The Non-Malignant Face of CA-125

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Summary

Carbohydrate antigen 125 (CA -125) is widely used as a tumor marker for ovarian cancer, but elevations can occur in benign conditions, leading to diagnostic dilemmas. We report a case of markedly elevated CA 125 in a 62-year-old woman due to pericardial effusion secondary to idiopathic pericarditis. Her CA -125 normalized following pericardiocentesis and treatment, highlighting the importance of interpreting tumor markers within clinical context.

Keywords

CA-125; Pericardial Effusion; Non-malignant cause; Tumor Marker

Introduction

CA- 125 is a high molecular weight transmembrane glycoprotein. It was first detected in ovarian cancer cells, but several studies showed that it is normally expressed on different cell surfaces present in various organs (lung, prostate, pleura, pericardium, and peritoneum). (1-4) With rich oligosaccharide chains, the physiological role of CA-125 is considered to protect the epithelial luminal surfaces from physical stress through hydration or lubrication process thus protecting them from mechanical stress. (1)

Clinically, it has been used as a marker of ovarian cancer, in monitoring, risk stratification and prognostication. CA 125 levels also rise in other malignancies such as lung cancer, mediastinal teratoma and non-Hodgkin lymphoma. (5, 6) Although CA 125 is a well-known marker of ovarian cancer, its serum levels are also upregulated in multiple nonmalignant pathological states but also in physiologic conditions: pregnancy, menstruation, liver cirrhosis, pelvic inflammatory disease, peritoneal trauma, ascites, lung cancer and congestion due to heart failure. (7,8)

Understanding the alternative causes of raised CA 125 is essential for appropriate clinical decision-making. Elevated CA 125 in the absence of malignancy can lead to unnecessary anxiety, invasive procedures, and delays in identifying the actual underlying condition. Therefore, this case is reported to aware healthcare professional's that they should interpret CA 125 results within the broader context of the patient's clinical presentation, imaging findings, and other relevant laboratory parameters to avoid diagnostic pitfalls.

Case Report

A 62-year-old woman with a history of hypertension and coronary artery disease presented with progressive dyspnea and pleuritic chest pain for two weeks. She had no abdominal symptoms or weight loss. An incidental CA 125 test showed a markedly elevated level of 680 U/mL (normal <35 U/mL), while other tumor markers including CEA and AFP were within normal limits. Pelvic ultrasound confirmed normal ovarian and uterine structures. CT imaging of the chest and abdomen revealed a large pericardial effusion without abdominal masses, lymphadenopathy, or pelvic abnormalities. Echocardiography demonstrated cardiac tamponade physiology. Pericardiocentesis drained exudative fluid with a protein concentration of 4.2 g/dL. Cytological examination showed no malignant cells, and a diagnosis of idiopathic pericarditis was established. Following pericardiocentesis and NSAID therapy, her CA 125 decreased to 85 U/mL within two weeks and normalized to 22 U/mL after complete resolution of the effusion.

Discussion

CA 125 is produced by mesothelial cells lining the serous cavities, including the pericardium, pleura, and peritoneum. Elevated levels can therefore be seen in non-malignant conditions such as serosal inflammation and heart failure. In this patient, pericardial inflammation likely led to mesothelial activation and increased CA 125 release.

Stressed mesothelial cells produce CA 125 in response to both fluid overload and inflammation. For example, in heart failure, elevated venous pressure results in fluid congestion within mesothelial-lined spaces, triggering the release of inflammatory markers such as IL-6, IL-10, and TNF. (9) Mesothelial cells can be stimulated by inflammation, mechanical stress, or fluid accumulation to produce CA 125, and studies have shown that inflammatory cytokines such as IL-1 are potent inducers of CA 125 production. (10)

In pericardial effusion, congestion often causes fluid buildup not only in the pericardium but also in the pleural and abdominal cavities, worsening inflammation in a vicious cycle. High venous pressure in these areas, rich in mesothelial cells, further promotes CA 125 release. (11) Additionally, bacterial translocation or endotoxin production, especially in right heart failure with bowel congestion, can enhance CA 125 production even more. (11)

In large ovarian tumors with pleural effusion, as seen in Meigs syndrome, CA 125 levels are typically high. Here, the tumor induces fluid accumulation in the peritoneal cavity, and mechanical irritation from the fluid stimulates mesothelial cells to produce CA 125. Similarly, in our case, pericardial fluid accumulation and inflammation likely irritated the mesothelial cells lining the pericardium, resulting in elevated CA 125 levels. This rise reflects mesothelial activation rather than direct tumor secretion.

This case highlights the importance of interpreting CA 125 results in the context of clinical findings and imaging studies, and of considering benign causes before pursuing oncological referrals to avoid unnecessary investigations and patient anxiety.

Conclusion Clinicians should interpret elevated CA-125 with caution, especially in patients with serosal effusions, to avoid unnecessary oncologic referrals and patient anxiety

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