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Case report

Collision of Primary Adenocarcinoma of the Lung with Metastatic Adenocarcinoma in the Colon: A Case Report

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SUMMARY

Introduction. Collision tumors occur when two tumors of different histological origin develop simultaneously at the same site, such as sarcoma and carcinoma combinations, carcinoma and lymphoma combinations, or others. Notably, collision tumors are less common in the lungs compared to other organs.
Case report. A 65-year-old woman with a history of surgically and chemotherapeutically treated colon adenocarcinoma underwent a regular chest radiographic check-up at a hospital. A follow-up examination and computed tomography revealed two oval lesions in the right lung lobe, later confirmed through histopathological and immunohistochemical analysis. One lesion was identified as primary lung adenocarcinoma, while the other was a metastasis of colon adenocarcinoma. Diagnosis of lesions with distinct histological origins relies on determining the expression of specific markers. Lung adenocarcinoma typically expresses TTF-1 in 90% of cases, while metastases originating from colonic adenocarcinoma often exhibit CDX2 marker expression in 99% of cases.
Conclusion. Several theories attempt to explain the formation of collision tumors. The first hypothesis suggests that their origin lacks a specific pattern or predictable cause. The second hypothesis proposes that environmental changes, influenced by carcinogenic stimuli, promote the simultaneous growth of two tumors. Lastly, it is hypothesized that tumors modify the organ's microenvironment, increasing the likelihood of nearby metastatic colonization. To ensure effective treatment of collision tumors, accurate and precise diagnosis, along with a comprehensive understanding of the tumor's characteristics, is crucial.

Keywords: **collision tumors, lung adenocarcinoma, thyroid transcription factor 1 (TTF-1), CDX2 transcription factor**

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INTRODUCTION

A collision tumor is a rare occurrence characterized by the presence of two tumors of different histological origin in the same organ. These tumors can involve various combinations, including benign with benign tumors, benign with malignant tumors, and two malignant tumors. Numerous studies have been conducted on the existence of this type of tumor (1). Although collision tumors are infrequent, they tend to have a higher frequency in men compared to women, with the peak occurrence observed in individuals over the age of 65. The only way to diagnose collision tumors is through pathohistological analysis of the affected tissue. They have been identified in various organs, including the liver, uterus, abdomen, esophagus, and lungs (2). In comparison to other organs, collision tumors in the lungs are extremely rare (3). It is important to note that collision tumors do not interfere with each other, even when they grow in close proximity and coexist within the same location (4). Collision tumors most often occur as a collision of carcinoma and sarcoma, carcinoma and lymphoma, but they rarely occur as a collision between two carcinomas (5).

CASE REPORT

A 65-year-old woman underwent a routine X-ray examination that revealed the presence of two oval-shaped abnormalities in the middle and lower lobe of her right lung. The patient had a previous history of colorectal adenocarcinoma, which led to her admission to the emergency center due to symptoms of ileus. Following the diagnostic procedures, she underwent a subtotal colectomy with the creation of terminal ileostomy. The pathohistological analysis revealed invasive low-grade invasive colorectal adenocarcinoma, classified as T3a, Nx (0/1) M0, Dukes B. It infiltrated the entire thickness of the colon wall and discrete pericolic fat tissue. The treatment plan includes adjuvant chemotherapy following the 5-fluorouracil and leucovorin protocol, with a prescription of six cycles of chemotherapy. During a routine follow-up examination, performed one month after completing the chemotherapy and 10 months after the subtotal colectomy, a control X-ray revealed the presence of two oval-shaped masses with diameters of approximately 10 mm in the middle and lower lobes of the right lung (Figure 1).

A CT (Computed tomography) scan of the thorax and upper abdomen revealed a subpleural lobular spiculated zone measuring 17 x 11 mm in the III segment of the right lung (Figure 2, A). Additionally, a nodular lesion measuring 9 mm was found in the IX segment of the same lung. (Figure 2, B).

No abnormalities were observed in other intrabdominal and intrathoracic organs, including the bone structures. Tumor markers CEA and CA 19 - 9 were measured at 16.3 ng/ml and 13.0 U/ml, respectively. The patient expressed a lack of motivation for continuing with second-line chemotherapy, leading to an expectant attitude (a process of waiting) but continued to attend regular follow-up appointments.

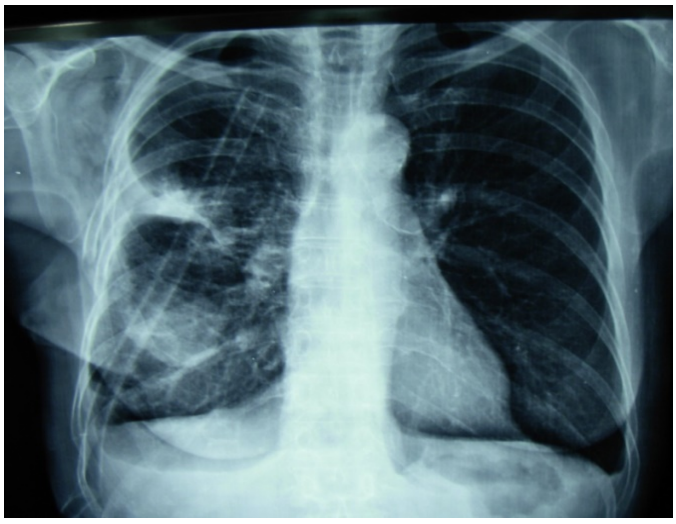

Figure 1. *Two oval hypodensity changes measuring approximately 10 mm in the middle and lower lobes of the right lung*

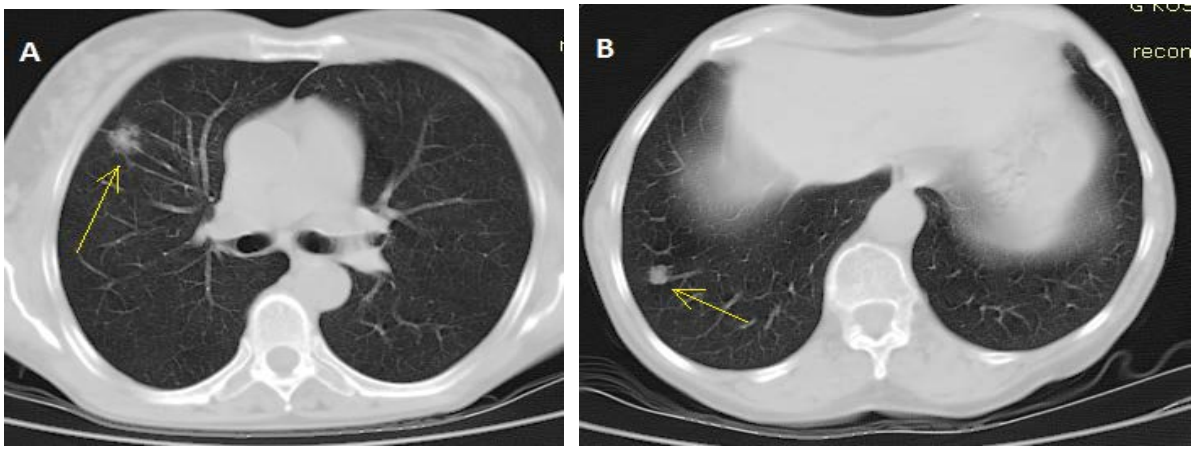

Figure 2. *CT of a thoracic subpleural lobular spiculated lesion (arrow on A part), with dimensions 17 x 11 mm; Nodular lesion with dimensions 9 mm (arrow on B part)*

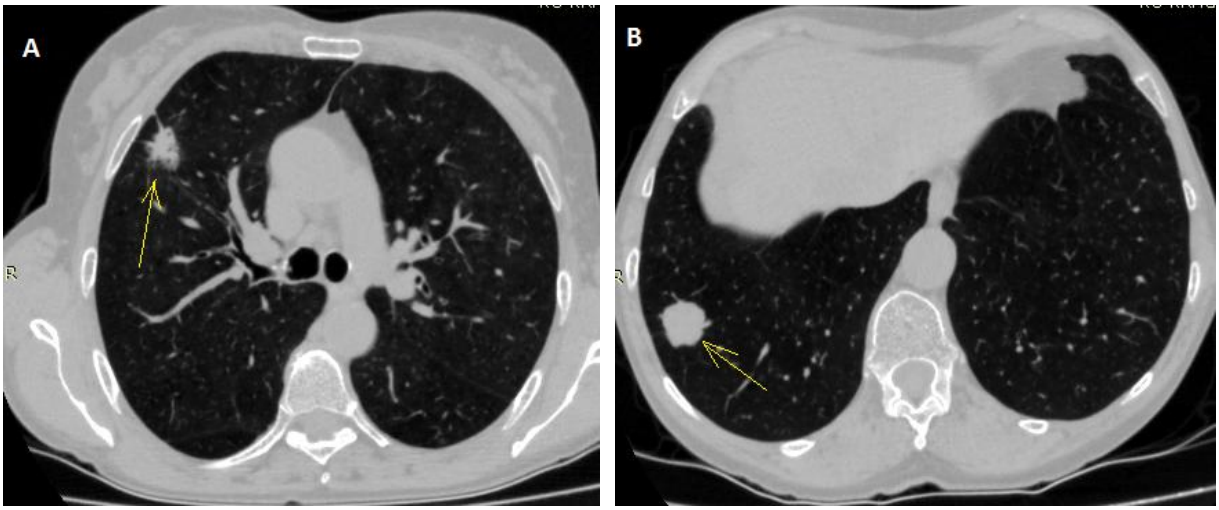

Figure 3. *An anterior segment of the upper lobe lesion, with dimensions 18 x 15 mm (arrow on A part); A lesion located laterobasally, with dimensions 20 x 22 mm (arrow on B part)*

After one year, a follow-up CT scan revealed the presence of previously observed lobular focal lesions with unclear contours in the lung parenchyma. The larger lesion was located laterobasally, measuring approximately 20 x 22 mm (Figure 3, A), while the lower lesion was found in the anterior segment of the upper lobe, measuring approximately 18 x 15 mm (Figure 3, B). No lesions were observed in other intrabdominal or intrathoracic organs, including the bone structures. Tumor marker CEA was measured at 227.3 ng/ml, and CA 19 - 9 at 16.4 U/ml. Both tumor markers showed higher values compared to previous measurements, with CEA exhibiting a particularly significant increase.

The patient was referred to a thoracic surgeon for the evaluation of resectability of the lung changes recorded in the medical documentation, indicating the need for surgical treatment. During the exploration, the thoracic surgeon observed a tumor lesion in the anterior segment of the right upper lobe, measuring approximately 2 x 2 cm. The lesion exhibited a solid consistency and retracted the visceral pleura. In the laterobasal segment of the right lower lobe, a change measuring approximately 2 x 2 cm

was observed, which raised suspicion of a metastatic lesion. The surgeon decided to perform an atypical resection of the anterior segment of the right upper lung, followed by the excision of the metastatic lesion in the laterobasal segment of the right lower lobe.

The histopathology findings from a tissue sample indicated the presence of acinar-predominant invasive adenocarcinoma of the lung, with a good differentiation type (histologic grade I). Necrosis was not observed and desmoplasia was of low-grade. There were no signs of lymphatic invasion, and infiltration of the visceral pleura was not present. The tumor cells showed diffuse positivity for cytokeratin 7 (CK7), carcinoembryonic antigen (CEA), and thyroid transcription factor 1 (TTF1), but were negative for cytokeratin 20 (CK20) and caudal type homeobox transcription factor 2 (CDX2). Based on these findings, the diagnosis was invasive pulmonary adenocarcinoma (Figure 4).

The other tissue represented mucinous colorectal adenocarcinoma with pulmonary metastases and tumor's cells were diffuse positive for CK20, CEA and CDX2 but negative for CK7 and TTF-1 (Figure 5).

It is noteworthy that, except for CEA, there is an opposite pattern of marker expression between these two tumor types.

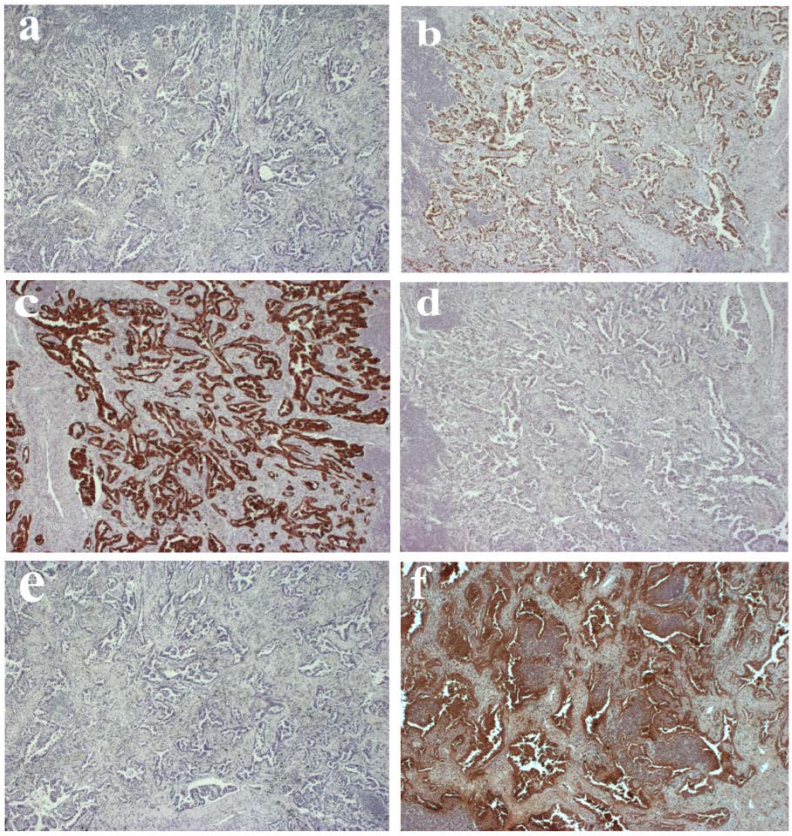

Figure 4. *Histopathological finding of the primary tumor. a) H&E; b)TTF-1+; c) CK7+; d) CK20-; e) CDX2-; f) CEA+*

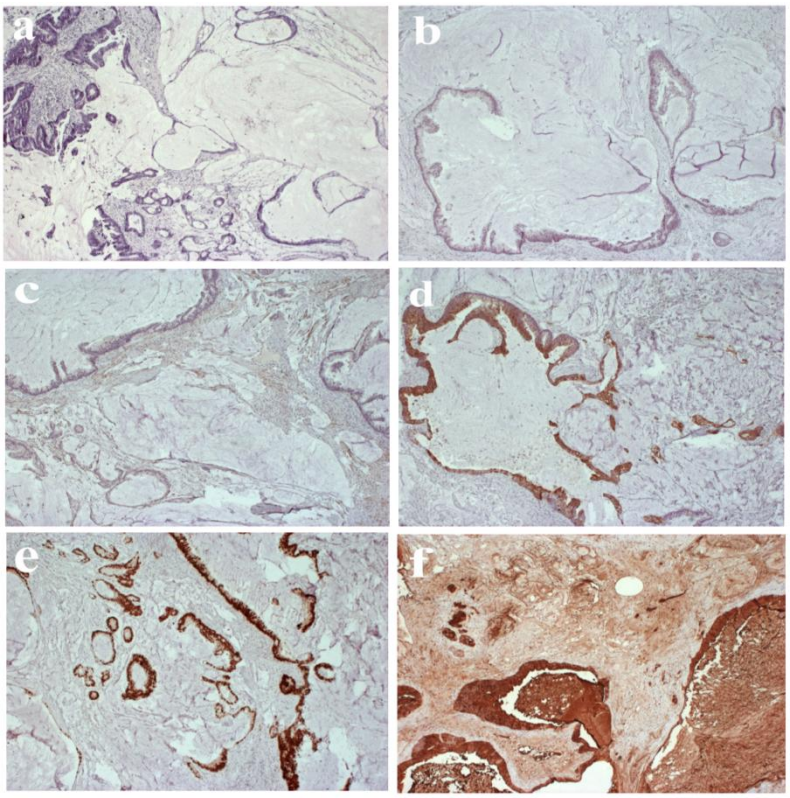

Figure 5. *Histopathological finding of colon adenocarcinoma metastasis. a) H&E; b)TTF-1-; c) CK7-; d) CK20+; e) CDX2+; f) CEA+*

DISCUSSION

Our case illustrates an interesting occurrence of two pathohistologically distinct tumors in lung tissue that were diagnosed simultaneously. The first tumor in our case is primary adenocarcinoma of the lung, which has become the most prevalent subtype of lung cancer with an increasing incidence. It is a primary epithelial neoplasm characterized by glandular differentiation. The five-year survival rate for this cancer type is typically 12% - 15%, regardless of recent advancements in therapeutic treatments. The incidence of lung adenocarcinoma in women has significantly risen in recent years, likely attributed to smoking. This tumor is rare before the age of 20, with the average age of onset being around 70 years. Over the past two decades, adenocarcinoma has surpassed squamous carcinoma as the leading type of non-small cell carcinoma (6).

On the other hand, there was a metastasis from colorectal carcinoma, which was diagnosed as mucosal adenocarcinoma. Metastasis is the primary cause of mortality in patients with colorectal cancer, with the liver and lungs being the most frequent sites of metastatic spread. The resectability of metastases plays a critical role in determining the prognosis and treatment strategy, especially when the metastasis is confined to a single site (7). Approximately, 10% - 15% of patients with colorectal carcinoma develop lung metastases during the course of the disease (8, 9). Compared to metastases from colorectal carcinoma in other organs, lung metastases tend to exhibit a slower growth rate and are associated with better survival outcomes (10).

The accurate diagnosis of pulmonary tumors and differentiation between primary tumors and lung metastases often depend on the use of immunohistochemical markers. Vidarsdottir H et al. conducted a study on 665 primary lung carcinomas and 425 lung metastases to evaluate the diagnostic value of markers and the potential to distinguish between primary and secondary lung lesions. The findings revealed that TTF-1 was expressed in 90% of primary lung adenocarcinomas, while CDX2 showed positive expression in only 7% of cases. Additionally, 68% of lung adenocarcinomas exhibited positivity for CK7,

TTF-1, and napsin A. In the case of lung metastases from colorectal carcinoma, CK20 showed positive expression in 83% of cases, while CDX2 demonstrated positive expression in 99% of cases. Only 4% of tumors showed positivity for TTF-1 (11).

SU YC et al. conducted a study to investigate the expression of CK7, CK20, and TTF-1 as a panel of markers for distinguishing primary adenocarcinoma from metastatic lesions in the lungs. The expression of the CK20 marker was significantly higher in metastases originating from the gastrointestinal tract (GIT) compared to metastases from other organs. The combination of markers TTF-1+, CK7+, and CK20- was significantly more common in primary lung adenocarcinomas, while the combination of markers TTF-1-, CK7-, and CK20+ was significantly more expressed in metastases of GIT origin compared to metastases from other organ origins (12). This suggests that TTF-1 is an important marker for diagnosing primary lung adenocarcinoma, while the expression of CD20 is an important marker for diagnosing metastasis from the colon.

There are three theories that try to explain the formation of collision tumors. One of the theories says that the occurrence of two lesions in the same location is coincidental. The second hypothesis assumes that a common carcinogenic stimulus changed the cellular environment and in such an environment two different neoplasms arise. While the last hypothesis says that the first tumor may have changed the microenvironment inside the organ and increased the probability of the development of a second primary tumor or facilitated the settlement of metastases in the vicinity (13).

Also, the exact diagnosis of pulmonary tumors is essential for treatment decision. Indicators for a possible metastasectomy in the lungs include an adequate state of the cardiovascular and respiratory system, a well-controlled primary tumor, a possibility of complete resection of the metastasis, the absence of a metastasis outside the lungs, or if it exists, it can be well controlled by resection or other local therapy. All this also applies to metastases originating from the colon (14). When metastasectomy is not possible, the main treatment methods are chemotherapy and targeted therapy. An analysis of 25 non-randomized studies carried out between 2000 and 2011 showed that the 5-year survival of patients who underwent pulmonary metastasectomy was between 27% - 68%, while the 5-year survival of patients with metastatic colorectal cancer receiving only supportive therapy was less than 5% (15). For primary lung adenocarcinomas in the early stage, if they are larger than 2 cm, segmentectomy is the method of choice, while for smaller tumors, wedge resection is the method of choice (16). Our patient underwent segmentectomy of the right upper lobe of the lung.

CONCLUSION

From this case, we can make a conclusion that coexisting two pathohistological different tumors must be correctly evaluated, diagnosed and adequately treated for better outcome.

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Kolizija primarnog adenokarcinoma pluća sa metastazom adenokarcinoma debelog creva: prikaz slučaja

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SAŽETAK

Uvod. Kolizioni tumori predstavljaju istovremenu pojavu dvaju tumora različitog histološkog porekla na istoj lokalizaciji. Tumori mogu biti kombinacija sarkoma i karcinoma, karcinoma i limfoma, a postoje i druge mogućnosti. Kolizioni tumori ređe se pojavljuju na plućima nego na drugim organima.
Prikaz slučaja. Šezdesetpetogodišnja žena sa ličnom anamnezom o postojanju adenokarcinoma kolona koji je hirurški i hemioterapijski tretiran javila se na redovan radiografski pregled pluća. Na kontrolnom snimku otkrivene su dve ovalne promene u desnom plućnom krilu, koje su kasnije verifikovane i kompjuterizovanom tomografijom. Patohistološkom i imunohistohemijskom obradom jedna promena identifikovana je kao primarni adenokarcinom pluća, dok je druga promena predstavljala metastazu adenokarcinoma kolona. Određivanje ekspresije pojedinih markera glavni je metod dijagnostikovanja lezija histološki različitog porekla. Adenokarcinom pluća u 90% slučajeva pokazuje ekspresiju tireoidnog transkripcionog faktora 1 (TTF-1), a 99% metastaza koje vode poreklo od adenokarcinoma kolona pokazuje ekspresiju CDX2 markera.
Zaključak. Postoje brojne teorije kojima se pokušava objasniti nastanak kolizionih tumora. Prema prvoj hipotezi, nastanak kolizionih tumora je slučajan. U drugoj hipotezi ističe se da pod uticajem karcinogenih stimulusa dolazi do promene okruženja i potom do istovremenog rasta dvaju tumora u takvoj izmenjenoj sredini. U poslednjoj hipotezi navodi se da jedan tumor menja mikrookruženje unutar organa i samim tim povećava mogućnost naseljavanja metastaza u blizini. Za pravilan tretman kolizionih tumora neophodna je tačna i precizna dijagnoza, kao i poznavanje karakteristika tumora.

Ključne reči: **kolizioni tumori, adenokarcinom pluća, tireoidni transkripcioni faktor 1, CDX2 transkripcioni faktor**