



Markedly Elevated Serum CA 19-9 in Metastatic Lung Adenocarcinoma: A Diagnostic Challenge

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Abstract

Carbohydrate antigen 19-9 (CA 19-9) is a tumour-associated biomarker predominantly linked to pancreatic and colorectal cancers. Elevated serum levels of CA 19-9 in lung adenocarcinoma are rare, with few cases documented in the literature. Herein, we present two cases of metastatic lung adenocarcinoma with markedly elevated CA 19-9 levels, initially leading to a diagnostic suspicion of a pancreatic malignancy.

Subject Areas

Respiratory Medicine

Keywords

CA 19-9, Lung Adenocarcinoma, Tumour Markers

1. Introduction

Carbohydrate antigen 19-9 (CA 19-9) was first identified by Koprowski and colleagues and is recognised as a tumor-associated mucin glycoprotein antigen. While it is most commonly associated with malignancies, such as pancreatic and colorectal adenocarcinomas, CA 19-9 can also be elevated in certain non-malignant conditions, including benign gastrointestinal diseases and hepatobiliary disorders. Clinically, CA 19-9 serves as a valuable biomarker primarily used for the surveillance, prognosis, and monitoring of treatment response in patients with pancreatic cancer, gastric cancer, and colorectal adenocarcinoma. Despite its

utility, the specificity of CA 19-9 is limited, and elevated levels should be interpreted cautiously in the context of the overall clinical picture.

2. Case Report 1

A 19-year-old female presented with lower back pain and bilateral lower limb weakness. Clinical examination revealed lower limb muscle strength graded at 3/5, accompanied by diminished sensation at the T10 level. Urgent magnetic resonance imaging (MRI) of the spine revealed a paravertebral collection extending from T1 to T5, with significant compression of the spinal cord at the T2 to T4 levels. The patient underwent an immediate laminectomy with posterior spinal fusion instrumentation.

Tumour marker screening revealed a markedly elevated CA 19-9 level of 20,909 U/ml. Positron emission tomography-computed tomography (PET-CT) identified a hypermetabolic mass in the left lower lung lobe (**Figure 1(A)**), measuring 7.3 cm with a maximum standardised uptake value (SUV_{max}) of 23 with hypermetabolic activity in the upper thoracic spine (SUV_{max}: 15.5). Bronchoscopy results were normal.

Histopathological analysis of the spinal biopsy confirmed metastatic adenocarcinoma, with immunohistochemical staining positive for CK7 and CK20 and negative for TTF-1. A subsequent lung biopsy confirmed adenocarcinoma with mucinous differentiation. Immunohistochemical staining was negative for TTF-1 but positive for CK7, CK20, CA 19-9, CK19, and CA 125. Genetic testing did not detect driver mutations for EGFR, ALK, or ROS-1. The patient was diagnosed with advanced lung adenocarcinoma with spinal metastasis and was subsequently treated with spinal radiotherapy and chemotherapy consisting of gemcitabine and cisplatin.

3. Case Report 2

A 55-year-old woman was referred to our respiratory department due to a chronic cough and a 5-month history of weight loss. Chest radiography revealed a retrocardiac opacity. Contrast-enhanced computed tomography (CECT) of the brain, thorax, abdomen, and pelvis demonstrated an irregular, heterogeneously enhancing mass in the left lower lobe with air bronchogram and subcentimeter mediastinal lymph nodes (**Figure 1(B)**). Bronchoscopy results were unremarkable.

A CT-guided tru-cut lung biopsy was performed, which identified adenocarcinoma with mucinous differentiation. Immunohistochemical staining showed positivity for CK7, CK20, CK19, and CA 19-9, and negativity for TTF-1 and Napsin A. Serum CA 19-9 was markedly elevated at 4674 U/ml. Further investigations to determine the cause of CA 19-9 elevation, including esophagogastroduodenoscopy, colonoscopy, and multiphase CT of the pancreas, yielded normal results.

The patient was diagnosed with lung adenocarcinoma (T3N0M0) and underwent video-assisted thoracoscopic lobectomy with mediastinal lymph node dissection. The mediastinal lymph node biopsy showed no evidence of nodal

metastases. Following surgical resection, adjuvant chemotherapy with gemcitabine and cisplatin was administered. However, the patient developed solitary cerebral recurrence six months after the surgery (**Figure 1(C)**).

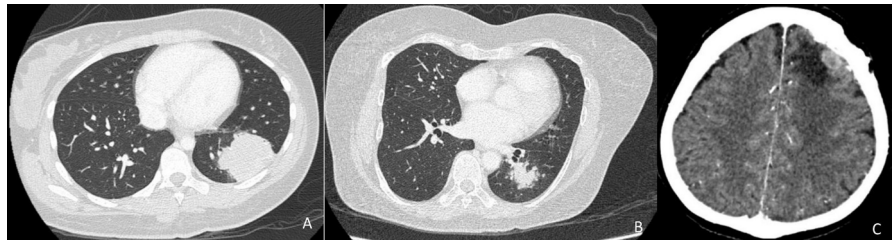


Figure 1. (A) CT thorax reveals a heterogeneously enhancing mass located in the posterobasal segment of the left lower lobe. (B) CT thorax shows an irregular, heterogeneously enhancing lesion in the posterobasal segment of the left lower lobe, with an air bronchogram present within it. (C) CT brain demonstrates an irregular hypodense mass in the left high frontal region, accompanied by extensive white matter oedema in the left frontal lobe.

4. Discussion

Most lung cancers are diagnosed at an advanced stage. Even when non-small cell lung cancer (NSCLC) is detected at a lower TNM stage and is potentially curable through surgery, the risk of recurrence remains high [1]. Studies have shown that the combined use of CA 19-9 and serum cytokeratin 19 fragments (CYFRA 21-1) can serve as prognostic markers in patients with advanced lung adenocarcinoma. Elevated pre-operative serum CA 19-9 levels may be associated with an increased risk of disease recurrence in resectable lung adenocarcinomas [2].

Serum CA 19-9 levels tend to be higher in lung cancer compared to benign pulmonary diseases, and elevated CA 19-9 levels are particularly associated with advanced lung adenocarcinoma. There is no significant difference in CA 19-9 levels among different subtypes of lung cancer [3]. Research indicates that patients who are CA 19-9 positive have shorter overall survival compared to those who are CA 19-9 negative [4]. Additionally, CA 19-9 in bronchoalveolar lavage fluid has been identified as a potential diagnostic tumour marker for lung cancer [5].

Although serum CA 19-9 elevation is non-specific, it has been detected in histopathological specimens of both small-cell and non-small-cell lung cancers. CA 19-9 may be synthesised by various epithelial cells, including those in the pancreas, biliary ducts, salivary glands, colon, stomach, and endometrium. It is also found in the mucous cells of the bronchial glands and bronchiolar epithelium, suggesting that elevated serum CA 19-9 could originate from neoplasms of the bronchiolar epithelium [6].

In both of our cases, patients had pulmonary adenocarcinoma with negative thyroid transcription factor 1 (TTF-1) and elevated serum CA 19-9. One patient also tested negative for EGFR-sensitizing mutations [7]. These findings are consistent with studies showing that TTF-1 negative NSCLC adenocarcinoma patients have poorer overall survival, regardless of whether they are treated with radical or palliative intent and a lower frequency of EGFR mutations [8]. It is

noteworthy that in our patients, both TTF-1 and cytokeratin markers were negative, which aligns with the distinct immune profile often observed in invasive mucinous adenocarcinoma compared to other lung adenocarcinoma subtypes [2].

High pre-operative serum CA 19-9 levels may be linked to an increased recurrent disease in resectable lung adenocarcinomas [8]. This was evident in our second patient, who experienced disease recurrence six months after undergoing radical resection followed by chemotherapy [2].

Serum CA 19-9 levels can be markedly elevated in lung adenocarcinoma, and a comprehensive tumour survey should include an evaluation of the lungs in patients with elevated serum CA 19-9. Monitoring serum CA 19-9 levels could be a valuable tool for identifying patients at high risk for recurrent lung cancer. However, the interpretation of CA 19-9 levels must be integrated with clinical findings, imaging, and histopathological examination.

Authors' Contribution Statement

The work conducted and presented in this manuscript has not been published or submitted for publication in another journal. All authors named in the manuscript have made substantial contributions to qualify for authorship according to BIMJ authorship criteria and have approved of the content of the manuscript. We have disclosed all financial support for our work and other potential conflicts of interest.

Ethics Statement

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Kelsey, C.R., Marks, L.B., Hollis, D., Hubbs, J.L., Ready, N.E., D'Amico, T.A., *et al.* (2009) Local Recurrence after Surgery for Early Stage Lung Cancer. *Cancer*, **115**, 5218-5227. <https://doi.org/10.1002/cncr.24625>
- [2] Isaksson, S., Jönsson, P., Monsef, N., Brunnström, H., Bendahl, P., Jönsson, M., *et al.* (2017) CA 19-9 and CA 125 as Potential Predictors of Disease Recurrence in Resectable Lung Adenocarcinoma. *PLOS ONE*, **12**, e0186284. <https://doi.org/10.1371/journal.pone.0186284>
- [3] LI, X., Asmitananda, T., Gao, L., Gai, D., Song, Z., Zhang, Y., *et al.* (2012) Biomarkers in the Lung Cancer Diagnosis: A Clinical Perspective. *Neoplasma*, **59**, 500-507. https://doi.org/10.4149/neo_2012_064
- [4] Sato, Y., Fujimoto, D., Uehara, K., Shimizu, R., Ito, J., Kogo, M., *et al.* (2016) The Prognostic Value of Serum CA 19-9 for Patients with Advanced Lung Adenocarcinoma. *BMC Cancer*, **16**, Article No. 890. <https://doi.org/10.1186/s12885-016-2897-6>
- [5] Ghosh, I., Bhattacharjee, D., Das, A.K., Chakrabarti, G., Dasgupta, A. and Dey, S.K.

(2012) Diagnostic Role of Tumour Markers CEA, CA15-3, CA19-9 and CA125 in Lung Cancer. *Indian Journal of Clinical Biochemistry*, **28**, 24-29.

<https://doi.org/10.1007/s12291-012-0257-0>

- [6] Takayama, S., Kataoka, N., Usui, Y., *et al.* (1990) CA 19-9 in Patients with Benign Pulmonary Diseases. *Nihon Kyobu Shikkan Gakkai Zasshi*, **28**, 1326-1331.
- [7] Cordoba Ortega, J.F., Morales, S., Rodriguez, J.V., Galindo, Á.R. and Salud, A. (2019) TTF1 Negative in Non Small Cell Lung Cancer Adenocarcinoma: A Prognostic Factor. *Annals of Oncology*, **30**, ii5. <https://doi.org/10.1093/annonc/mdz072.014>
- [8] Rossi, G., Murer, B., Cavazza, A., Losi, L., Natali, P., Marchioni, A., *et al.* (2004) Primary Mucinous (So-Called Colloid) Carcinomas of the Lung. *The American Journal of Surgical Pathology*, **28**, 442-452.
<https://doi.org/10.1097/00000478-200404000-00003>