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Original Research Article

The role of carbohydrate antigen 19-9 in the clinical evaluation of mature cystic teratomas: an observational study at a tertiary care centre

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ABSTRACT

Background: Carbohydrate antigen (CA) 19-9 is a tumour marker mainly used in the evaluation of gastrointestinal tract malignancies including pancreas, colon and biliary tract. Cases of ovarian tumours such as mucinous neoplasms have been reported to have high levels of CA 19-9. However, its role in the management of cystic teratomas (MCT) which are the most common benign ovarian tumours encountered in gynaecology, is not studied in depth in literature.
Methods: In our study, we observed the levels of CA 19-9 in 40 patients presenting with MCT. Its association to the cyst size, contents, laterality and torsion or rupture were documented.
Results: The various clinical parameters evaluated in our study such as larger cyst size, presence of torsion and tooth as a content had a positive association with elevated CA 19-9 levels ($p<0.05$). However, CA 19-9 had no significant relationship with the laterality of the cyst. Thus, CA 19-9 may serve as an important adjunct tool to ultrasonography in the management of dermoid cysts (MCT), particularly in those with larger sizes and at risk of torsion.
Conclusions: High levels of CA 19-9 can be observed in benign ovarian tumors like mature cystic teratoma (MCT) and it need not always be associated with malignancy or malignant transformation of benign tumors. Levels more than 100 IU may warrant further imaging studies to rule out gastro-intestinal pathologies. Unnecessary medical investigations or patient anxiety can be avoided in cases of moderate elevation in CA 19-9 levels

Keywords: MCT, Dermoid cyst, Tumour markers, CA 19-9, Size, Torsion

INTRODUCTION

All through the reproductive years in a woman's lifetime, the most common ovarian masses she develops are benign. The chance that a primary ovarian tumour is malignant in a patient younger than 45 years is <1 in 15. In other words, 90% of all ovarian masses in premenopausal women end up being histologically proven of benign origin, whereas in post-menopausal women, malignancy is detected in 40% of cases.

Dermoid cyst, also called as MCT is the most common germ cell tumour of the ovary in reproductive-aged women. It accounts for 10-25% of all ovarian neoplasms and 60% of all benign ovarian tumours. It is mostly common in women aged between 20 and 40 years.[1]

Bilaterality is found in 10% of cases, 15% of cases develop torsion; however, rupture is rare <1%, probably due to thick cyst wall. Malignant transformation occurs in only 1-3% of cases, especially in postmenopausal women. Squamous cell carcinoma is the most common type (80-90%) of malignant transformation.[2]

Carbohydrate antigen (CA) 125 has been used in the diagnosis of ovarian cancer, and serum levels of this antigen are elevated in approximately 80% of women with epithelial ovarian cancer.

However, CA 125 levels can also be increased in endometriosis, adenomyosis, leiomyoma, and pelvic inflammatory disease. Therefore, some institutions have incorporated CA 19-9 as a tumour marker for the prediction of adnexal malignancy, although its usefulness in tumour differentiation is still controversial.[3]

CA/cancer antigen 19-9 is usually raised in gastrointestinal tumours, pancreatic malignancy, pseudocyst of pancreas, colon and biliary tract carcinomas.[4] It can be increased in certain benign conditions, however, not many studies have been done to warrant its diagnostic and prognostic aid in benign ovarian tumours.

METHODS

This is a cross-sectional study undertaken at Apollo hospitals, Chennai from June 2022 to June 2023. 40 women of different age groups presenting with dermoid tumours to the gynaecology outpatient department were included in the study. Women with any other ovarian/adnexal cysts were excluded. All patients were evaluated with ultrasound, pre-operative tumour markers CA 19-9 and CA 125. All underwent laparoscopic ovarian cystectomies and all specimens were retrieved via endo-bags.[5] Intraoperative findings such as cyst diameter, laterality, torsion and contents of the cyst were documented and their association with elevation in CA 19-9 were observed. All operative specimens were histo-pathologically confirmed to be MCTs. Figure 1 shows the laparoscopic removal of a large dermoid cyst.

Statistical analyses

Descriptive statistics were presented with frequency (percentage) and mean ± SD for the categorical and continuous factors respectively. Median (IQR) was presented while the data skewed. The normality of the data was checked by using Shapiro-Wilk test. Student's t test/Mann Whitney U test were used to determine the significant changes between torsion. ANOVA/Kruskal Wallis test were used to determine the difference between laterality. Chi-square test was used to find out the association between two independent categorical factors. $P<0.05$ considered as statistical significance. All the analysis was carried out by using the statistical software SPSS (IBM, 28.0)

RESULTS

The descriptive data of the study is represented in Table 1.

Age of the study population varied between 8-42 years with a mean ± SD as 26.15±7.03 (in years). Of the 40 patients, 27 presented with symptoms, such as abdominal pain (45%), irregular cycles (20%) and heavy menstrual bleeding (2.5%). 13 patients were asymptomatic (32.5%). Clinical presentation of the partakers in shown in Figure 2. We found that left sided cysts (50%) were commoner than right sided ones (37.5%). Bilateral ovarian dermoid cysts were found in 5 patients (12.5%).

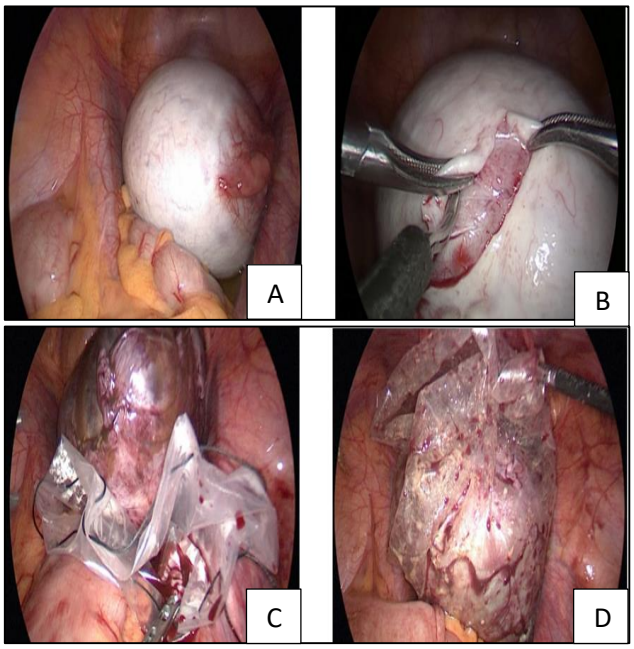

Figure 1 (A-D): Laparoscopic ovarian cystectomy. Large right ovarian dermoid cyst, peeling cyst wall with laparoscopic scissors, introduction of the endo-bag and placement of cyst inside the endo-bag for retrieval.

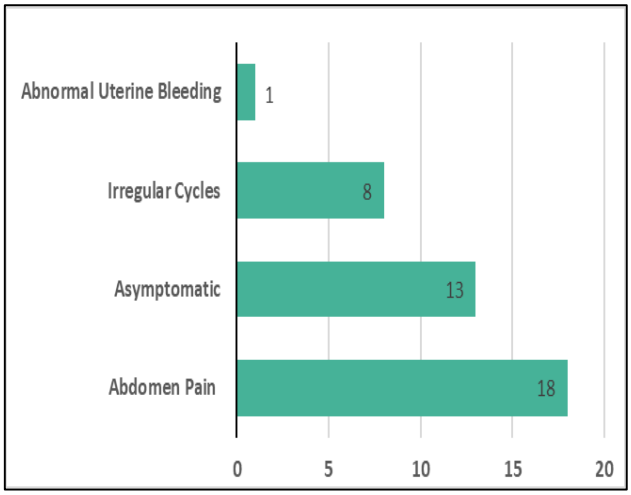

Figure 2: Clinical presentation of the patients.

Mean cyst diameter was 6.08±2.24 cm (ranging from 3-12 cm), 19 had size <6 cm and 21 patients had size ≥6 cm.

8 out of the 18 patients who presented with abdominal pain had torsion of the cyst. Total torsion rate accounted for 20% as shown in Figure 3. We also studied if the presence of tooth had a correlation with CA 19-9. 9 patients had tooth in the Histopathology report and had a positive association with the CA 19-9 levels (Figure 4).

Table 1: Descriptive statistics, (n=40).

Parameters	N (%)
Age (In years)	
Mean ± SD	26.15±7.03
Range	8-42
Presentation	
Abdominal pain	18 (45)
Irregular cycles	13 (32.5)
Asymptomatic	8 (20)
Abnormal-uterine bleeding	1 (2.5)
Laterality	
Right	15 (37.5)
Left	20 (50)
Bilateral	5 (12.5)
CA125	
Median (IQR)	14.5 (9.7-24.5)
Range	7-59.1
CA19-9	
Median (IQR)	25 (15.13-61.25)
Range	7.5-1041
Size	
Mean ± SD	6.08±2.24
Range	3-12
Size category	
<6 cm	19 (47.5)
>6 cm	21 (52.5)
Torsion	
Yes	8 (20)
No	32 (80)
Content	
Presence of tooth	9 (22.5)
No tooth	31 (77.5)

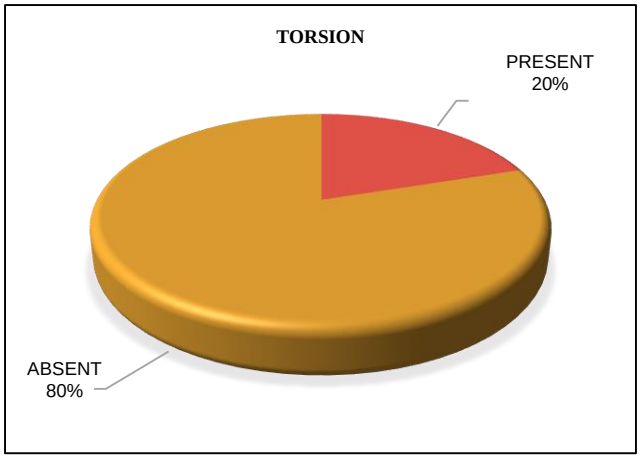

Figure 3: Torsion rates.

Table 2: Correlation of cyst size and CA 19-9.

Size-CA 19-9	Value
Correlation coefficient (Spearman Rho)	0.609**
Sig (2 tailed)	<0.001
N	40

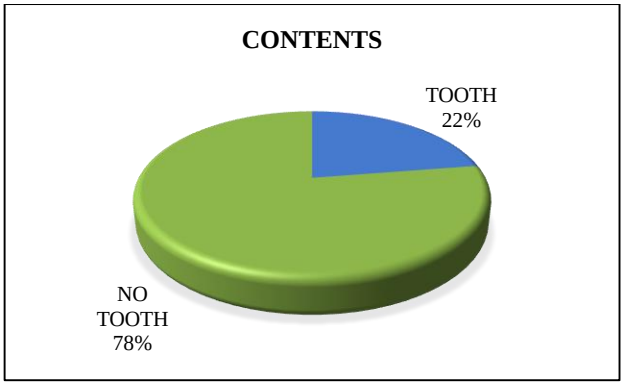

Figure 4: Rates of tooth in the cyst.

Table 3: Correlation of cyst size and torsion.

Size-torsion	Value
Correlation coefficient (Spearman Rho)	29.500**
Sig (2 tailed)	<0.001
N	8

**Correlation is significant at the 0.05 level (2-tailed).

Table 4: Correlation of torsion and CA 19-9.

Torsion-CA 19-9	Value
Correlation coefficient (Mann-Whitney U)	246**
Sig (2 tailed)	<0.001
N	40

**Correlation is significant at the 0.05 level (2-tailed).

Table 5: correlation of tooth and CA 19-9.

Tooth - CA 19-9	Value
Correlation coefficient (Mann Whitney U)	26.0**
Sig (2 tailed)	<0.001
N	40

**Correlation is significant at the 0.05 level (2-tailed).

Table 6: Association between various cyst parameters and CA19-9.

Parameters	CA19-9	P value
Size^	0.609	<0.001*
Torsion^^		
No	21 (14.2-38.7)	<0.001[#]
Yes	19 (72.5-720.2)	
Contents^^		
Presence of tooth	90.2 (44.5-210)	<0.001[#]
No tooth	20 (14-38)	
Laterality	0.388	0.823 (Kruskal-Wallis H)

^-Correlation/rho value; ^^- Median (Inter-quartile range); *Spearman rank order correlation median (IQR); [#]Mann Whitney U test- Boldface indicates statistical significance.

We noted that as the size of the cyst increased, there was a positive correlation with the elevated levels of CA 19-9 (Table 2). As well documented in literature, we found that larger cyst size was directly proportional to torsion rates.[6] All cases with torsion (n=8) had a cyst diameter ≥ 6 cm (Table-3). There was also a statistically significant association between CA 19-9 and torsion rates as shown in (Table 4). CA 19-9 also significantly differed across cysts which had tooth as one of its contents (Table 5). There were no statistical association found between laterality and CA 19-9 ($p>0.05$). The statistical association of all the cyst parameters and CA 19-9 is shown in Table 6.

DISCUSSION

Dermoid cysts/ MCT are one of the common benign ovarian cysts occurring in women of reproductive age group. 60% of them are 5-10 cm in diameter. They contain elements of 3 germ cell layers. Sebaceous material, hair, tooth, cartilage and thyroid tissue are the elements frequently observed. Bilaterality is seen in 10% cases, if unilateral, they have a more common occurrence in the right adnexa.

Torsion is found in 15% cases. USG findings of a dermoid cyst include shadowing echo density, fat-fluid levels, intra cystic floating balls, tip of the iceberg sign and diffuse or regional high amplitude echoes.[7] However, it is difficult to notice torsion in an ovary with dermoid cyst. This is due to the shadowing pattern of these tumors which hinders the accurate diagnosis. Supplementary means are maybe useful to diagnose torsion, as early recognition and treatment is paramount. Recent studies indicate that CA 19-9 and CA125 may be used as adjuncts in diagnosis and management of dermoid cysts. [8]

In our study we did not find any statistical significance of CA 125 across the various clinical parameters that were assessed ($p>0.05$), nor was malignancy detected in any case. CA 19-9 may serve as an important prognostic tool in the management of dermoid cysts among various other tumor markers. [9,10]

Many case reports show extreme elevation of CA 19-9 serum levels, observed in young women with benign dermoid cyst.[2,4,5]

In another study involving 163 women concluded that elevated serum 19-9 levels correlated with larger tumor diameters and higher torsion rates. A systematic meta-analysis encompassing 7 studies including 995 patients supported that CA 19-9 could raise a high degree of clinical suspicion of torsion in dermoid cysts, thereby aiding in early surgical management. However, the researchers concluded that its diagnostic value is still limited and it can only serve as a supplementary diagnostic tool in MCTs.[11]

The various clinical parameters evaluated in our study such as larger cyst size, presence of torsion and tooth as a content had a positive relation with elevated CA 19-9 levels ($p<0.05$). However, CA 19-9 had no significant relationship with the laterality of the cyst. Thus, CA 19-9 may serve as an important adjunct tool to ultrasonography in the management of dermoid cysts, particularly in those with larger sizes and at risk of torsion.

CONCLUSION

From our study, we conclude that high levels of CA 19-9 can be observed in benign ovarian tumors like the dermoid cyst and it need not always be associated with malignant tumors or malignant transformation of benign tumors. Alarmingly high levels may warrant further imaging studies such as CT scan and MRI to rule out gastro-intestinal pathologies.[12] Unnecessary medical investigations or patient anxiety can be avoided in cases of moderate elevation in CA 19-9 levels.[13] Although malignant transformation in a dermoid cyst is extremely rare, cases have been reported of squamous cell carcinoma occurring in postmenopausal women with ovarian dermoids. However CEA and SCCA have been found useful in these cases, rather than CA 19-9.[14–15]

Larger case studies are needed to further evaluate and support the routine use of this tumour marker in the clinical evaluation of MCTs.

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