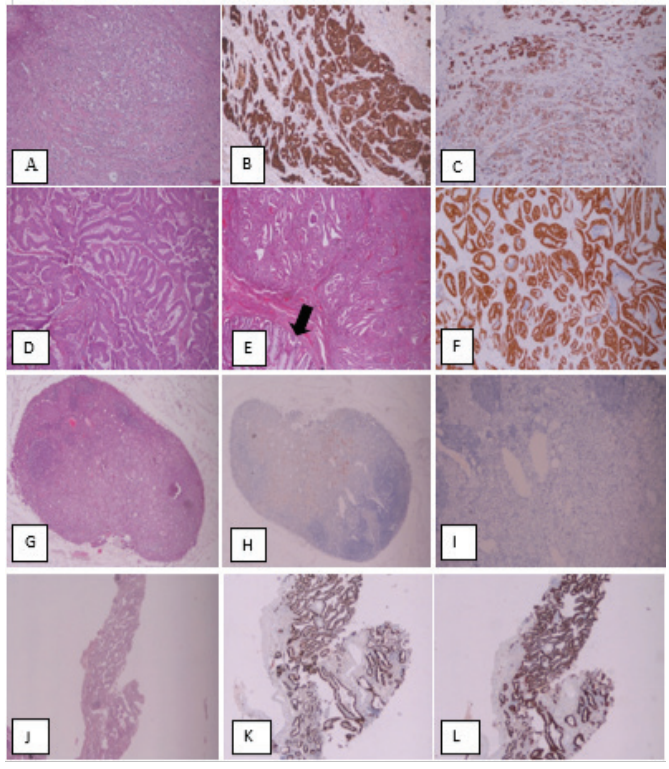

Figure 2. Microscopic examination of prostatic acinar adenocarcinoma (A-C), colon adenocarcinoma (D-F), metastatic pericolonic lymph node (G-I), and lung adenocarcinoma (J-L) Characteristic features of prostate adenocarcinoma (A), Tumor cells show cytoplasmic expression with immunohistochemical AMACR (B), Tumor cells show focal nuclear positivity with immunohistochemical p63 (C), Glandular pattern of colonic adenocarcinoma (D), Colon adenocarcinoma and non-tumor colonic mucosa (black arrow) (E), Tumor cells show cytoplasmic expression with immunohistochemical CDX2 (F), Pericolonic lymph node shows tumoral metastasis (G), Tumor cells show focal nuclear positivity with immunohistochemical p63 (H), Prostatic specific acid phosphatase (PSAP) staining shows positive for tumor cells (I), Lepidic pattern of lung adenocarcinoma (J), Tumor cells show nuclear expression with TTF-1 immunohistochemically (K), Tumor cells show cytoplasmic expression with immunohistochemical CK-7 (L)

Accordingly, if there is less than six months between the definitions/occurrence of primary cancers, these tumors are synchronous while primary tumors with a duration of more than six months are called metachronous. In the presented patient, tumors fit into the metachronous tumor class because of the duration of more than 6 months among the four tumors described. The mechanisms of occurrence of multiple primary cancers are not fully known. However, many hypotheses have been described, such as family history, immunological and genetic defects, prolonged exposure to carcinogens with similar characteristics, or receiving chemotherapy/radiotherapy for primary cancer. The presented patient has no known family history of cancer. However, he had a history of adjuvant radiotherapy due to the diagnosis of squamous cell carcinoma with location in the hypopharynx, which was the first cancer he was diagnosed as having. Post-radiotherapy-associated tumors are generally seen after 10 years, and they are known to be more likely to have sarcoma-type histology.[6] Again, among the chemotherapy-related secondary tumors, hematolymphoid neoplasms have been defined most frequently.[7] All of the tumors described in the presented patient were in the carcinoma group.

There is no established treatment rule in the treatment of multiple primary cancers. Optimal treatment should be determined by considering the type of cancer, the stage of the disease, the response to treatment, the expected life expectancy, and the general condition of the patient.

While retrospectively examining the extremely rare multiple primary cancers presented in this study, the importance of knowing the medical history of previous disease and their specific diagnostic evidence when evaluating patients with cancer was highlighted. Similarly, accurate and complete immunophenotypic studies in determining the histopathological types of tumors reveal the importance of distinguishing separate primary tumors from metastatic tumors. In some cases where the same histological type, for example squamous cell carcinoma, is shown in different locations, the differentiation of multiple primary and metastases may be more difficult, and in such cases the molecular characteristics of the tumors become increasingly important.

Ethics

Informed Consent: Written informed consent was obtained from the patient for the presented study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Z.Ş., B.G., T.G., N.K.T., Design: Z.Ş., B.G., T.G., N.K.T., Data Collection or Processing: Z.Ş., B.G., T.G., N.K.T., Analysis or Interpretation: Z.Ş., B.G., T.G., N.K.T., Literature Search: Z.Ş., B.G., T.G., N.K.T., Writing: Z.Ş., B.G., T.G., N.K.T.

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

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

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