Lung cancer associated with a single simultaneous solitary metastatic lesion in stomach: a case report with the review of literature

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ÖZET
Midede izole, eş zamanlı metastatik lezyon ile seyreden akciğer kanseri: Literatür eşliğinde olgu sunumu

Mideye ait metastatik tümörler oldukça nadirdir. Pek çok doku neoplazmının mideye metastaz yapabileceğini bildirilmiş ol-
sa da, akciğer kanseri nadir bir metastaz nedenidir. Burada, ilk başvuru bulgusu vena kava sendromu olan 46 yaşındaki
erkek olguyu sunmayı amaçladık. Primer akciğer tümörün histopatolojisibilgisayarlı tomografi eşliğinde alınan biyopsi ile
küçük hücreli dış akciğer kanseri olarak rapor edildi. Takipleri sırasında gastrik yakınmaları olan hastaya üst gastrointes-
tinal sistem endoskopisi uygulandı. Endoskopî bulguları primer skuamöz hücreli kanserin metastazını teyit etti ve yapılan
taramaları da farklı uzak organ metastazının olmadığını, gastrik bölgenin tek bir metastaz odağı olduğunu işaret etti.

Anahtar Kelimeler: Akciğer kanseri, mide metastazı.

SUMMARY
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with the review of literature

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Lung cancer is the major cause of death all over the world. Approximately 40 percent of patients have metastatic disease at the time of presentation (1). The most common site of extrapulmonary spread include liver (35%), bones (25%), adrenals (22%), kidneys (10-15%) and heart-pericardium (20%) (2). However, a metastasis to the stomach is uncommon; hence, it’s rarely diagnosed during the patients lifetime. Although these patients are often asymptomatic, gastric metastasis mark advanced disease and poor prognosis.

We report a case of lung cancer associated with a single simultaneous solitary metastatic lesion in the stomach with a review of the literature about this rare entity.

**CASE REPORT**

A 46-years-old male patient admitted to hospital with a two months’ history of shortness of breath, cough, night sweats and weight loss. His chest radiography revealed an appearance of mass lesion and atelectasis in the right middle zone.

He had a history of smoking (20 package-year) and quitted just two months before hospitalization. His father has died because of lung cancer at age of 58.

Physical examination findings were edema in the face and neck region, formation of collateral veins in chest wall suggesting vena cava syndrome (VCS). Oscultation findings were cracles in the lower lung areas. Also during oscultation breath sounds in the right upper lobes of chest was decreased.

X-ray film of the chest showed volume loss of right lung with tracheal deviation to the right. In the right upper lobe mass lesion is observed near to the assending aorta (Figure 1).

Computed tomography (CT) scan of lung showed vascular invasion of mass lesion with atelectatic areas in the right upper lobe. A large trombus was observed in internal jugular and subclavian vein. There were also multiple mediastinal enlarged lymph nodes and thickening of pericardium with minimal pericardial effusion (Figure 2).

He was undertaken bronchoscopic examination. Bulging of main carina and obstruction of right upper lobe bronchus with submucosal lesion is observed pathological examination of the specimen obtained from tumor by transbronchial biopsy was non-diagnostic. Patient refused second bronchoscopic procedure.

Because of patient’s poor general condition urgent palliative radio therapy was performed for VCS findings. Mediastinal and right lung region was radiated totally with dose of 3600 cGy for two weeks period. By the improvement of his general condition after radiation therapy, CT-guided transthorasic fine needle biopsy was performed as a second diagnostic procedure. Histological examination of biopsy specimen was consistent with the diagnosis of non-small cell
lung cancer. Immunohistochemical stainings for Pan CK and CK 7 were positive but negative for CK 20 and CEA (Figure 3).

Distant site metastasis including abdomen and cranium were investigated and no pathological spread was observed. After radio therapy, chemotherapy was planned; however just before the initiation of chemotherapy the patient had a complaint of disphagia and epigastric pain. Upper gastrointestinal endoscopy (UGIE) revealed a giant ulcer with central ulceration located in the lesser curvature of the gastric body which was assessed as a malignant ulcerative lesion macroscopically by the endoscopist. Histopathological examinations of gastric specimens showed a low differentiated malignant infiltration of the stomach. The histopathological result of gastric specimen was reported as “low-differentiated malignant infiltration of tumor”. Tumor cells were positively stained with CK 7 and CK 5/6 which was diagnosed as metastasis of gastric region secondary to primary squamous cell lung cancer (Figure 4). Gastric region was the only metastatic site obtained in our patient.
The patient’s survival was only one month after the diagnosis.

**DISCUSSION**

Lung cancer has been shown to metastasize to almost anywhere within the gastrointestinal tract. The esophagus has been described as the most common sites largely secondary to local extension of the primary lung tumor (1). The hematogenous spread of lung cancer to stomach is extremely rare, but recent reports suggest that they may be more frequent than previously thought, because they are rarely symptomatic (3). The gastrointestinal tract has been reported throughout the literature as a site of metastatic lung cancer with an estimated incidence of 4 to 12 percent (4,5). But only 0.2-1.7% of them are detected as gastric metastasis during autopsy findings (6). The presence of gastric metastasis suggests poor prognosis (Table 1).

Metastatic disease to stomach can occur with breast, melanoma, ovary, liver, colon and testicular cancer with breast cancer being the most frequent (7). Other rare tumors that can involve stomach include Kaposi’s sarcoma, schwannoma and glomus tumors (7,8).

Only 51 cases of lung carcinoma metastasis to gastrointestinal tract have been reported in the literature since 1961 (seven cases with stomach metastasis, 37 cases with small bowel metastasis, three cases with colon metastasis, two cases with anus metastasis, and two cases with duodenum metastasis) (3). The most frequent site of metastasis was reported as small bowel and perforation in gastrointestinal tract was observed among 55.1% of all cases (3).

Patients with gastric metastases from any types of malignancy are often asymptomatic unless the metastases invade the gastric mucosa or serosa, or occupy the gastric lumen. However, further evaluation of gastrointestinal tract is unlikely to be performed because the symptoms, such as nausea and vomiting, are usually regard as side effect of chemotherapy or a involvement of the central nervous system (6). For our patient, complaint of dysphagia was considered as to be local invasion of the primary tumor to esophagus or as a complication of radio therapy. However, UGIE revealed only a malignant ulcerative lesion located in the corpus of the stomach.

The most common symptoms and complications according to gastrointestinal tract metastasis are gastrointestinal bleeding, abdominal pain, perforation and peritonitis (6). Up to date three cases were reported with perforation due to stomach metastasis and one of the perforation occurred during application of chemotherapy (9-11). For this reason, gastrointestinal symptoms observed during chemotherapy need careful management.

Maeda et al. and Casella et al. reported two cases with small cell carcinoma of lung metastasized to stomach (12,13). In our case histopathological type of tumor was squamous cell cancer and did not have gastric symptoms until advanced stage of his disease. For this reason, there was a diagnostic delay both for his primary disease and metastatic procedure.

Some mechanisms of gastric metastasis are considered as follows;

1. Direct invasion such as pancreatic cancer or esophageal cancer,
2. Disseminated involvement of peritoneum such as in ovarian cancer,
3. Hematogeneous metastasis most often occurring in lung cancer (12,14,15).

Although the stomach receives plenty of blood supply, both the mechanism of gastric metastasis and the reason of rarity of metastasis to stomach from lung cancer could not be explained up to now. Recently, it is suspected that some types of cytokines may affect the organ specificity in hematogenous metastasis. Recently, it is suspected that some types of cytokines may affect the organ specificity in hematogenous metastasis (12). Hematogeneous metastatic tumor cells to the stomach are situated in the submucosal layer and develop into submucosal tumors (12). Endoscopically nearly all the metastatic cases present submucosal tumors with bridging folds and small ulcerations at the top which is named “volcano-like ulcers” (3,6,12,13,17,18).
<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Clinical presentation</th>
<th>Diagnostic procedure</th>
<th>GIT localisation</th>
<th>Stomach biopsy/Lung biopsy (HP)</th>
<th>Pulmonary localisation</th>
<th>Metastasis localisation (except GIS positive)</th>
<th>Time interval (months)*</th>
<th>Survival after diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al. (2007) (20)</td>
<td>82/M</td>
<td>Melena</td>
<td>Gastroscopy</td>
<td>Cardia</td>
<td>Adenocarcinoma</td>
<td>Indetermined</td>
<td>Location not positive</td>
<td>108 reported</td>
</tr>
<tr>
<td>73/M</td>
<td>Melena</td>
<td>Gastroscopy</td>
<td>Cardia carcinoma</td>
<td>Squamous cell</td>
<td>Indetermined reported</td>
<td>Location not positive</td>
<td>5</td>
<td>Indetermined</td>
</tr>
<tr>
<td>70/M</td>
<td>Epigastric pain</td>
<td>Gastroscopy</td>
<td>Gastric corpus</td>
<td>Adenocarcinoma</td>
<td>Indetermined</td>
<td>Location not positive</td>
<td>5</td>
<td>Indetermined</td>
</tr>
<tr>
<td>Casella et al. (2006) (13)</td>
<td>63/M</td>
<td>Epigastric pain</td>
<td>Gastroscopy</td>
<td>Gastric corpus</td>
<td>Small cell/small cell</td>
<td>Left upper lobe + pleurisy</td>
<td>Brain + liver</td>
<td>The same time</td>
</tr>
<tr>
<td>Altintas et al. (2006) (16)</td>
<td>55/M</td>
<td>Melena + hematemesis</td>
<td>Gastroscopy</td>
<td>Greater curvature of stomach</td>
<td>Adenocarcinoma</td>
<td>Indetermined</td>
<td>Brain + bone + skin</td>
<td>12</td>
</tr>
<tr>
<td>Yamamoto et al. (2002) (3)</td>
<td>80/M</td>
<td>Epigastric pain</td>
<td>Gastroscopy</td>
<td>Upper stomach</td>
<td>Adenocarcinoma/adenocarcinoma</td>
<td>Left lower lobe</td>
<td>Brain</td>
<td>?</td>
</tr>
<tr>
<td>Suzuki et al. (2002) (9)</td>
<td>45/M</td>
<td>Epigastralgia + gastric perforation</td>
<td>Gastroscopy</td>
<td>Greater curvature of stomach</td>
<td>Adenocarcinoma</td>
<td>Right middle lobe</td>
<td>No metastasis</td>
<td>7</td>
</tr>
<tr>
<td>Kim et al. (1993) (19)</td>
<td>66/M</td>
<td>Epigastric pain + weakness</td>
<td>Gastroscopy</td>
<td>Upper body + fundus of stomach</td>
<td>Small cell?</td>
<td>Left upper lobe</td>
<td>No metastasis</td>
<td>-</td>
</tr>
<tr>
<td>Kim et al. (1993) (19)</td>
<td>68/M</td>
<td>Polydipsia + headache</td>
<td>Gastroscopy</td>
<td>Greater curvature side of mid-body</td>
<td>Squamous cell/squamous cell</td>
<td>Left upper lobe</td>
<td>Brain (diabetes insipidus)</td>
<td>The same time</td>
</tr>
<tr>
<td>Maeda et al. (1992) (12)</td>
<td>60/F</td>
<td>Nausea + vomiting</td>
<td>Gastroscopy</td>
<td>Whole stomach</td>
<td>Small cell/small cell</td>
<td>Right upper -lower lobe</td>
<td>Skin</td>
<td>4</td>
</tr>
</tbody>
</table>

* Time between primary tumour diagnosis and GIS metastasis.
As observed in Table 1 which is the review of cases in literature, all of the patients with gastric metastasis was symptomatic and diagnostic procedure was gastroendoscopy for all of the cases. Upper lobe localization was pre-dominant among all cases just like our case. It has also been reported that a high percentage of gastric metastases are localized in the fundus and cardias, but in our experience, the lesions were present in the gastric corpus region which is in agreement with Casella et al. and Kadakia et al. (3,19). In clinicopathological study of Ming-Hsun Wu et al., the sites of metastasis in the stomach were solitary for 94.4% of patients and only 5.6% developed multiple lesions in the stomach (20). In previous reports as shown in Table 1, most of the lung cancer patients with gastric metastasis were associated with other organ metastasis when the diagnosis of gastric metastasis was established. In our patients, stomach was found to be a single site of metastasis with careful review of imaging studies.

Because of advanced improvement in chemotherapy and supportive care in lung cancer and extending life expectancy, we may come across an increasing number of this kind of metastatic tumor in the future. Therefore, we should pay more attention to these GI metastatic signs including gastrointestinal bleeding, epigastric pain, nausea, vomiting, acute abdominal pain or less commonly ileus. Cases with new development of gastrointestinal symptoms after chemotherapy, should be carefully managed because of the possibility of chemotherapy induced perforation or ulceration. Chemotherapy may be beneficial to the improvement of the survival rate in individual cases (6). The definite role of FDG-PET in the diagnosis of gastrointestinal metastasis from lung cancer is still controversial because of the few cases and lack of enough clinical data (6).

Therefore since the stomach metastases of lung cancer is rarely seen, commonly lethal and pre-emptive diagnosis of the metastatic disease affects survival; gastroendoscopy which is the gold standard diagnostic procedure is not recommended as a routine screening test unless the patients are symptomatic. The suitable time for endoscopy can be before initiation of chemotherapy or as soon as the gastric symptoms are observed. When patients with lung cancer present with gastrointestinal symptoms like bleeding and obstructive symptoms semi elective surgery should be considered.

This case and review of literature support that the prevalence of gastric metastasis in patients with lung cancer is very low. The clinician should be aware of the possibility of gastric metastasis. During the follow up of lung cancer, gastrointestinal symptoms should be questioned and gastroscopy associated with biopsy should be performed especially in symptomatic patients. Unfortunately, the diagnosis of metastasis in a symptomatic patient signifies a late diagnosis which a stage that renders any treatment procedure ineffective. Further research is required to clarify the timing of gastroscopy in patients with lung cancer.

REFERENCES


