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CA-125 – AS A NOVEL MARKER IN DISSEMINATED TUBERCULOSIS

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ABSTRACT

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INTRODUCTION

Tuberculosis is a menace in disguise and is one of the widely prevalent diseases in our country. The World Health Organisation TB statistics for India in the year 2019 reports an incidence of 2.64 million cases. Despite many effective strategies that are being employed to control the spread of tuberculosis, the numbers are in a rise. Tuberculosis can affect virtually every other organ system and has a very varied presentation. Extrapulmonary forms of tuberculosis prove to be diagnostic challenge and remain hidden for long, before being diagnosed. Chance observation of a relation of CA-125 and disseminated tuberculosis in our hospital sparked an interest in this novel marker.

CASE REPORT 1: A 63-year-old female patient was brought to our emergency department as a case of acute onset of breathlessness for 4 hours, more on lying down and relieved to a certain extent in the sitting position. No history of fever, cough, expectoration, chest pain, palpitations. No history of swelling of legs, decreased urine output, abdominal distension, abdominal pain or vomiting or loose stools. History of loss of weight of about 5 kgs in 2 months.

Patient was treated for COVID pneumonia about 7 months back. Known diabetic on regular treatment with OHAs. No other comorbidities.

Patient was admitted with similar complaints at a private hospital where she was treated as acute pulmonary edema. Due to unresolving nature of the breathlessness, she was further evaluated. Patient was discharged against medical advice and the patient came to our hospital.

On examination: Patient was conscious, oriented Afebrile, dyspneic and tachypneic, mild dehydration + Pallor +, not icteric, no cyanosis, no clubbing, no pedal edema, no palpable lymphadenopathy.

Systemic examination: CVS: S1 S2 heard, no murmurs RS: NVBS+ Decreased air entry in the right and left infra axillary and infra scapular areas.

P/A: Mild hepatomegaly with doughy abdomen CNS: NFND

Initially treated as pulmonary edema and then investigations were carried out. Routine investigations of CBC, RFT and LFT was within normal limits.

Viral markers – Negative. COVID RT-PCR - Negative

ECHO: No Regional wall motion abnormality, EF-60% Normal LVSF.

CT CHEST: Bilateral Ground glass opacities with bilateral pleural effusion right more than left.

Multiple mediastinal and hilar lymphadenopathy noted, largest measuring 3.1*2 cm

CECT ABDOMEN: Multiple pre aortic, para-aortic, pre aortic, peri pancreatic necrotic nodes with hepatomegaly.

With the above investigations in mind, our differential diagnosis was narrowed down to:

1. Tuberculosis.
2. Lymphomas
3. Malignancy with metastasis.

Further evaluation: Peripheral smear – microcytic hypochromic anemia Sputum AFB, Sputum CBNAAT – Negative, Gene Xpert - Negative Pleural fluid ADA – 38 U/L

Tumor markers: CA 125 – 230.70 U/ml (REF VALUE: <35.00) CA – 19-9 – 18.00 U/ml (<37.00)

CEA – 20.00 ng/ml (<3.00)

CECT abdomen: Atrophic ovaries.

OG opinion obtained – PAP smear – inflammatory cells.

Despite the elevation in tumor marker CA-125, the ovaries were atrophic and other sources of malignancy couldn't be identified.

Hence, repeat workup for tuberculosis was carried out and the following results were obtained.

Repeat ADA values: 55 U/l

Pleural fluid AFB – Mycobacterium tuberculosis - detected

With the above findings, the diagnosis of disseminated extra pulmonary tuberculosis was made and the patient was started on ATT. The pleural fluid ADA elevation, the presence of multiple nodal involvements with the elevation of CA- 125 sparked an interest and another case of disseminated tuberculosis in a male was evaluated.

CASE REPORT-2: A 46-year-old male patient was brought with complaints of fever for 6 months with evening rise of temperature. Associated with chills, loss of appetite, myalgia with easy fatiguability and abdominal pain. Patient also reports a significant weight loss of about 10 kgs in the last 3 months. No other significant history could be elicited. No history of comorbidities. Patient consumed mixed diet. Patient is a chronic alcoholic and a chronic smoker for 25 years.

On examination patient was conscious, oriented, afebrile, poorly built and nourished.

Generalised lymphadenopathy was present. VITALS: BLOOD PRESSURE: 90/60 mmHg

PULSE RATE: 80/min SPO2: 98% RA

CBG: 112mg/dl

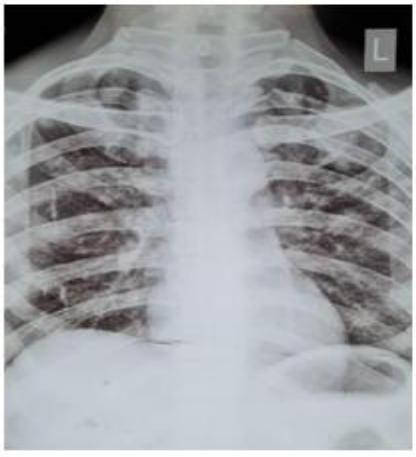
Investigations: CBC, RFT, LFT were within normal limits. PERIPHERAL SMEAR: NORMAL

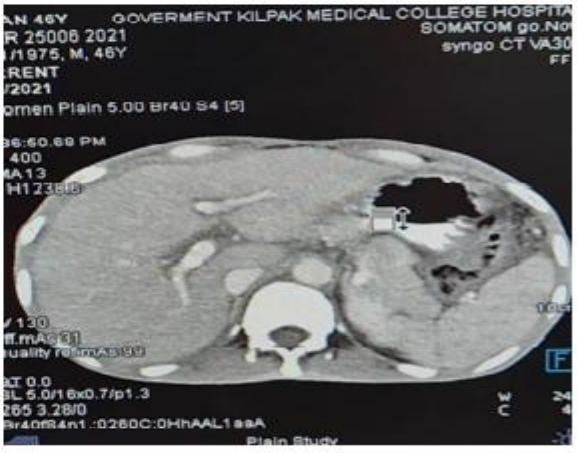
ESR: 60mm

VIRAL MARKERS: NEGATIVE COVID RT-PCR – NEGATIVE

SPUTUM AFB- Mycobacterium tuberculosis detected 1+

CECT ABDOMEN: Peritoneal thickening with nodes suggestive of possible tuberculous etiology.





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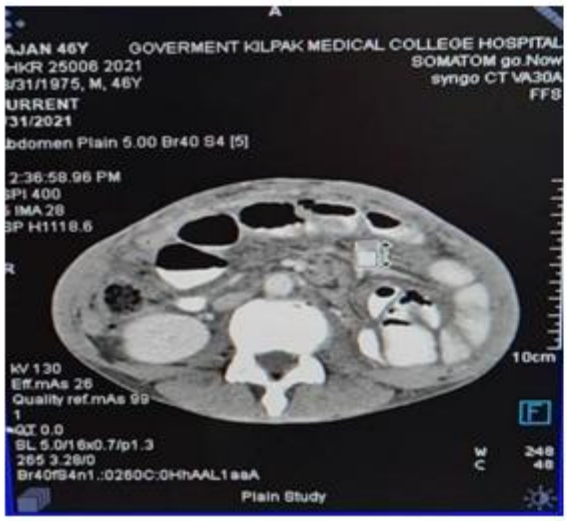

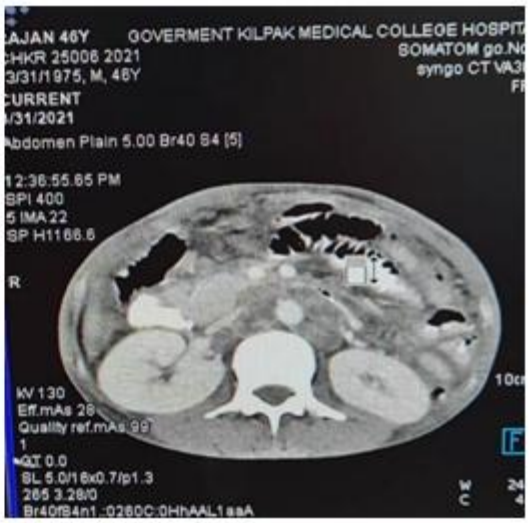

CA -125 – 46.88 U/ml (<35.00 U/ml) DISCUSSION:

CA 125 is an antigenic determinant on a high molecular weight glycoprotein recognized by a monoclonal antibody. It contains more than 11000 amino acids and has a mucin like nature. It is expressed usually in more than 80% of non-mucinous epithelial ovarian carcinomas and is also found in most of the carcinomas of Mullerian origin. It is elevated in 90% of advanced ovarian cancers and has a sensitivity of 57-80% and specificity of 100%. Its levels can be affected by a variety of benign, malignant and physiological conditions as well.

MALIGNANT	**BENIGN**
Epithelial ovarian carcinoma	Endometriosis
Endometrial carcinoma	Cirrhosis
Endocervical adenocarcinoma	Acute peritonitis
Pancreatic carcinoma	Acute pancreatitis
Breast carcinoma	Acute PID
Lymphoma	First trimester of pregnancy
Lung carcinoma	Colorectal carcinoma
Squamous carcinoma	cervical/vaginal

After having ruled out the above conditions in our first patient, the increased levels of CA-125 sparked our interest and further evidence and literature was reviewed.

Hence, as a support to our finding, CA-125 levels were estimated in a male patient with evidence-based sputum positive TB and was found to be elevated. The patient is being followed up to look for the decline of the levels with treatment.

Disseminated TB is defined as having two or more non-contiguous affected sites resulting from lymphohematogenous spread of Mycobacterium tuberculosis. Tuberculosis, being a rampant disease in our country, can present in diverse fashions. CA-125 is strongly associated with the idea of ovarian malignancy in our minds and its elevation is always viewed with a high index of suspicion.

POSSIBLE MECHANISMS: The exact pathophysiology behind the elevation of CA-125 in tuberculosis is not well explained but, Ronay et al. determined that Ca-125 was immunohistochemically localized and sharply demarcated around the tuberculous granuloma, and this suggested the possible explanation that the proliferating inflammatory mesothelial cells are the source of CA-125 in patients with tuberculosis. Another study demonstrated that the epitheloid and giant cells in both pleural effusion and ascites were stained with antibodies to Ca-125 in a patient with pleural and peritoneal tuberculosis.

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Apart from the gynecological and other malignant conditions in which the marker can be elevated, the possibility of tuberculosis should be ideally borne in mind. This can prevent unwanted surgical interventions and excess morbidity and psychological stress in part of the patients as well.

Aoki et al., demonstrated a sensitivity, specificity and accuracy of 100%, 75% and 84%, respectively, for serum Ca 125 >35 IU/ml in patients with pleural tuberculosis. At a serum Ca 125 of ⩾34.6 U/ml as a cut-off value, it had sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of 81.4%, 95%, 95.6%, 79.2% and 87.2%, respectively, among patients with active pulmonary TB. Results obtained with serum Ca 125 levels were similar or better than those obtained using pleural ADA (adenosine deaminase) levels >45 IU/ml, with a sensitivity, specificity and accuracy for this test of 81.8%, 89.3% and 87.2%, respectively. (1)

Hence, if Ca-125 level is <34.6 U/ml in a suspected pulmonary tuberculosis case, one should prompt a search for alternate diagnosis than TB. It is definitely useful in the monitoring of therapeutic responses to anti-tuberculosis drugs, predicting the prognosis.

CONCLUSION: In conclusion, the purpose of the article is to highlight that apart from the other possible malignant and grave causes of CA-125 elevation, a treatable cause like disseminated tuberculosis must also be considered. This will save both the physician and the patient from undergoing extensive investigations and morbidity. Taking the above into consideration, in patients with no definite evidence of TB, CA-125 can be used as a predictor.

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