

# CA 19-9 in Ovarian Immature Teratoma- A Potential Tumour Marker or A Masquerade?

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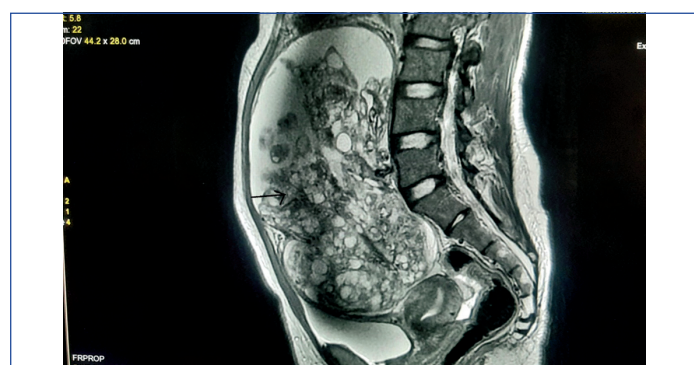
## ABSTRACT

Carbohydrate antigen 19-9, also known as Cancer Antigen (CA 19-9) is a tumour marker found elevated in certain ovarian tumours. Although, reports of its association with mature teratoma are considerable, little is mentioned about its association with immature teratoma. This could be attributed to immature teratoma being a rare tumour with only a few studies on its tumour markers. Authors present the case of a 24-year-old female presenting with ovarian immature teratoma who also showed unusually high serum levels of CA 19-9 which reduced drastically after surgery. This association therefore may warrant further investigations to establish the clinical relevance and its importance in future.

**Keywords:** Abdominopelvic mass, Adjuvant chemotherapy, Carbohydrate antigen 19-9, Multiloculated solid-cystic lesion

## CASE REPORT

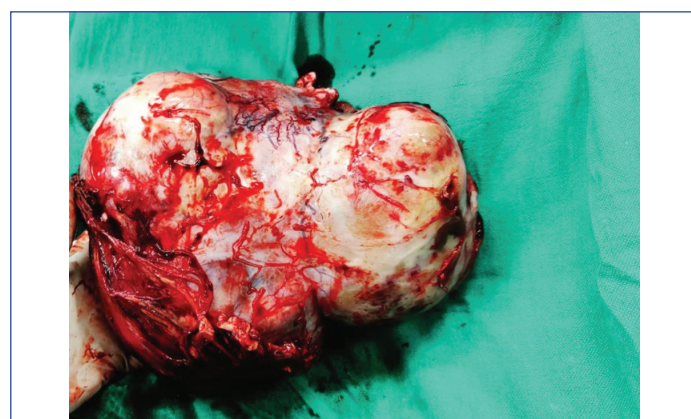
A 24-year-old P0A1 married for the past seven months, presented with rapidly increasing abdominopelvic mass over the past three months. Her menstrual cycles were normal with a history of first trimester pregnancy loss two months earlier. On per abdominal examination, the mass was 25×20 cm in size, firm in consistency, and non tender. On vaginal examination, uterus was not separated from the mass. Her Magnetic Resonance Imaging (MRI) suggested right sided well defined multiloculated solid cystic lesion measuring 20×11×18 cm with right ovary not seen separate from the mass [Table/Fig-1]. Tumour markers were significantly increased. The  $\beta$ -Human Chorionic Gonadotropin ( $\beta$ -HCG) was 4.03 mIU/mL, Carcinoembryonic Antigen (CEA) was 3.82 ng/mL, Lactate Dehydrogenase (LDH) was 200 U/mL, Cancer Antigen 125 (CA-125) was 222 U/mL, Alpha Fetoprotein (AFP) was 16.9 IU/mL and CA-19.9 was 1336 U/mL. Upper abdominal imaging and colonoscopy was done to rule out gastrointestinal pathology and was found to be normal.



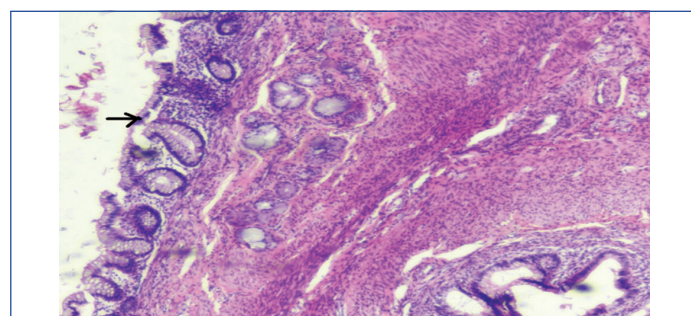
**[Table/Fig-1]:** Sagittal T2 weighted image (MRI) showed right sided well defined multiloculated solid cystic lesion with right ovary not separated from the mass.

Intraoperatively, a 22×11×18 cm, irregular, bosselated surfaced right ovarian mass with an intact capsule and dilated blood vessels on the surface was seen, which was adherent to the anterior surface of uterus, pushing it inferiorly. Left fallopian tube and ovary were grossly normal, while the right fallopian tube was stretched over the mass [Table/Fig-2]. Systematic survey of peritoneal cavity revealed no other organ involvement or metastasis. Operative team proceeded with fertility preserving ipsilateral salpingo-oophorectomy assisted by frozen section histopathology of the specimen. Postoperative period was uneventful. Final histopathology report revealed immature teratoma

grade 3 and pathological stage was T1aN0Mx [Table/Fig-3,4]. On postoperative day 14, CA-19.9 was reported as 109 U/mL. Patient is currently in remission after having received adjuvant chemotherapy with Bleomycin, Etoposide and Platinum (BEP) based regimen for two cycles and is on regular follow-up.



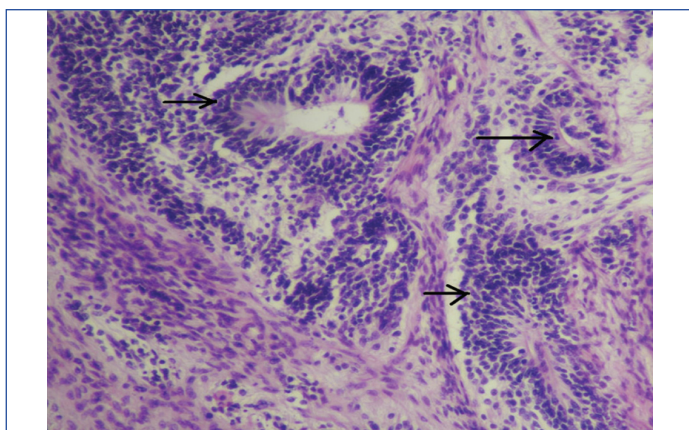
**[Table/Fig-2]:** Gross specimen of right ovarian mass showing irregular, bosselated surfaced with dilated blood vessels over the intact capsule.



**[Table/Fig-3]:** Photomicrograph showing immature neural tissue formed of sheets of small round neuroblasts and rosettes and primitive neural tubules lined by stratified columnar neuroepithelial cells displaying nuclear pseudo stratification and hyperchromasia (H&E stain, 100X).

## DISCUSSION

Sialylated Lewis A antigen or cancer antigen 19-9 is structurally a carbohydrate moiety which is widely employed as a tumour marker [1]. An ideal tumour marker should be highly sensitive and organ-specific, correlate well with the tumour size, should be epidemiologically homogenous, with minimal interobserver variability. Among the tumour markers, CA 19-9 stands out as a predictable



**[Table/Fig-4]:** Photomicrograph showing endodermal components composed of gastric mucosa (H&E stain, 100X).

marker for the diagnosis of solid organ tumours of abdominopelvic origin. It is made up of transmembrane proteinaceous moieties with glycosylated assimilation of oligosaccharides. It is a member of the mucinous epicellular marker's league [2]. Physiologically, the ductal cells of pancreas and epithelial lining of biliary tracts, gastric, colonic, endometrial structures all synthesize CA19-9 antigen as a part of its normal immunological homeostasis. As an established tumour marker of hepatobiliary and pancreatic malignancies, its concentration level correlates with the size of the mass. However, not only in malignant masses, but the serum levels also spike in multiple benign and inflammatory conditions in source organs of gynaecological, pulmonary, urological and thyroid system [3].

It has been shown that statistically significant relationship exists between ovarian mature cystic teratoma and CA19-9 levels with mean level being  $71 \pm 17$  U/mL [4]. There are case reports describing the elevated CA19-9 levels in mucinous cystadenoma and mature cystic teratoma of the ovaries [5-8]. Steinberg W, concluded that high levels of CA19-9 are associated with malignant tumours [9]. While the study by Cho HY et al., suggested high levels are seen in mucinous borderline and malignant tumours [10]. However, study by Lahdenne P et al., found reporting immature teratoma in association with CA19-9 marker [11]. Although, it has been stated that 50% immature teratoma can have raised CA19-9 [6, 12].

Immature teratoma is a less prevalent (1% of all ovarian cancers) germ cell tumour accustomed to present either as an isolated pure form or as a component of mixed germ cell growth affecting individuals in early 30s [13].

Although, the marker most commonly linked to immature teratoma is alpha-fetoprotein [14]. The combined estimation of CA 125, CA 19.9, CEA and AFP accentuate the sensitivity of diagnosis and severity of progression. In terms of specificity, none is superior. Having the knowledge of widely used cut-off values of the serum CA-125 (>35 U/mL), CA 19-9 (>39 U/mL) and CEA (>3.8 U/mL) aids in suggesting the possibility of malignancy, however, not organ-specific. In the

present case, authors found increased values of both CA 125 and CA 19-9. The up scaling of CA 19-9 was much higher i.e., 1336 U/mL. Its elevation is well associated with mature teratomas and size progression, pertaining to the secretion from the apical cytoplasm of the epithelial lining [15]. The utility of CA 19-9 as a follow-up marker for recurrence after radical removal can be culminated as observed in the present case. The carbohydrate markers i.e., CA 125 and CA 19-9, although less studied can be used as an adjunct in the follow-up of immature teratoma [11].

## CONCLUSION(S)

The CA 19-9 has been found elevated in various ovarian malignancies- both benign and malignant. The use of CA19-9 as a diagnostic modality may be difficult due to its lack of specificity. However, if employed as a prognostic marker and for follow-up of ovarian neoplasms, it may succor the smooth management of these neoplasms. The limited literature available on immature teratoma and tumour markers associated with it, however, obligates the need for further studies on it.

## REFERENCES

- [1] Duffy MJ, Sturgeon C, Lamerz R, Haglund C, Holubec VL, Klapdor R, et al. Tumour markers in pancreatic cancer: A European Group on Tumor Markers (EGTM) status report. *Ann Oncol*. 2010;21(3):441-47.
- [2] Magnani JL, Brockhaus M, Smith DF, Ginsburg V, Blaszczyk M, Mitchell KF, et al. A monosialoganglioside is a monoclonal antibody-defined antigen of colon carcinoma. *Science*. 1981;212(4490):55-56.
- [3] Dyckhoff G, Warta R, Gonnermann A, Plinkert PK, Flechtenmacher C, Volkmann M. Carbohydrate antigen 19-9 in saliva: Possible preoperative marker of malignancy in parotid tumors. *Otolaryngology-Head and Neck Surgery*. 2011;145(5):772-77.
- [4] Abide QY, Ergen EB. Retrospective analysis of mature cystic teratomas in a single center and review of the literature. *Turk J Obstet Gynecol*. 2018;15(2):95.
- [5] Pandey D, Sharma R, Sharma S, Salhan S. Unusually high serum levels of CA 19-9 in an ovarian tumour: Malignant or benign? *J Clin Diagn Res*. 2017;11(3):QD08.
- [6] Singh A, Srivastava A, Chauhan D, Guatam RG. CA-19-9 as an Emerging Marker of Ovarian Tumour: A Rare Entity. *J Clin Diagn Res*. 2019;13(5):QD01-03.
- [7] Madaan M, Puri M, Sharma R, Kaur H, Trivedi SS. Unusually high levels of CA19-9 associated with mature cystic teratoma of the ovary. *Obstet Gynecol Sci*. 2014;2014.
- [8] Prodromidou A, Pandrakakis A, Loutradis D, Haidopoulos D. Is There a Role of Elevated CA 19-9 Levels in the Evaluation of Clinical Characteristics of Mature Cystic Ovarian Teratomas? A Systematic Review and Meta-analysis. *Cureus*. 2019;11(12):e6342.
- [9] Steinberg W. The clinical utility of the CA 19-9 tumor-associated antigen. *Am J Gastroenterol*. 1990;85(4):350-55.
- [10] Cho HY, Kyung MS. Serum CA19-9 as a predictor of malignancy in primary ovarian mucinous tumors: A matched case-control study. *Med Sci Monit*. 2014;20:1334-39.
- [11] Lahdenne P, Pitkanen S, Rajantie J, Kuusela P, Shmes MA, Lanning M, Heikinheimo M. Tumour markers CA 125 and CA 19-9 in cord blood and during infancy: Developmental changes and use in pediatric germ cell tumors. *Pediatr Res*. 1995;38(5):797-01.
- [12] Novaković S. Tumour markers in clinical oncology. *Radiology and Oncology*. 2004;38(2):73-83.
- [13] Smith HO, Berwick M, Verschraegen CF, Wiggins C, Lansing L, Muller CY, et al. Incidence and survival rates for female malignant germ cell tumors. *Obstet Gynecol*. 2006;107(5):1075-85.
- [14] Saba L, Guerriero S, Sulcis R, Virgilio B, Melis G, Mallarini G. Mature and immature ovarian teratomas: CT, US and MR imaging characteristics. *Eur J Radiol*. 2009;72(3):454-63.
- [15] Coskun A, Kiran G, Ozdemir O. CA 19-9 can be a useful tumor marker in ovarian dermoid cysts. *Clin Exp Obstet Gynecol*. 2008;35(2):137-39.

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