Be Wary Of CA 125 Levels

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KEYWORDS

ABSTRACT
Ca 125 a tumour marker for ovarian neoplasms. We did a retrospective study to assess the levels of CA 125 in patients with ovarian masses. It was surprising to find CA 125 levels being elevated in both malignant and benign ovarian masses. It is a well-known fact that in Cancer ovaries the CA 125 is elevated. But what about benign condition? Here we try to reason out why CA 125 is elevated in benign conditions also.

Introduction:

Ovary is a part of the female reproductive system. It an endocrine gland that secretes hormones which play a role in menstrual cycle and fertility. It starts to function at puberty by secreting hormones. These hormones are responsible for the development of secondary sexual characters in a female. The ovaries also play an important role in fertility and pregnancy. Once the ovary releases an egg, there are a lot of feedback mechanisms involving the pituitary and hypothalamus. These signals make the ovary secrete their own hormone. (1)

The ovaries not only produce but also release the egg or the mature oocyte. The development of oocyte happens within the ovary. Once the oocyte is mature, the pituitary gland secrets luteinizing hormone to release the egg from the follicle. This process is called ovulation. This follicle becomes a corpus luteum and secrets progesterone to maintain a pregnancy once the egg is fertilised.(2)

As the woman ages, there is a decline in these hormones causing menopause. The events that lead to ovarian aging are unclear but it can be attributed to environmental factors, lifestyle and/or genetic factors.(2)

Ovarian diseases can be classified as endocrine or reproductive disorders. Ovarian cysts are most common among reproductive age groups. Cancer of the ovary can be classified into germ cell tumours and non-germ cell tumours. (2)

Ovarian carcinomas are the sixth most common cancers among women, and they are the seventh leading cause of death. In the Indian scenario, ovary is the third leading site for cancer after cervix and breast. (3)

Ovarian cancers increase with age. Hence more common among post-menopausal women. In most patients, these are symptoms free until several months. These are often painless. Some of the symptoms include bloating, abdominal or pelvic pain or discomfort, back pain, irregular menstruation or postmenopausal vaginal bleeding, pain or bleeding after or during sexual intercourse, loss of appetite, fatigue, diarrhea, indigestion, heartburn, constipation, nausea, feeling full, and possibly urinary symptoms. All these occur because the ovarian mass begins as pelvic and becomes an abdomino-pelvic mass. And the diagnosis was with the help of a biomarker, CA 125. This is usually elevated in case of ca ovary and hence can be differentiated from benign conditions.(4)

Hence the aim of this study:

To assess the CA 125 levels of all patients with ovarian masses and to find out how many of these patients did really have cancer ovaries.

Methodology:

After institutional ethical clearance, a retrospective study was conducted at the ACS Medical College and Hospital from Jan 2018 to Jan 2024. all data pertaining to patients with ovarian mass was collected from the medical records department of our hospital. All these were analysed to find out the following in each patient

1. age of patients
2. history and symptoms
3. presence of CA 125
4. history of previous medication
5. socioeconomic status of these patients
6. examination findings
7. treatment given for patients
8. previous treatment or surgery history
9. final diagnosis

All necessary data was collected from the medical records department of our institute. The names of these patients were masked and the data coded in order to get an unbiased statistical output.

There was a total of 50 patients. Patients with CVA or stroke, debilitated patients, patients who underwent major surgeries in the past year were all excluded from this study. Patients whose CA 125 were within normal levels were excluded. After exclusions, a total of 20 patients remained.

The collected data was analysed using SPSS 18.0 (PASW Statistic, SPSS Inc., IBM, Chicago, IL).

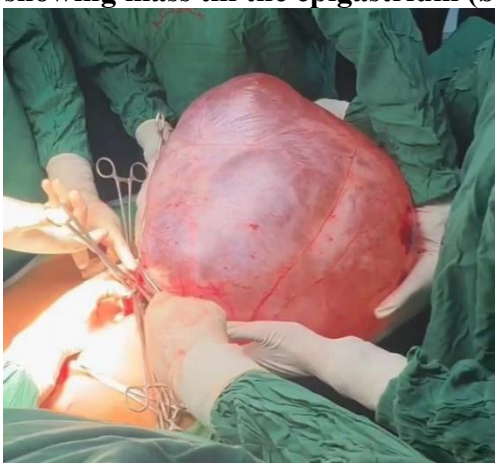
Results:

Parameter			Percentage
Total no of patients	20		100%
Age	20-40years	2	10%
	40-60 years	6	30%
	>60 years	12	60%
Menstrual status	Pre menopausal	5	75%
	Post menopausal	15	25%
Symptoms	pain	15	75%
	Bloated abdomen	18	90%
	Post menopausal bleeding	5	25%
	Abnormal vaginal bleeding	1	5%
Per Abdomen findings	Mass palpable just above the pubic symphysis	6	30%
	Mass palpable just below the umblicus	11	55%
	Mass palpable just above the umblicus	3	15%
CA 125	Elevated	20	100%
	More than 1500	8 (later proven Ca ovary)	40%
	Less than 1500	12(later proven benign)	60%
Treatment	Two stage procedure (cystectomy followed by further management)	15 (4 of these patients underwent a second procedure)	75%

	TAH with BSO	5 (one was benign but in view of the age we decided to go ahead with single step procedure)	25%
Diagnosis	Benign	12	60%
	Cancer	8	40%

Pic 1: Intra op picture showing ovarian mass – below the umbilicus. (malignant)

Pic 2: showing mass till the epigastrium (benign)



Pic 3: intra op pic – mass till the epigastrium

Discussion:

Biomarker used in ovarian cancer is CA125, this is otherwise called as serum ovarian cancer biomarker.(5) This however has the drawback of being less sensitive and specific. There are other biomarkers for ovarian tumours like the CEA (mucinous tumour) LDH (dysgerminoma, mixed germ cell

tumours), α-fetoprotein (embryonal cell tumours, yolk sac tumour), β-hCG (choriocarcinoma), inhibin B (granulosa cell tumours), and HE4 (Human epididymis protein 4). (6,7)
In this study, we evaluated CA-125 as the marker, since it is the most commonly done first-line tumour marker for screening ovarian malignancies.
In 1981 Robert Bast, Robert Knapp and their team discovered the CA 125. CA-125 was found using the murine monoclonal antibody designated OC125. The protein was named "cancer antigen 125" because OC125 was the 125th antibody produced against the ovarian cancer cell line that was being studied.(8)
CA 125 also known as Mucin-16 or MUC-16 is a protein that is encoded by MUC 16 gene. It is from the mucin family of glycoproteins. Serum CA 125 levels are usually elevated in ovarian cancer, endometrial cancer, fallopian tube cancer, lung cancer, breast cancer, and gastrointestinal cancer. Its levels are also used to monitor response to chemotherapy and disease progression in ovarian cancer. (8–10)
Studies suggests MUC16 binds selectively to mesothelin, a glycoprotein normally expressed by the mesothelial cells of the peritoneum (the lining of the abdominal cavity) hence participates in cell-to-cell interactions that enable the metastasis of tumour cells. MUC16 and mesothelin interactions are thought to provide the first step in tumour cell invasion of the peritoneum. (11)
CA-125 is best known as a marker for ovarian cancer, is often found to be elevated in other conditions: benign and malignant, gynaecological and non-gynaecological. The elevation associated with benign conditions is usually mild. (12)Generally, high concentrations of CA-125 are suggestive of malignancy, thus posing a diagnostic challenge to the physician.(11)
In our study, the CA 125 levels were less than 1500 in patients with benign ovarian disease and more in malignant patients.
The interesting find in our study was that there was no relation seen between the size of the tumour and CA 125 levels. Larger tumours had lower CA 125 and smaller tumours had higher CA 125.
With this in mind, it is interesting to note that, CA-125 is a membrane glycoprotein which is found in the female genital tract of Mullerian duct origin (uterus, fallopian tube, upper part of vagina).(13) Ovarian cystic epithelium is also of Mullerian origin; thus, expansion of cystic epithelium in larger cyst could have shown correlation with the CA-125 levels. But this lack of correlation may be due the fact that high-grade sporadic epithelial ovarian tumours arise from serous tubal intraepithelial carcinoma (STIC) lesions of fallopian tube. Possibly, due to this, there was lack of direct correlation with ovarian cyst size.(8,14,15)
The dilemma due to CA 125 is further worsened because the RMI and risk of malignancy algorithm (ROMA) which places emphasis on the CA 125 levels. Thus, for these reasons, the RMI and ROMA may be unreliable estimates of the risk of malignancy in women of reproductive age.(16–18)

Conclusion:
In conclusion, this article demonstrates the diagnostic challenge of elevated levels of CA-125. Therefore, a multidisciplinary team, fertility-sparing surgery, and follow-up are essential for better treatment and patient satisfaction. To say it in an old-fashioned way, lets take CA 125 levels with a pinch of salt.

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