

CASE REPORT

Dual Primary Squamous Cell Carcinoma of the Lung and Adenocarcinoma Rectal

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ARTICLE INFO	ABSTRACT
<p><i>Article history:</i> Received 29 October 2022 Received in revised form 12 December 2022 Accepted 23 December 2022 Available online 30 January 2023</p>	<p>Introduction: Lung and colorectal carcinoma are commonly found in cancer and often cause mortality worldwide. Colorectal cancer (CRC) is the third most common cause of death. Although multiple primary cancers can exist, these two malignancies rarely happen simultaneously. This case report shows a patient diagnosed with squamous cell carcinoma of the lung and rectal adenocarcinoma with metastases to the liver, ocular, and cerebrum.</p>
<p><i>Keywords:</i> Cancer, Dual primer, Rectal adenocarcinoma, Squamous cell carcinoma.</p>	<p>Case: A 54-year-old woman came with chest pain accompanied by persistent and progressive breathing difficulty, cough, loss of appetite, and weight loss of almost 15 kg. The patient experienced sudden lower and upper extremities weakness two weeks after being hospitalized. The patient also experienced blurred vision and swelling of the eyes. At that time, the patient had an endoscopy procedure, and the biopsy showed colitis with severe dysplasia. Based on clinical and radiologic findings, the patient had lung and colon cancer.</p>
<p><i>Cite this as:</i> Haikal SMS, Irawiraman H, Putra AD. Dual Primary Squamous Cell Carcinoma of the Lung and Adenocarcinoma Rectal. <i>J Respi</i> 2023; 9: 44–48.</p>	<p>Conclusion: Dual primary carcinoma rarely happens, and metastases from different neoplasms are difficult. Warren and Gates' criteria could be used to diagnose dual primary carcinoma, especially if diagnostic studies could not be performed. Signal that the hedgehog gene is still active when the neonate is born is suspected of causing these carcinomas.</p>

INTRODUCTION

Lung and colorectal cancer (CRC) are common forms of cancer and often cause mortality. Approximately about 1.08 million people die from pulmonary cancer. Meanwhile, CRC causes 0.916 million deaths. Pulmonary cancer is the leading cause of death in men with cancer (21.8%). It is also responsible for the death of women (9.1%) after breast cancer.¹ Most lung cancer cases can only be diagnosed in advanced stages, resulting in high mortality rates.^{2,3} The most common type of tumor in pulmonary cancer is squamous cell carcinoma (SCC). SCC mainly affects men and is more strongly associated with smoking than any other type of lung cancer. Other risk factors for SCC include age, family history, exposure to second-hand smoke, mineral and metal particles, or asbestos.^{1,4}

CRC is the third most common cause of death after pulmonary and breast cancer (1.93 million cases).³ About 1,096,000 new cases of colon cancer are estimated to be diagnosed in 2018, while about 704,000 new cases of rectal cancer are expected. Together, these comprise 1.8 million new cases of CRC, the most diagnosed cancer among men. Certain dietary and lifestyle choices can promote intestinal inflammation and modify the intestinal microflora to promote an immune response, both of which can facilitate polyp growth and conversion to cancer.^{5,6}

These two tumors rarely occur at the same time. The presence of multiple primary cancers in a single patient was first reported more than 100 years back.⁷ This report describes a unique case of dual primary squamous cell carcinoma of the lung and rectal adenocarcinoma with metastases to the liver, ocular, and cerebrum.

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Jurnal Respirasi, p-ISSN: 2407-0831; e-ISSN: 2621-8372.

Accredited No. 200/M/KPT/2020; Available at <https://e-journal.unair.ac.id/JR>. DOI: [10.20473/jr.v9-i.1.2023.44-48](https://doi.org/10.20473/jr.v9-i.1.2023.44-48)



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CASE

A non-smoking 54-year-old woman came with chest pain for the past month. It was accompanied by persistent and progressive breathing difficulty, cough, loss of appetite, and weight loss of almost 15 kg. Two weeks after being hospitalized, the patient experienced sudden lower and upper extremities weakness. The patient also experienced blurred vision and swelling of the eyes. The patient had a history of a mass on the right lower abdomen. The symptom was accompanied by defecation difficulty and the stool's consistency turning into liquid in the past two years. At that time, the patient had an endoscopy procedure, and the biopsy showed colitis with severe dysplasia.

Physical examination showed proptosis in the left eye. Thorax percussion showed dullness, and the vesicular sound was diminished on the right side. Abdominal examination showed no abnormality. Extremities examination showed reduced motoric power on the right side. Tumor marker examination results were lactate dehydrogenase 749 U/L; alpha-fetoprotein (AFP) 4.12 ng/mL; and carcinoembryonic antigen (CEA) 1.100 ng/mL.

Thorax computed tomography (CT) scan (Figure 1) showed a solid mass absorbing the contrast on the right lung's superior lobe with a size around 10 cm x 6.9 cm x

11.7 cm with multiple nodules with varied sizes on both lungs' hemithorax.

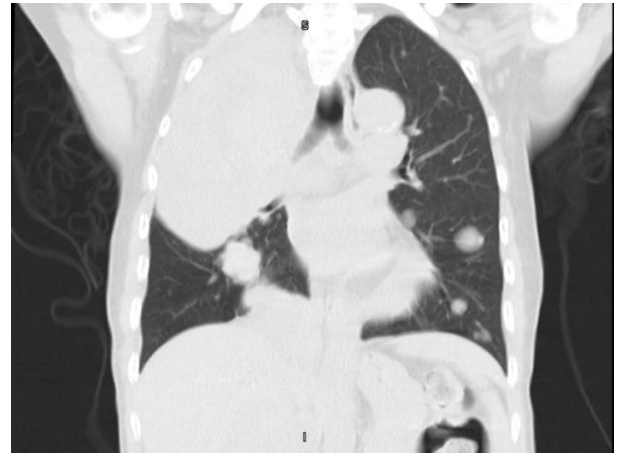


Figure 1. Thorax CT scan

An abdominal CT scan showed an eccentric mass found on 1/3 medial of the sigmoid colon with a size of 2.73 cm x 4.81 cm. Multiple lymphadenopathies were found on the abdominal paraaortic. The liver was not enlarged, the parenchyma's shape and density were normal, the edge's surface was smooth, and a nodule was found on the liver's lobule with a diameter of around 3.25 cm (Figure 2).

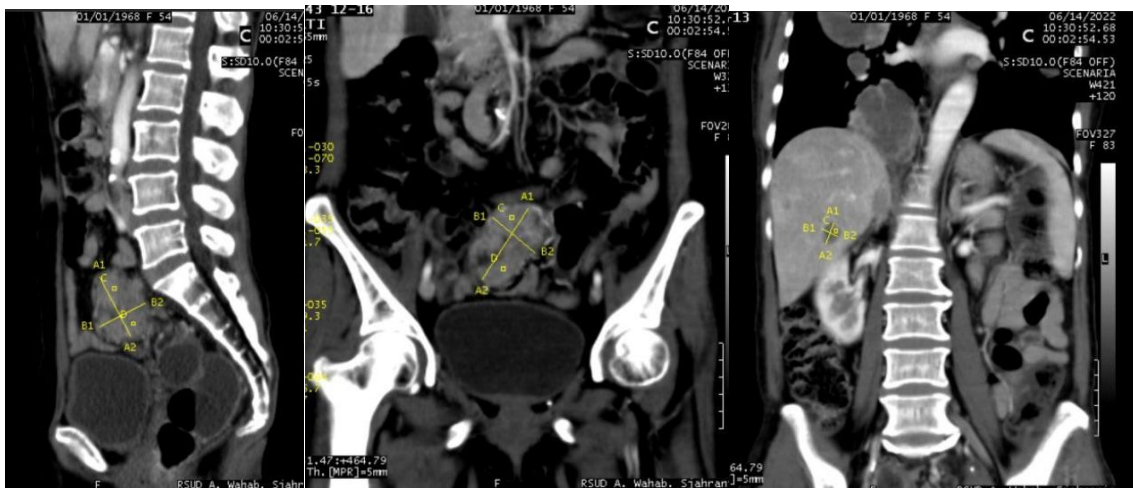


Figure 2. Abdomen CT scan

CT scan of the head showed an isodense lesion absorbing the contrast on ethmoidal sinus, expanding into the posterior cavum orbita with a size of 1.4 x 2.7 cm. An isodense lesion was found on the right temporal

bone with a diameter of around 1.7 cm (Figure 3). Based on the clinical and radiological examination, the primary diagnosis was lung carcinoma with multiple extrathoracic metastases.



Figure 3. Head CT scan

Fine needle aspiration biopsy (FNAB) of the lung with CT guiding showed an atypical clustered epithelial tumor, polymorphic with basophilic cytoplasm and showing necrosis in the background. The conclusion was squamous cell carcinoma of the lung (Figure 4). A tissue biopsy of the rectum by endoscopy was also performed, showing the rectum's mucosa epithelial tumor infiltrating the surrounding tissue, hyperchromatic and polymorphic atypical cells. The conclusion was rectal adenocarcinoma (Figure 5).

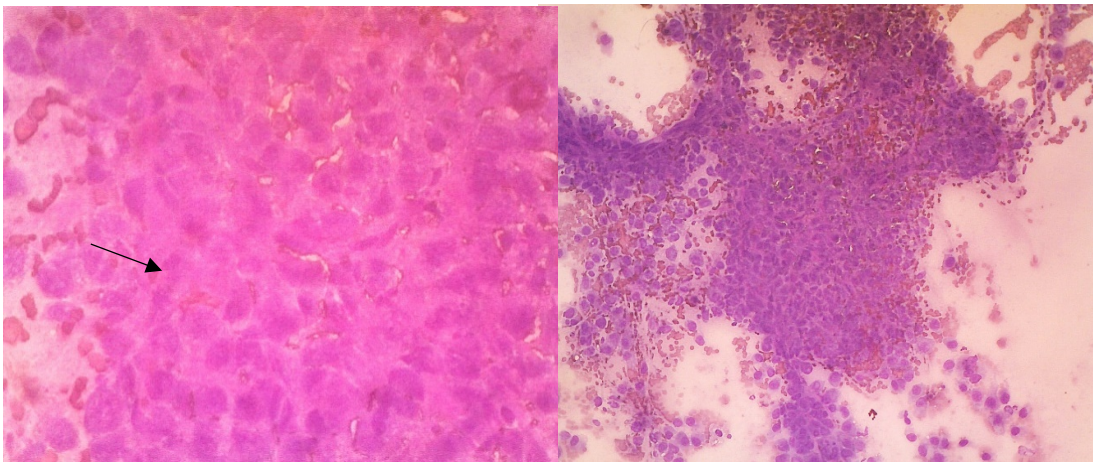


Figure 4. Cytopathology examination showing several polymorphic epithelial cells with a hyperchromatic nucleus (arrow) spreading diffusely with erythrocytes and vast necrosis in the background

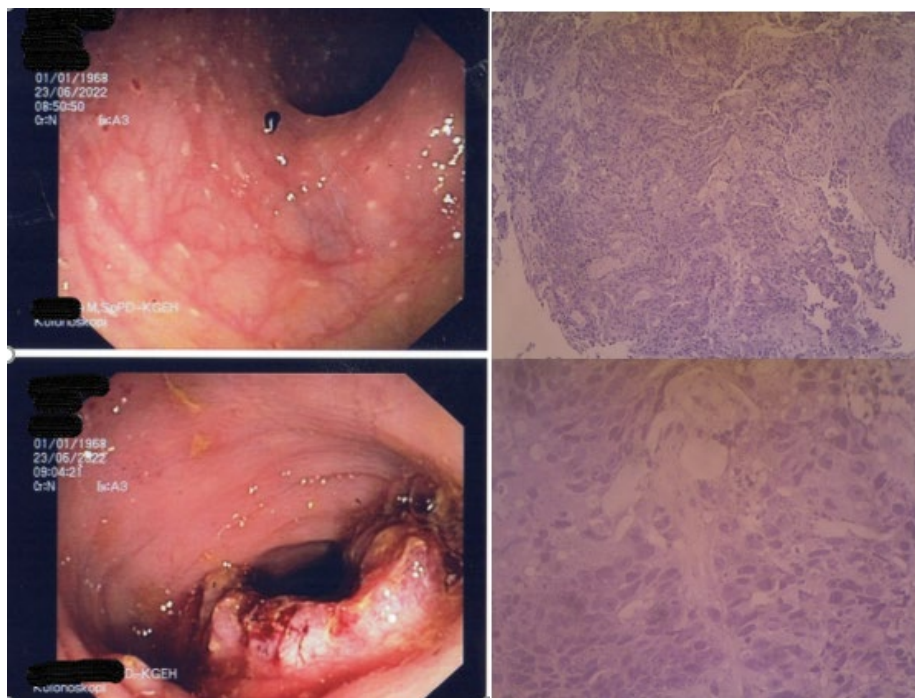


Figure 5. Endoscopic examination showed a fragile lumpy mass that easily bled, covering half of the lumen, 20 cm from the anocutaneous line. Histopathology examination showed the intestine's mucosa with tubular and papillary epithelial tumor infiltrating the surrounding tissue. The tumor cells were atypical, polymorphic, and hyperchromatic with pathological mitosis.

DISCUSSION

Clinically, the patient showed symptoms of lung cancer with chest pain accompanied by persistent and progressive breathing difficulty, chronic cough, and loss of appetite and weight.^{8,9} Respiratory and systemic manifestations can be found in lung cancer. Chest pain could be caused by cancer invasion into the surrounding tissue, causing neuropathic pain.¹⁰ The suspicion of lung cancer was strengthened by dullness on chest percussion and reduced vesicular sound caused by the lung mass filling the thorax cavity. The patient also experienced an extremities problem and blurry vision. It can be assumed that there were other organs involved. A history of mass on the abdomen with digestive tract disorder for the last two years indicated a different progressivity between the lung tumor and the rectum tumor.

CEA test result was 1.100 ng/ml, as tumor marker showed a response from the body's cells to the cancer cell. CEA increases in some cancers, including lung and colon cancer. However, CEA examination cannot determine which cancer is primary cancer. Immunohistochemistry staining is commonly performed to identify metastatic cancer cells in uncommon places. CK7 and TTF-1 immunohistochemistry staining specific for carcinoma of the lung and CK20 and CDX2 expressed by intestinal carcinoma were not performed on the patient.¹¹

The incidence of ocular metastases from lung cancer is 2-7%. The diagnosis of ocular metastases is based on clinical findings and radiological imaging. The spread of these metastases indicates that the spread of cancer is hematogenous. Radiotherapy, surgical resection, transpupillary thermotherapy, and intravitreal chemotherapy are available.¹² Radiotherapy is an effective treatment modality for ocular metastases. According to Yang (2009), patients with ocular metastases with primary pulmonary cancer have a survival rate of no longer than six months.¹³ Hence, an immediate clinical suspicion of ocular metastases is required if there are any visual complaints. Although the treatment is only palliative, a thorough ocular and systemic evaluation is required for the patient.

The brain is one of the most common distant metastatic sites in non-small cell lung cancer (NSCLC). It was found that 40% of NSCLC patients had brain metastases.¹⁴ Based on a study by He, *et al.* (2021), 39% of lung squamous cell carcinoma patients had brain metastases.¹⁵ Li, *et al.* (2017) said that females and high CEA levels are factors associated with the incidence of brain metastases.¹⁴ Both factors are consistent with the patient in this case report. Iwasaki, *et al.* (2004) reported that the 3-year survival rate of patients with high CEA was 0%, and the 3-year survival rate of patients with

normal CEA was 39.6%.¹⁶ CEA is expressed in cancer cells, especially in non-squamous cell carcinomas. Elevated serum CEA levels can reliably reflect body-wide metastases, but the exact mechanism remains unclear.

The liver is the most common site of metastases in patients with colorectal cancer because of its anatomical relationship to portal circulation. As many as 70% of colorectal cancer patients will develop liver metastases. The process of metastasis occurs with a series of mutations in the epithelial cells of the colon, followed by spreading through the blood or lymphatic circulation, which then attaches to the hepatic sinusoids. Cancer cells will interact with sinusoid cells, such as Kupffer cells and stellate cells, resulting in damage to the liver parenchyma.¹⁷

Based on clinical and radiologic findings, the patient had lung and colon cancer. Whether the second lesion of cancer was truly primary or metastatic was difficult to decide. Warren and Gates (1932) proposed criteria that the diagnosis of dual primary carcinoma requires the following: (1) each tumor must present a definite picture of malignancy; (2) each tumor must be distinct histologically; and (3) the possibility that one is metastatic to the other must be ruled out.⁷⁻¹⁸

The biopsy showed squamous cell carcinoma of the lung and adenocarcinoma of the colon. This proved that the two cancers are histologically different. Metastases from the lung to the rectum are extremely rare. Generally, lung cancer spreads through the aerodigestive tract (larynx, nasopharynx, esophagus, oral cavity, and hypopharynx). In this patient, there was no abnormality in that tract.¹⁵ However, the condition of metastases can still be ruled as a differential diagnosis.

Even though the mechanism of this dual primary cancer could not be determined, some studies hypothesize the hedgehog gene's role. Hedgehog (Hh) is one of the few signaling pathways frequently used during development for intercellular communication.¹⁹ The signaling path of the hedgehog gene is responsible for cell growth through signal transmission between the cell membrane and nucleus. It plays an important role in the proliferation and differentiation of the cell for increasing the number of cells. The signaling pathway of the hedgehog gene is still active when the fetus is in the mother's womb. When the baby is born, this signaling pathway deactivates or is minimally active. If this signaling pathway is still active in adulthood, excessive proliferation of the cell will occur. This can lead to malignancy. The type of hedgehog gene often studied is the sonic hedgehog gene. This gene is expressed in many organs, including the pulmonary and colorectal tissues. Dual primary cancer can be suspected when this gene is still active in both organs.²⁰

CONCLUSION

The case for primary dual carcinoma rarely happens in one person. This case challenges many physicians, especially when the tumor metastases in the nearby tissues. It is difficult to distinguish between dual primary metastases from a neoplasm of different organs. Warren and Gates' criteria can be used to diagnose this dual malignancy when the diagnostic studies are limited. The hedgehog gene that is still active is suspected to be the cause of this phenomenon.

Consent

Written informed consent was obtained from the patient.

Acknowledgments

None declared.

Conflict of Interest

The authors declared there is no conflict of interest.

Funding

This study did not receive any funding.

Author's Contributions

Concepting, designing, and collecting the data: SMSH. Providing access to the data: ADP and HI. Reviewing and revising: SMSH. All authors contributed and approved the final version of the manuscript.

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