Introduction

Tumor markers are biochemical indicators of the presence of neoplastic proliferation. The main utility of tumor markers is monitoring the response to cancer treatment and recurrence during the follow-up. Nevertheless, it is known that tumor markers may also be raised in various benign diseases, especially those involving the pleura or peritonium or with some drugs. There are a few reports about serum CA72-4 elevation with colchicine use in the literature. A 62-years-old female patient was admitted to hospital with chest pain, malaise and palpitation. Computed tomography of the thorax showed pericardial effusion and multiple lymphadenopathies. For pericardial effusion ibuprofen and colchicine was initiated. CA72-4 was found 300 U/mL (0-6.9 U/mL). The cause of CA72-4 was investigated, malignancy is excluded. CA72-4 elevation was considered to be associated with colchicine, so colchicine was discontinued. Follow-up CA72-4 level of the patient ordered about 3 weeks later was 4.8 U/mL (0-6.9 U/mL) within normal limits. With this case, we wanted to underline the importance of considering the drugs or supplements that patients use when evaluating their laboratory results. Serum tumor marker elevations may not always associated with malignancy.

An Unusual Cause of Serum CA-72-4 Elevation: Colchicine

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Abstract

Tumor markers are biochemical indicators of the presence of neoplastic proliferation. Nevertheless, it is known that tumor markers may also be raised in various benign diseases, especially those involving the pleura or peritonium or with some drugs. There are a few reports about serum CA72-4 elevation with colchicine use in the literature. A 62-years-old female patient was admitted to hospital with chest pain, malaise and palpitation. Computed tomography of the thorax showed pericardial effusion and multiple lymphadenopathies. For pericardial effusion ibuprofen and colchicine was initiated. CA72-4 was found 300 U/mL (0-6.9 U/mL). The cause of CA72-4 was investigated, malignancy is excluded. CA72-4 elevation was considered to be associated with colchicine, so colchicine was discontinued. Follow-up CA72-4 level of the patient ordered about 3 weeks later was 4.8 U/mL (0-6.9 U/mL) within normal limits. With this case, we wanted to underline the importance of considering the drugs or supplements that patients use when evaluating their laboratory results. Serum tumor marker elevations may not always associated with malignancy.

CA72-4 antigen, first discovered in the early 1980s, is an antigenic marker of glycoprotein TAG-72, which is also recognized by the B72.3 and CC-49 monoclonal antibodies [1]. CA72-4 antigen is expressed in various adenocarcinomas including gastric, colorectal, ovarian, breast and lung, and rarely in benign and normal tissues [2-5]. CA72-4 is considered one of the most sensitive and specific markers in gastrointestinal system cancers [6,7]. Therefore CA72-4 is widely used in clinical practice.

Colchicine is a drug that binds to the intracellular tubuline protein and shows antimitotic activity by inhibiting new microtubule polymerization. Colchicine disrupts neutrophil chemotaxis by reducing the expression of adhesion molecules in membranes such as L-selectins and E-selectins[8]. Colchicine has been used for gout, familial Mediterranean fever, pericarditis and other inflammatory conditions[9]. Furthermore, it has been found to exhibit an anticancer effect [10]. There are a few reports about serum CA72-4 elevation with colchicine use in the literature. Here we report serum CA72-4 elevation in a patient receiving colchicine for pericardial effusion.
Case Presentation

A 62-years-old female patient was admitted to hospital with chest pain, malaise and palpitation. Laboratory tests revealed leukocytosis, elevated sedimentation rate and c-reactive protein. The body temperature was 38.5°C, heart rate and blood pressure was normal. Cardiomegaly was seen on chest x-ray. Computed tomography of the thorax showed pericardial fluid measuring 2 cm at the most prominent level, multiple lymphadenopathies, the largest of which measuring 24x10 mm in mediastinal perivascular space, subaortic, subcarinal and paratracheal areas, no pleural fluid was visualized.

The patient is referred to our hospital for the differential diagnosis of pericardial effusion. CK-MB, Troponin I, blood tests for liver and kidney functions were within normal levels. The white blood cell count was 20.000/microL (4500-11000); hemoglobin was 12.3 g/dL (12.6-17.4 g/dL); platelet count was 418.000/microL (150000-40000/microL); CRP was 309 mg/L (0-5 mg/L); sedimentation rate was 106 mm/h; procalcitonin level was 0.12 ng/mL. HBsAg, anti-HCV and anti-HIV tests were negative. TSH was 2.25 µIU/ml; vitamin B12:313 pg/ml (126-505 pg/ml); folic acid:23.33 ng/ml (5.9-24 ng/ml); ferritin:201.2 ng/ml (23-336 ng/ml), albumin: 34.5 g/L (35-52 g/L).

Blood samples for culture was taken when the patient was febrile and ampicillin/subbactam therapy was initiated empirically. The transthoracic echocardiography of the patient showed 0.9 cm pericardial fluid behind the left ventricle during diastole and minimal fluid around other cardiac cavities. For pericardial effusion ibuprofen and colchicine was initiated. Sputum gram stain test was negative for acid-resistant bacilli, tuberculin test was measured as 2 mm, quaniferon test and tuberculosis culture was negative. ANA, RF, anti-CCP, anti-DNA, ANCA, anti-SSA, anti-SSB, anti-Jo1, anti-Ro-52, AMA, anti CMV IgM, anti-CMV IgG, EBV-VCA IgM, EBV-VCA IgG and Brucella agglutination test were negative. Blood and urine culture results were negative. With these findings, tuberculosis, viral enfection and rheumato logical disease diagnoses were mostly excluded.

In order to exclude malignancy, upper gastrointestinal system endoscopy, colonoscopy, mammography and breast ultrasound was performed and no findings suggestive of malignancy were detected. Tumor markers CEA, CA-19-9, CA-15-3, AFP were within normal limits but CA-72-4 was 300 U/mL (0-6.9 U/mL). The positron emission tomography of the patient revealed increased 18F-FDG uptake on mediastinal lymph nodes (SUV max: 6.8) and pericardium (SUV max: 4.9). Endobronchial ultrasonography (EBUS) and fine-needle aspiration biopsy was obtained from subcarinal 7 and 11L lymph node stations. The cytopathological diagnosis came back negative for malignancy.

CA-72-4 elevation was considered to be associated with colchicine, so colchicine was discontinued. Follow-up CA72-4 levels of the patient ordered about 3 weeks later was 4.8 U/mL (0-6.9 U/mL) within normal limits.

Discussion

Benign conditions, drugs or supplements may cause elevations on serum tumor markers. Some dietary supplements like ganoderma lucidum spore powder (Reishi mushroom) used by cancer patients all over the world have been shown to cause elevation in CA72-4 [11,12]. There is also publications about serum CA72-4 elevations in patients using colchicine refersans. Zhao et al. Reported a patient taking colchicine for his gouty arthritis, serum CA72-4 levels significantly increasing during colchicine treatment and reducing when stop taking colchicine. After this observation they conducted a trial with 9 patients and results showed that serum CA72-4 levels were within normal range in all the patients before treatment, but significantly increased 5 days after colchicine treatment and reduced within normal range again 3 weeks after discontinuing treatment [13]. After that, they conducted a trial with 143 gout patients and 40 healthy individuals. In that trial serum CA72-4 level was significantly higher in gout patients receiving colchicine than that in healthy control and gout patients without any treatment or who were receiving other treatments [14]. In another study CA72-4 elevation has been reported in familial Mediterranean fever (FMF) patients. In this study, CA72-4 has been reported to be higher in patients with frequent attacks and was thought to be associated with inflammation. All patients were taking colchicine for FMF in this study. Although not specified, elevation of CA72-4 may be associated with the use of colchicine, and CA-72-4 levels may be higher in patients with a high frequency of attacks due to the higher dose of colchicine [15]. And lastly, Trape et al. Reported CA72-4 elevation in three patients taking anti inflammatory treatment for pericardial efusion [16].

Serum tumor markers are widely used for monitoring treatment response or for detecting recurrence during follow-up. But they are not sensitive or specific enough for screening cancer. Clinicians often ask for multiple serum tumor marker tests in patients they think may have cancer. Incorporating serum tumor markers into routine clinical practice for screening cancer is not cost effective, it does not contribute to diagnosis and cause anxiety. When assessing patients and interpreting laboratory results it is necessary to know the drugs they use and it is also very important to assess drug interactions in order to prevent economical and mental burden.

References


