

# Multiple Primary Malignancy of Esophageal and Gastric Synchronous and Colon Metachronous

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## ABSTRACT

Multiple primary cancer is an incidence when a patient has multiple malignancy in two or more organs without possibility of metastatic lesion. There have been many reports on multiple primary cancer since Billroth reported it for the first time in 1879. Patients who have been diagnosed with a cancer have higher risk for developing another cancer, thereby physician and the patients should raise more awareness toward possibility of developing a new metachronous or synchronous cancer. We report a patient who has three histologically distinct cancers. Resected primary colon adenocarcinoma and 3 years after came with hematemesis and diagnosed to have a metachronous squamous cell carcinoma of the oesophagus synchronous with gastric adenocarcinoma. This case is interesting due to the clustering of three primary cancers (synchronous and metachronous) which is a rare occurrence in a single patient.

**Keywords:** multiple primary cancer, esophageal squamous cell carcinoma, colonic adenocarcinoma, gastric adenocarcinoma, triple primary cancer

## ABSTRAK

Multiple primary cancer adalah suatu insidensi ketika pasien memiliki beberapa keganasan pada dua organ atau lebih tanpa kemungkinan lesi metastatik. Ada banyak laporan tentang multiple primary cancer sejak Billroth melaporkannya pertama kali pada tahun 1879. Pasien yang telah didiagnosis menderita kanker memiliki risiko lebih tinggi untuk berkembangnya kanker lain, oleh karena itu dokter dan pasien harus meningkatkan kesadaran lebih terhadap kemungkinan berkembangnya kanker metachronous atau kanker synchronous. Dilaporkan seorang pasien yang memiliki tiga kanker histologis yang berbeda. Adenokarsinoma primer kolon yang telah pulih dan 3 tahun setelah kedatangan dengan hematemesis dan didiagnosis memiliki karsinoma sel skuamosa metachronous dari synchronous kerongkongan dengan adenokarsinoma lambung. Kasus ini menarik karena pengelompokan tiga kanker primer (sinkron dan metachronous) yang jarang terjadi pada satu pasien.

**Kata kunci:** multiple primary cancer, karsinoma sel skuamosa kerongkongan, adenokarsinoma kolon, adenokarsinoma lambung, triple primary cancer

## INTRODUCTION

Multiple primary cancer is an incidence when a patient has multiple malignancy in two or more

organs without possibility of metastatic lesion. Based on Billroth findings, multiple primary cancer could occur in highly cancer-susceptible patients. Multiple

primary cancer mainly classified based on whether it occur together in a 6-months period (synchronous) or in consecutive time period (metachronous).<sup>1</sup>

Moertel et al otherwise classified multiple primary cancer into three type: (1) Two or more cancer from the same organs or similar histopathologic findings in a different organs; (2) Several malignancy in different tissues and organs; (3) A combination of both type 1 and 2. Estimated in 20 year follow-up period, almost a quarter of patient with cancer would develop secondary cancer.<sup>1,2</sup> The cumulative incidence was 5.0%, 8.4%, 10.8%, and 13.7% in 5, 10, 15, and 25 years after the first malignancy incidence.<sup>3</sup> Most of elderly patients aged 60 or more would developed secondary cancer.<sup>4</sup>

Prevalence of cancer in Indonesia until 2013 was 1.4% and ranked as the 4<sup>th</sup> most cause of death in 2015 until 2019, generally found more in female population (2.2%) rather than male (0.6%).<sup>5,6</sup> A study by Bagri et al in Iran from 2009 to 2012 showed that patients with primary multiple cancer was mostly found in female than male in 5<sup>th</sup> to 6<sup>th</sup> decades with 1.56:1 ratio. Metachronous incidence was higher than synchronous multiple primary cancer.<sup>7</sup> Incidence of esophagus, gastric, and colon cancer as a single cancer was high, although multiple primary cancer involving esophagus and gastric was rare (0.08-0.87% in China), although it was increasing in recent years.<sup>8,9</sup>

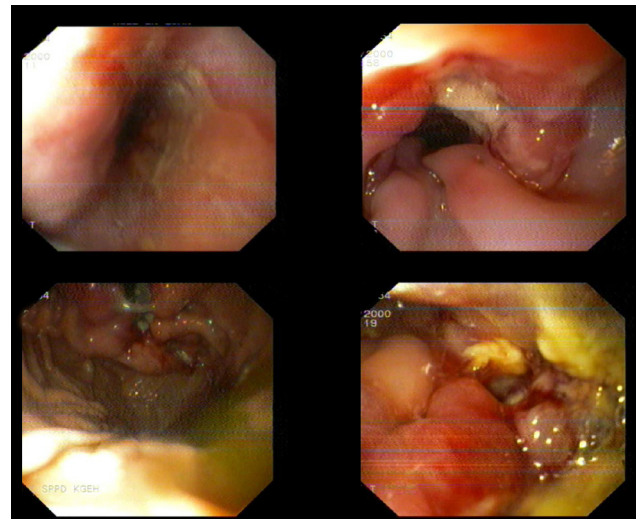
## CASE ILLUSTRATION

A male, 62 years old, with a history of adenocarcinoma colon three years ago, come to emergency unit with the chief complaint of hematemesis for three hours before admission. The vomit was found without any clot and food, but precede with nausea and heartburn from chest to neck. Patient also complained dark stool from seven days ago. During physical examination, patients was found to be pale with a positive epigastric pain. Laboratory examination showed a low hemoglobin (2,5 g/dL), leukocytosis (18.600/uL), hypoalbuminemia (1.62 g/dL), hyponatremia (119 mmol/L), and hyperglycemia (217 mg/dL). Otherwise, potassium, calcium, chloride, AST, ALT, ureum, and creatinine level was in normal range.

Patients was previously hospitalized because of vomiting after meal with watery stool 8-10 times daily with yellowish content. He also had a 9-kg body weight reduced during the last two years. Patients was smoking since 40 years ago, but alcohol consumption was denied. There was no malignancy history among family. During previous hospitalization,

EGD result showed a frail circular mass that tend to bleed in distal esophagus and esophagogastric junction. Histopathologic examination revealed a poorly differentiated squamous cell carcinoma with invasion to muscularis layer (T2). There were also lymphovascular embolus. Abdominal X-ray and CT Scan did not show other significant information. Colonoscopy was also done, but no abnormality was found.

In present admission, 2<sup>nd</sup> EGD was done showing a frail circular mass that tend to bleed in distal esophagus, fulfilling gastric lumen. Histopathologic examination showed adenocarcinoma with moderate-to-severe differentiation. Patients was refusing a referral for further treatment.



## DISCUSSION

Multiple primary cancer was a rare finding. In this case, patient was diagnosed esophageal squamous cell carcinoma two years after previous colon resection following its colonic adenocarcinoma diagnosis. Three months later, patient was diagnosed to have a gastric adenocarcinoma.

There were several case reports of more than two multiple primary cancer cases. In those reports, esophageal carcinoma or premalignant lesion was the preceding cancer, but other studies also report an esophageal carcinoma incidence during or following a cancer diagnosis in other organs.<sup>10,11,12,13,14,15</sup> Xubai Ahmad et al reported a male with metachronous gastric adenocarcinoma that occur 4.5 years after right colon adenocarcinoma diagnosis, while Effat et al reported an esophageal cancer in a patient with colorectal cancer history.<sup>16,17</sup>

This was an interesting case because of the presence of three histologically distinct cancer in

one patient. Several factors that trigger development of secondary cancer were genetics, lifestyle such as alcohol consumption and cigarette smoking, and also radiotherapy or chemotherapy exposure. This patient did not have any significant risk factor nor family history for multiple cancer. Hereditary malignancy syndrome in gastrointestinal cancer was very rare, but should be explored further especially for genetic aspect in this patient.<sup>3</sup> In general, patient with cancer has multifactorial etiology for developing multiple cancer. For example, a patient with colorectal cancer has a susceptibility for developing primary extracolonic cancer as high as developing other primary cancer in colon.<sup>3,18</sup>

This patient has a bad prognosis since there were two synchronous cancer, with recently known successful therapy rate was still low.<sup>19</sup> Long-term screening in patient with malignancy history should be done for early detection purpose, mainly focused on multiple primary cancer, so that prompt treatment could be planned earlier.

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