

False-Positive Tumor Markers: CA 15-3 and CEA in a Patient with Breast Carcinoma Secondary to Inflamed Mediastinal Lymph Nodes: A clinical case

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Abstract- False-positive tumor markers occur when tests for specific proteins, known as tumor markers, reveal elevated levels of these proteins in the blood or other tissues. This can be mistakenly interpreted as an indication of cancer. Various factors can contribute to false-positive results, including other diseases like inflammatory processes or infections, as well as factors such as smoking, age, gender, or potential errors in test execution. While elevated levels of tumor markers can suggest the presence of cancer, they are not definitive diagnostic tools on their own. Further testing is typically required to confirm the presence of cancer.

Keywords: False-positive tumor markers, breast cancer, mediastinal lymph nodes, CA 15-3, CEA.

Introduction:

False-positive tumor markers occur when tests for specific proteins, known as tumor markers, reveal elevated levels of these proteins in the blood or other tissues. This can be mistakenly interpreted as an indication of cancer. Various factors can contribute to false-positive results, including other diseases like inflammatory processes or infections, as well as factors such as smoking, age, gender, or potential errors in test execution. While elevated levels of tumor markers can suggest the presence of cancer, they are not definitive diagnostic tools on their own. Further testing is typically required to confirm the presence of cancer.

Clinical Case

We present the case of a 59-year-old woman diagnosed with triple-negative breast cancer. In October 2022, she underwent a right mammary quadrantectomy with axillary lymph node dissection, receiving a histological diagnosis of invasive ductal carcinoma, T2N0M0. Immunohistochemistry confirmed triple-negative status: Estrogen receptor (ER)-0, Progesterone receptor (PR)-0, and Human epidermal growth factor receptor-2 (HER2) (1+).

The patient had comorbidities including type 2 diabetes, essential hypertension, and chronic ischemic heart disease.

She commenced post-operative radiotherapy from December 23, 2023, to January 24, 2023, using 6 MeV photons.

The right mammary gland area received a total dose of 50 Gy, with an additional 2 Gy.

The patient did not undergo immunotherapy or targeted therapy. Following radiotherapy, she began periodic medical check-ups every three months.

In February 2024, during a routine preventive breast cancer check-up, chest X-ray and abdominal ultrasound revealed newly appearing lymph nodes in the chest. A positron emission tomography (PET) scan on February 19, 2024, confirmed the presence of new metabolically active mediastinal lymph nodes with an SUV max (Maximum standardized uptake value) of up to 10.8 score 5.

A multidisciplinary team discussed the findings and recommended a biopsy in the Department of Thoracic Surgery.

During the prophylactic examination, elevated levels of the tumor markers CA-15.3 and CEA were noted. Although these markers had been within the normal range in previous months, they had increased during the follow-up.

On March 16, 2024, the patient underwent excision of two lymph nodes, yielding a scant amount of extravasate.

Histological examination diagnosed chronic desquamative lymphadenitis. Subsequent laboratory tests showed decreased levels of the tumor markers CA-15.3 and CEA following the biopsy.

Discussion

False-positive tumor markers present a significant challenge in cancer diagnosis and monitoring [1]. While tumor marker tests serve as valuable tools for assessing cancer risk and tracking disease progression, they can yield misleading results that suggest cancer presence due to reasons unrelated to cancer, such as other diseases or various factors[2].

From the patient's observation, we can chronologically track the development of the tumor marker CEA. Starting from March 9, 2023, it registered a value of 7 ng/mL, which dropped to 2 ng/mL by June of the same year. Throughout subsequent follow-ups, the tumor marker showed a slight increase, rising from 2.4 ng/mL in September 2023 to 3.8 ng/mL in January 2024, which was the date of the last preventative examination. At this time, an imaging study revealed lesions in the chest area. Following a manipulation performed on April 24th, the indicator decreased to 2.16 ng/mL.

Similarly, the gradual rise of the tumor marker CA 15.3 can be observed. Sequentially, its values increased from 19.5 in March 2023 to 20.55 ng/mL in June 2023. Subsequently, there was a significant rise to 29.15 ng/mL in September 2023, and during the last preventative examination in January 2024, it was 39.11 ng/mL. Post-manipulation, it also exhibited a downward trend, with values at 19.10 ng/mL.

These trends suggest that an inflammatory process is likely, as histologically confirmed by fibrobronchoscopy. Given these findings, it is plausible that the tumor markers CEA and CA 15.3 could be false positives due to inflammatory processes within the body. It's crucial to note that each elevation in tumor markers does not necessarily indicate a cancer recurrence but warrants thorough investigation in consideration of all possible nosological entities.

Causes of false-positive tumor markers range from infections and inflammatory processes to factors like smoking, age, and gender. Certain health conditions and medications can also influence tumor marker test outcomes. Technical errors or misinterpretation can further contribute to false-positive results^[3,4].

To mitigate the risk of false positives, clinicians should consider patients' clinical and medical histories and combine tumor marker tests with other diagnostic methods. Patients should be made aware of the potential for false-positive results and undergo additional tests to confirm or rule out cancer presence. This approach ensures more accurate cancer diagnosis and monitoring, reducing unnecessary stress and inappropriate medical interventions^[5].

CA-15.3 is a protein biomarker used to monitor breast cancer. It's measured through blood tests and helps track therapeutic responses in women with breast cancer. While normal CA-15.3 levels vary by lab, elevated levels may indicate the presence of cancer cells. However, elevated CA-15.3 levels alone aren't diagnostic of breast cancer and are typically used alongside other diagnostic methods^[6].

Carcinoembryonic antigen (CEA) is among the most recognized tumor markers used in cancer diagnosis and monitoring. CEA, a glycoprotein produced by normal epithelial cells, can be elevated in the blood due to certain cancers and other conditions^[7].

Primarily, it's used to monitor colorectal cancer patients post-treatment to detect recurrence or disease progression. Additionally, CEA aids in diagnosing and monitoring other cancers like lung, gallbladder, and pancreatic cancers. While elevated CEA levels may suggest cancer, they aren't exclusive to cancer and can also rise due to inflammatory processes, liver cirrhosis, or smoking. Notably, not all cancer patients exhibit elevated CEA levels, especially in early disease stages, and not all CEA elevations signify cancer presence^[8].

Inflammation can elevate levels of certain tumor markers. Conditions like infections, inflammatory processes, and other inflammatory disorders can increase specific tumor markers in the blood or tissues. The immune system's response to inflammation involves producing various proteins and substances detectable by tumor marker tests^[9,10].

However, an increase in tumor markers due to inflammation doesn't necessarily indicate cancer presence. While inflammation can result in false-positive tumor marker test results, these findings are typically validated or refuted by additional diagnostic tests. Hence, physicians should consider potential inflammatory factors when interpreting tumor marker test results and integrate these findings with other clinical data for an accurate diagnosis^[10,11].

Clinical Case Implication

Based on the presented patient case, we hypothesize that the elevated CA 15.3 and CEA levels were likely associated with the identified lymph nodes in the mediastinum and their specific histology.

Conclusion

False-positive tumor markers play a crucial role in cancer test result interpretation but shouldn't be relied upon as standalone diagnostic tools. Elevated tumor marker levels can stem from various factors, including other medical conditions or external influences. For a reliable assessment of potential cancer presence, test results should be combined with clinical data and other diagnostic procedures. Both physicians and patients should be aware of the possibility of false-positive results, emphasizing the need for consistent evaluations and examinations to either rule out or confirm cancer presence.

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REFERENCES:

1. Thakur S., Grover R.K., Gupta S., Yadav A.K., Das B.C. Identification of Specific miRNA Signature in Paired Sera and Tissue Samples of Indian Women with Triple Negative Breast Cancer. *PLoS ONE*. 2016;11:e0158946. doi: 10.1371/journal.pone.0158946.
2. Radojicic J., Zaravinos A., Vrekoussis T., Kafousi M., Spandidos D.A., Stathopoulos E.N. MicroRNA expression analysis in triple-negative (ER, PR and Her2/neu) breast cancer. *Cell Cycle*. 2011;10:507–517. doi: 10.4161/cc.10.3.14754.
3. Ellis G.K., Livingston R.B. Feasibility of dose-intensive continuous 5-fluorouracil, doxorubicin, and cyclophosphamide as adjuvant therapy for breast cancer. *Cancer* 1993; 71: 392–6.
4. Mar-Aguilar F., Mendoza-Ramírez J.A., Malagón-Santiago I., Espino-Silva P.K., Santuario-Facio S.K., Ruiz-Flores P., Rodríguez-Padilla C., Reséndez-Pérez D. Serum circulating microRNA profiling for identification of potential breast cancer biomarkers. *Dis. Markers*. 2013;34:163–169. doi: 10.1155/2013/259454.
5. Iero M., Valenti R., Huber V., Filipazzi P., Parmiani G., Fais S., Rivoltini L. Tumour-released exosomes and their implications in cancer immunity. *Cell Death Differ*. 2007;15:80. doi: 10.1038/sj.cdd.4402237.
6. Zhang H.-G., Grizzle W.E. Exosomes: A Novel Pathway of Local and Distant Intercellular Communication that Facilitates the Growth and Metastasis of Neoplastic Lesions. *Am. J. Pathol*. 2014;184:28–41. doi: 10.1016/j.ajpath.2013.09.027.
7. Piao Y.J., Kim H.S., Hwang E.H., Woo J., Zhang M., Moon W.K. Breast cancer cell-derived exosomes and macrophage polarization are associated with lymph node metastasis. *Oncotarget*. 2017;9:7398–7410. doi: 10.18632/oncotarget.23238.
8. Rupp A.-K., Rupp C., Keller S., Brase J.C., Eehalt R., Fogel M., Moldenhauer G., Marmé F., Sülthmann H., Altevogt P. Loss of EpCAM expression in breast cancer derived serum exosomes: Role of proteolytic cleavage. *Gynecol. Oncol*. 2011;122:437–446. doi: 10.1016/j.ygyno.2011.04.035.
9. Namer M., Fontana X. CA 15–3 versus CEA in monitoring of breast cancer. *Reviews on Endocrine-Related Cancer* 1991; 35: 19–24.
10. Lokich J.J., Moore C. Chemotherapy-associated palmar-plantar erythrodysesthesia syndrome. *Ann Intern Med* 1984; 101: 798–800.
11. Shin V.Y., Siu J.M., Cheuk I., Ng E.K.O., Kwong A. Circulating cell-free miRNAs as biomarker for triple-negative breast cancer. *Br. J. Cancer*. 2015;112:1751. doi: 10.1038/bjc.2015.143.