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Synchronous Gastric Diffuse Large B-Cell Lymphoma and Pulmonary Squamous Cell Carcinoma Presenting as a Cavitary Lung Lesion: A Case Report

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Abstract

Gastric diffuse large B-cell lymphoma (DLBCL) coexisting with pulmonary squamous cell carcinoma is uncommon. A cavitary lung lesion in this setting can complicate differentiation between infection, lymphomatous involvement, and a second primary malignancy. A 61-year-old man with a 40 pack-year smoking history was diagnosed with gastric DLBCL after worsening epigastric pain, vomiting, melena, and weight loss. Computed tomography revealed a concurrent 45 × 26 mm cavitary right lower lobe mass. A slight interval decrease in size initially favored infection, but microbiological investigations and bronchial biopsies were nondiagnostic. Following multidisciplinary reassessment and subsequent lesion enlargement, percutaneous transthoracic biopsy established poorly differentiated squamous cell carcinoma. His lymphoma was treated with chemotherapy and rituximab. Pulmonary resection was recommended, but financial constraints interrupted follow-up, and surgery was not performed. Subsequent imaging suggested metastatic progression, prompting palliative chemotherapy. A cerebellar lesion was later resected, with histopathology supporting pulmonary squamous cell carcinoma metastasis. The patient deteriorated postoperatively and subsequently died. The small initial decrease in lesion size and nondiagnostic bronchoscopic findings complicated assessment. Thoracic lymphadenopathy added staging uncertainty, and crush artifacts limited nodal histology. Direct sampling of the persistent pulmonary mass established its distinct malignant nature. A pulmonary lesion in a patient with lymphoma should not automatically be attributed to the same disease. Persistent cavitary lesions warrant multidisciplinary reassessment and targeted tissue diagnosis despite a slight decrease in size or nondiagnostic initial investigations.

Categories: Oncology, Pulmonology
Keywords: brain metastasis, cavitary lung lesion, diffuse large b-cell lymphoma, gastric lymphoma, squamous cell carcinoma, synchronous malignancies

Introduction

The synchronous occurrence of gastric diffuse large B-cell lymphoma (DLBCL) and primary pulmonary squamous cell carcinoma represents an unusual clinical co-existence. A previous study has described synchronous DLBCL with squamous cell lung carcinoma [1]. Observations specifically involving gastric DLBCL have more commonly reported associations with other pulmonary neoplasms, notably concomitant small-cell lung carcinoma and pulmonary adenocarcinoma [2,3].

Identifying a second primary pulmonary malignancy in a patient with lymphoma can be diagnostically challenging, particularly when imaging findings allow for several competing diagnoses. A cavitary pulmonary lesion may initially raise suspicion of infection or concomitant lymphomatous involvement. The associated mediastinal or hilar lymphadenopathy may further complicate interpretation and staging. Histopathological confirmation is therefore central to establishing the nature of the pulmonary lesion and guiding appropriate management.

We herein describe the case of a 61-year-old man with gastric DLBCL and a concurrent poorly differentiated squamous cell carcinoma presenting as a cavitary lesion in the right lower lobe.

Case Presentation

A 61-year-old man presented with a five-year history of epigastric pain and vomiting, accompanied by episodes of melena, fatigue, and anorexia. He also reported an unintentional weight loss of 10 kg over the four months preceding presentation. His medical history was notable for a 40-pack-year smoking history, occasional alcohol consumption, and a paternal history of lung cancer. He had no history of pulmonary tuberculosis or recent tuberculosis exposure.

At the initial presentation, upper gastrointestinal endoscopy with gastric biopsy established a diagnosis of gastric diffuse large B-cell lymphoma (DLBCL). Thoracoabdominopelvic computed tomography (CT) revealed gastric wall thickening, a cavitary mass measuring 45 × 26 mm with mildly irregular margins in the superior segment of the right lower lobe, and two approximately 6-mm nodules in the left lower lobe.

One month later, the patient was referred to hematology. He was normotensive, had preserved peripheral oxygen saturation, and was alert and oriented to time, place, and person. Abdominal examination revealed mild epigastric tenderness without a palpable mass or organomegaly. No cervical, axillary, or inguinal lymphadenopathy was detected, and his performance status was 1. He denied cough, purulent sputum, dyspnea, chest pain, and hemoptysis. Additional immunohistochemical analysis of the gastric biopsy, performed two months after the initial presentation, demonstrated CD20 and BCL6 expression, absent CD10 and CD3 expression, and a Ki-67 proliferation index of 58%. The patient received cyclophosphamide, vincristine, and prednisone (COP), followed by rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), with a favorable clinical response.

Four months after the initial assessment, the patient was referred to pulmonology and admitted for further investigation of the cavitary pulmonary lesion. Morning sputum molecular testing for tuberculosis using Xpert MTB/RIF was negative. Flexible bronchoscopy revealed mild diffuse inflammation of the left bronchial mucosa with mucoid secretions but no visible endobronchial lesion. Biopsies were obtained from the right and left lobar carinae, and bronchial aspirates were submitted for cytological and microbiological examination.

During this admission, chest CT showed a slight decrease in the lesion's dimensions to 42 × 26 mm, together with a right apical atelectatic band and apical emphysematous bullae. This modest reduction in size initially favored an infectious etiology. The patient was therefore discharged with a short course of antibiotics and instructed to return when the microbiological and histopathological results became available.

However, the subsequent investigations failed to establish an infectious or malignant diagnosis. Direct microscopy and Gram staining of bronchial aspirates, bacterial and fungal cultures, and examination for acid-fast bacilli were negative. Bronchial biopsies showed nonspecific chronic inflammatory changes without evidence of malignancy. Given the persistent diagnostic uncertainty, the case was discussed at a thoracic oncology multidisciplinary meeting. Review of the serial images raised greater concern for a primary pulmonary malignancy than for an infectious process or pulmonary involvement by DLBCL. Fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) was therefore requested.

Five months after the initial presentation, FDG-PET/CT demonstrated a thick-walled cavitary mass in the right lower lobe with intense fluorodeoxyglucose uptake (maximum standardized uptake value [SUVmax], 17.3). Additional uptake was observed in bilateral hilar and mediastinal lymph nodes at stations 10R, 10L, 7, 4R, and 5, with SUVmax values of 2.9, 2.2, 4.2, 3.4, and 2.9, respectively. No suspicious gastric hypermetabolism was identified (Figure *1*).

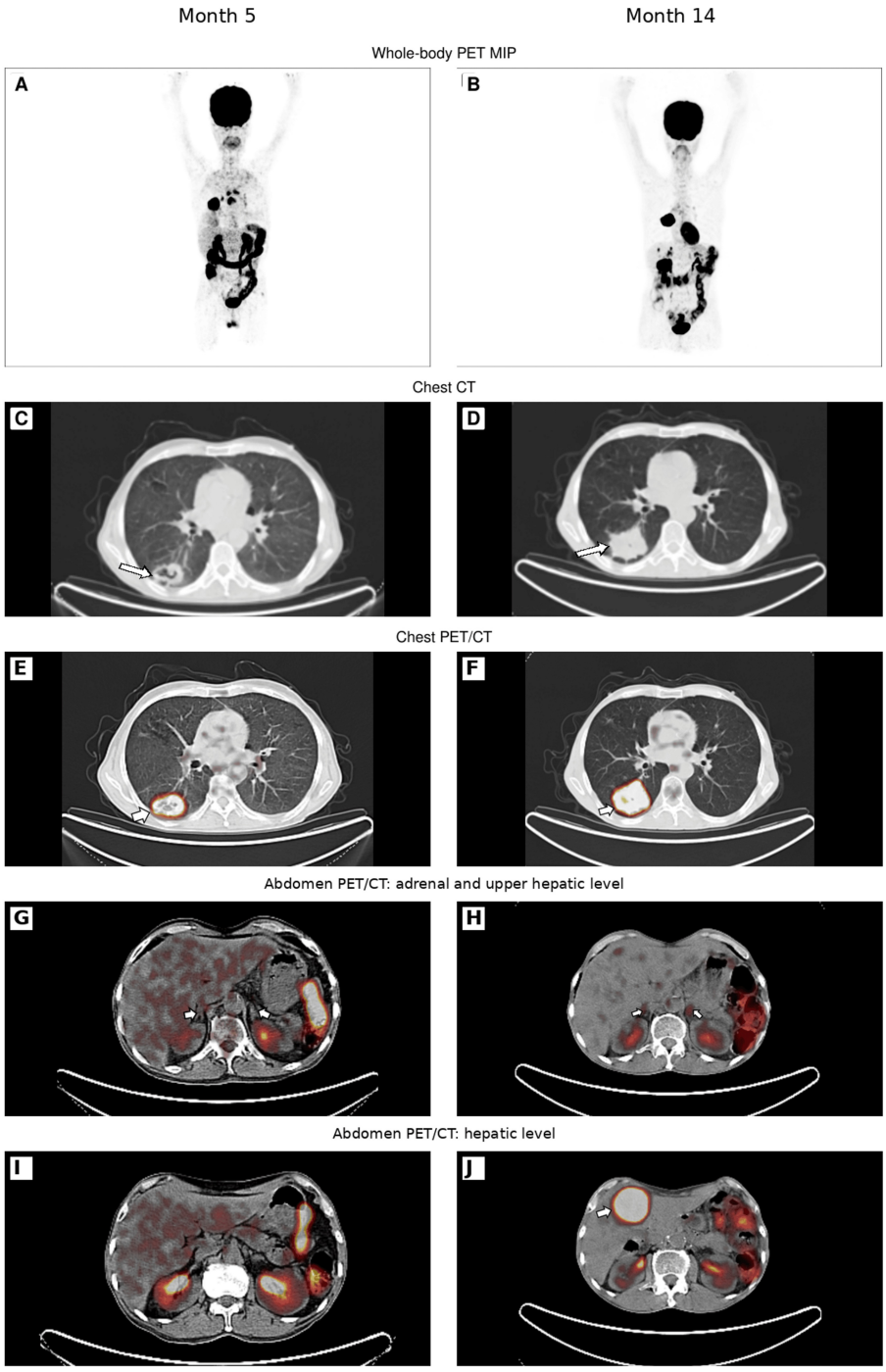


FIGURE 1: Systemic radiologic and metabolic progression between approximately five and 14 months after baseline.

Paired images obtained approximately five months (left) and 14 months (right) after the gastric lymphoma diagnosis (baseline) are shown at corresponding anatomical levels.
(A, B) Whole-body FDG-PET maximum-intensity projection images.
(C, D) Non-contrast axial chest CT demonstrating interval progression of the cavitary right lower lobe mass (white arrows).
(E, F) Fused chest FDG-PET/CT demonstrating metabolic progression of the pulmonary lesion (white arrows).
(G, H) Fused abdominal FDG-PET/CT at the adrenal and upper hepatic level. White arrows identify the bilateral adrenal regions for comparison, with adrenal lesions suspicious for metastases on the follow-up study.
(I, J) Fused abdominal FDG-PET/CT at a corresponding hepatic level, demonstrating development of a large hepatic lesion suspicious for metastasis at approximately 14 months after baseline (white arrow in J).

FDG-PET/CT: Fluorodeoxyglucose positron emission tomography/computed tomography

One month later, mediastinoscopy was performed to investigate the thoracic lymphadenopathy. Five lymph nodes were excised for histopathological examination. Histology and immunohistochemistry revealed anthracotic deposits without morphologically evident carcinomatous or lymphomatous proliferation. However, the interpretation was limited by crush artifacts, and the findings did not establish the etiology of the pulmonary lesion.

At the eight-month follow-up, a chest CT demonstrated enlargement of the cavitary mass to 45 × 35 mm, accompanied by ipsilateral pulmonary nodules and mediastinal lymph node enlargement. Given the radiological progression and the inconclusive results of the previous investigations, a percutaneous transthoracic biopsy was performed. Histopathological examination revealed an invasive, poorly differentiated carcinoma. Immunohistochemistry showed p40 expression and negative staining for TTF-1, CD56, and chromogranin A, supporting a diagnosis of poorly differentiated squamous cell carcinoma. The recorded tumor was classified as T2bN0M0.

Brain CT showed no intracranial secondary lesions. Following multidisciplinary review, surgical management was recommended, and the patient was referred to thoracic surgery for consideration of resection. However, financial constraints subsequently interrupted follow-up, and the planned surgery was not performed.

Fourteen months after the initial presentation, follow-up FDG-PET/CT demonstrated morphological and metabolic progression of the pulmonary mass, with new hepatic and adrenal lesions suspicious for metastases. A comparison with the examination performed five months after the initial presentation is shown in Figure *1*.

One month later, brain magnetic resonance imaging (MRI) revealed a cystic lesion in the right cerebellar hemisphere with marked peripheral enhancement and surrounding edema, highly suggestive of metastatic disease (Figure *2*). The patient remained asymptomatic at that time.



FIGURE 2: Right cerebellar lesion on brain magnetic resonance imaging.

Axial T2-weighted magnetic resonance imaging (MRI) obtained approximately 15 months after baseline showing a hyperintense lesion in the right cerebellar hemisphere (white arrow) with surrounding edema.

In view of the metastatic progression, treatment intent shifted to a palliative approach, and gemcitabine plus platinum-based chemotherapy was administered.

Twenty days after his last chemotherapy session, the patient developed rapidly progressive heaviness in all four limbs, dysarthria, and severe balance impairment, accompanied by vomiting and deterioration in his general condition. Neurological examination documented an ataxic gait, impaired coordination, absent deep tendon reflexes, and bilateral Babinski signs.

Eighteen months after the initial assessment, the patient underwent neurosurgical resection of the posterior fossa lesion. Histopathological examination revealed an invasive, poorly differentiated carcinoma compatible with squamous cell carcinoma. Tumor cells expressed p40, supporting a diagnosis of brain metastasis from the previously diagnosed pulmonary squamous cell carcinoma. His clinical condition deteriorated three days after surgery, and he subsequently died.

Representative histopathological and immunohistochemical images were unavailable for inclusion in this

report. The histopathological and immunohistochemical findings are described on the basis of the corresponding pathology reports. The chronology of the diagnostic investigations, treatment decisions, and subsequent disease progression is summarized in Figure 3.

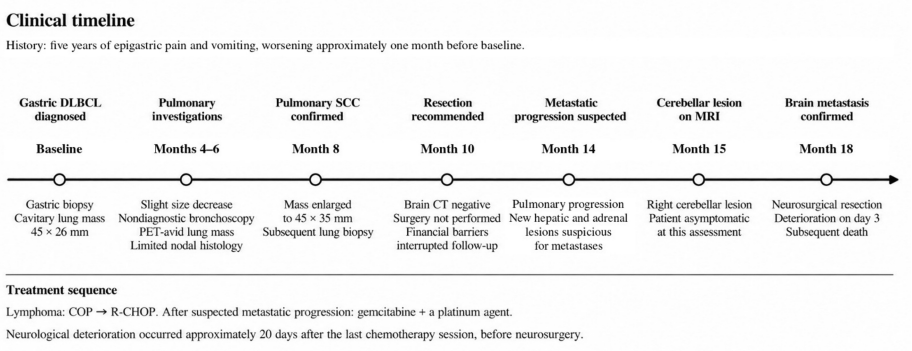


FIGURE 3: Clinical timeline from gastric lymphoma diagnosis to histologically confirmed brain metastasis.

DLBCL: diffuse large B-cell lymphoma; SCC: squamous cell carcinoma; CT: computed tomography; PET: positron emission tomography; MRI: magnetic resonance imaging; COP: cyclophosphamide, vincristine, and prednisone; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Discussion

The coexistence of primary gastric diffuse large B-cell lymphoma (DLBCL) and pulmonary squamous cell carcinoma is an uncommon clinical association that complicates both diagnosis and treatment planning.

Fujii et al. previously reported synchronous DLBCL and squamous cell lung carcinoma, with mediastinal and hilar lymphadenopathy complicating lung cancer staging [1]. Other reports have described gastric DLBCL occurring alongside small-cell lung carcinoma [2] or pulmonary adenocarcinoma with concomitant pulmonary cryptococcosis [3]. These cases illustrate the difficulty of interpreting pulmonary abnormalities in patients with lymphoma. Our case adds to this literature by describing gastric DLBCL accompanied by a cavitary pulmonary squamous cell carcinoma whose initial radiological evolution appeared reassuring.

The central diagnostic challenge was determining the nature of the pulmonary lesion in the context of gastric lymphoma. Pulmonary cavitation has a broad differential diagnosis, including bacterial, mycobacterial, and fungal infections; primary lung cancer; metastatic disease; and pulmonary involvement by hematological malignancies [4,5]. Infection was initially considered because of the cavitary morphology and the epidemiological relevance of tuberculosis in our setting. However, the patient had no respiratory symptoms, and the extensive microbiological workup did not identify an infectious cause. His substantial smoking history and the persistence of the cavitary mass warranted continued consideration of a primary pulmonary carcinoma. Moreover, the coexistence of pulmonary adenocarcinoma and cryptococcosis in the case reported by Yao et al. illustrates that pulmonary abnormalities in patients with lymphoma may have distinct, concurrent causes [3].

The slight interval decrease in lesion size complicated the interpretation of the imaging findings. The reduction from 45 × 26 mm to 42 × 26 mm was initially interpreted as favoring an infectious etiology, but the lesion persisted and subsequently enlarged. This course illustrates the limitations of relying on a small change in size to distinguish infection from malignancy. Cavitation is a recognized manifestation of primary lung cancer, particularly squamous cell carcinoma, and a thick or irregular cavity wall may raise suspicion of malignancy [6]. In our case, persistent radiological concern prompted multidisciplinary reassessment; subsequent enlargement of the mass, ipsilateral pulmonary nodules, and mediastinal lymph node enlargement reinforced the need for a definitive tissue diagnosis.

FDG-PET/CT showed intense uptake in the pulmonary mass (SUVmax, 17.3), with lower uptake in the hilar and mediastinal lymph nodes. However, FDG accumulation is not specific to malignancy and may also occur in bacterial, mycobacterial, and fungal infections, as well as inflammatory and granulomatous conditions [7]. The PET/CT findings therefore required interpretation alongside the lesion's morphology, clinical course, and microbiological results.

Thoracic lymphadenopathy introduced further uncertainty regarding diagnosis and staging. As illustrated by Fujii et al., interpreting FDG-avid lymph nodes can be particularly difficult when lymphoma and lung carcinoma coexist, because nodal involvement may reflect either malignancy [1]. In our case, mediastinoscopy showed anthracotic deposits without morphologically evident malignancy. However, crush

artifacts limited interpretation of these observations. These findings emphasize the value of pathological assessment of suspicious lymph nodes and the need to consider sampling limitations when interpreting a negative result. The nature of the pulmonary mass was ultimately established by percutaneous transthoracic biopsy, which revealed an invasive, poorly differentiated carcinoma. Expression of p40, together with negative staining for TTF-1, CD56, and chromogranin A, supported the diagnosis of poorly differentiated squamous cell carcinoma.

Management required multidisciplinary coordination to address the two concurrent malignancies. Previous reports describe individualized strategies that account for the extent and treatment requirements of each disease [1-3]. In our case, the pulmonary lesion was initially considered potentially resectable, and thoracic surgery was recommended. Financial constraints interrupted follow-up, and the planned procedure was not performed. Subsequent imaging demonstrated progression of the pulmonary mass and new intracranial, hepatic, and adrenal lesions suspicious for metastases, prompting a shift to palliative management. Later neurological deterioration led to resection of the cerebellar lesion, with histopathological findings supporting metastasis from the pulmonary squamous cell carcinoma.

Conclusions

This case highlights the importance of considering a separate primary malignancy when a pulmonary lesion is identified in a patient with lymphoma. A persistent cavitary mass warrants continued evaluation when its cause remains unproven, even after a slight decrease in size or nondiagnostic initial investigations. Multidisciplinary reassessment and tissue sampling of the unresolved lesion are central to clarifying the diagnosis and guiding management.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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