

# Elevated CA 125 in A Male Patient with Lung Carcinoma: A Laboratory Perspective

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## ABSTRACT

CA 125 is a tumour marker that is widely used for the management of patients with ovarian malignancy. However, elevated CA 125 has been reported in various non-ovarian cancer patients, including males. This report describes a case of an elevated CA 125 level in a 49-year-old male patient who presented with chronic cough associated with constitutional symptoms. The patient was diagnosed with lung carcinoma based on radiological investigations and tissue histopathological examination. According to recent studies, CA 125 has a potential role as a marker for lung malignancies. However, questions arise about the effectiveness of its measurement for such patients due to its poor specificity and improper utilization of the test. This report focuses on the clinical role of CA 125, the appropriateness of the test request for this patient, the significance of the result, and its implications for the patient and laboratory management.

## INTRODUCTION

Cancer Antigen 125 (CA 125) is a high molecular weight mucin glycoprotein encoded by the MUC16 gene. It is produced by cells derived from the coelomic epithelium (i.e., mesothelial cells of the pleura, pericardium, and peritoneum) and cells of Mullerian epithelial derivatives, such as tubal, endometrial, and endocervical tissues.<sup>1</sup>

CA 125 is a well-established tumour marker used in female patients to detect ovarian malignancy. It is recommended as a marker for the diagnosis and monitoring of epithelial ovarian carcinoma.<sup>2</sup> However, CA 125 is known to have poor sensitivity in the detection of the early phase of the disease and poor specificity as its concentration can be elevated in other conditions.<sup>3</sup> Recently, studies have investigated the role of CA 125 as a marker for non-ovarian benign and malignant pathological conditions, such as heart failure, liver cirrhosis, and lung carcinoma.<sup>4-6</sup> In parallel, we noticed several requests for CA 125 for patients with non-ovarian cancer, including male patients, despite limited data on the effectiveness of CA 125 level monitoring in the management of these patients. Here, we present a case of

a male patient with lung carcinoma and elevated CA 125. The indication of the request for CA 125, the outcome of the patient, and implications for laboratory management are discussed.

## CASE REPORT

A 49-year-old man who was a chronic smoker presented with prolonged cough and lethargy for 6 months duration, associated with loss of appetite and weight. There was no history of contact with the PTB patient. On examination, he was cachexic. Chest examination revealed reduced air entry with stony dullness on the left lung. Other findings were unremarkable. A blood sample for CA 125 test was sent to the laboratory along with samples for other tests such as renal function tests, liver function tests, and full blood count. All results were unremarkable, except for the CA 125 level that was elevated with the value of 204 U/mL. Chest X-ray was done and revealed left lung homogenous opacity, suggestive of pleural effusion. CT scan of thorax revealed massive left pleural effusion and lung collapse. Bronchoscopy revealed a hard mass

arising from the left lung. A diagnosis of small cell lung carcinoma was made based on the histopathological examination finding. The patient underwent a series of chemotherapy with follow-up. In this case, CA 125 level was measured only once, prior to the diagnosis and was never repeated on follow-up. The patient defaulted to treatment one year after the diagnosis was made and succumbed to death at home due to the complication of the disease.

## DISCUSSION

CA 125 is a biomarker that is known for its role in the monitoring of epithelial ovarian carcinoma. In healthy people, CA 125 is found in the ovaries and various tissues, such as endometrial, pleural, pericardial, and peritoneal tissues. Based on the knowledge of its origin, it is unquestionable that CA 125 is present and can be measured in males, despite its established role in malignancy in females. The cut-off level for CA 125 is 35 U/mL.<sup>1</sup> Elevated CA 125 has been reported in various malignant and benign pathological conditions, including lung carcinoma. In lung cancers, elevated levels result from the release of CA 125 by proliferating malignant pleural cells.<sup>6</sup>

Recently, various studies were done regarding the potential role of CA 125 in lung carcinoma. According to Li et al., a combination of CA 125 with CA-153 and CYFRA21-1 may serve as a tool to aid in the diagnosis of lung carcinoma.<sup>7</sup> Similarly, Dai et al. found that a combination of CA 125 and carcinoembryonic antigen (CEA) may have a role in predicting the risk of lung carcinoma among patients with interstitial lung disease.<sup>8</sup> These studies showed that CA 125 is an effective biomarker for screening and predicting the risk of lung carcinoma, however, it has to be used in combination with certain markers such as mentioned above. In our case, CA 125 was the only tumour marker measured. According to Zhou et al., CA 125 acts as an independent risk factor for bone metastasis in lung cancer.<sup>9</sup>

However in our case, CA 125 was not used to assess metastasis risk, as it was only measured once before the diagnosis of lung carcinoma was made. Therefore, the

reason for requesting the CA 125 test is unclear in this case. It is also doubtful whether or not the test result has helped the clinicians in diagnosing the patient. Furthermore, it is known that CA 125 has poor specificity. In this case, the clinicians relied on other diagnostic tools which were more reliable, such as radiological measures.

A survey regarding CA 125 requests in male patients has been carried out in our centre. We found that 5% of all CA 125 requests were for male patients. The indications for the requests were unclear. Based on the medical records, most of the patients were in suspicion of various malignancies, and CA 125 requests were sent randomly with other tumour markers such as prostate-specific antigen (PSA) and alpha-fetoprotein (AFP) for screening purposes. In most of the patients, the CA 125 was requested and measured only once, which was prior to the diagnosis and was not followed up. According to our analysis, there were concurrent medical disorders associated with elevated CA 125 in these patients, such as liver cirrhosis, heart failure, lung disease, and renal impairment, which implied the poor specificity of the test. Therefore, we conclude that a request for CA 125 measurement without clear indication in a male patient shall be considered a misutilisation of the test, as the result does not provide sufficient value to assist patient management. Moss et al. addressed the issue of improper use of CA 125 testing, which leads to useless findings for clinicians, has financial implications, and contributes to patient worry and clinical ambiguity.<sup>10</sup>

Based on these findings, several measures can be implemented to improve the use of the CA 125 test. First, there must be a clear indication, and this must be stated in the request form. Second, awareness should be raised among clinicians about the proper use of CA 125 as a tumour marker. This can be done via activities such as educational talks for new doctors who might not have sufficient knowledge about the use of CA 125 in clinical practice and regular discussions between laboratorians and clinicians. Additionally, the laboratory may create a 'flagged system' for test requests that do not adhere to the appropriate requirements.

## CONFLICT OF INTEREST

None

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