EJMO

DOI: 10.14744/ejmo.2020.03511
EJMO 2021;5(1):80–84

Case Report

Alpha Fetoprotein Secreting Mucinous Epithelial Ovarian Carcinoma in a Young Woman- a Rare Case Report and Review of Literature

Sangam Jha,[1] Jayanti Sinha,[1] Shreekant Bharti[2]

[1]Department of Obstetrics and Gynecology, AIIMS Patna, Bihar, India
[2]Department of Pathology, AIIMS Patna, Bihar, India

Abstract

Germ cell tumors are known to secrete alpha fetoprotein. Epithelial ovarian cancers rarely secret alpha fetoprotein and mucinous variety is rarest among them that too in young woman. In addition to the case discussion, literature on this entity has been reviewed.

A 24 years, parous woman presented with 28 weeks sized abdominopelvic mass. CECT confirmed this as right adnexal malignant mass. Tumor markers for ovarian cancer were within normal limits except alpha fetoprotein which was marginally raised (21.4ng/dl). Under the diagnosis of malignant germ cell tumor, she underwent staging laparotomy, right salpingo-oophorectomy performed. Final histology returned as stage I mucinous adenocarcinoma without any germ cell component. Cells of invasive mucinous gland expressed reactivity for AFP on immunostaining. AFP fell to normal level following surgery.

Only three case reports concerning this topic have been described in the literature till date. All were advanced stage disease in the postmenopausal women. Given the late stage diagnosis, mortality was also high. Owing to its atypical presentation, immunostaining was required for differentiating it from other AFP secreting tumors of ovary.

Keywords: Alpha fetoprotein, immunohistochemistry, mucinous adenocarcinoma

Cite This Article: *Jha S, Sinha J, Bharti S. Alpha Fetoprotein Secreting Mucinous Epithelial Ovarian Carcinoma in a Young Woman- a Rare Case Report and Review of Literature. EJMO 2021;5(1):80–84.*

Alpha fetoprotein (AFP) is a glycoprotein secreted from yolk sac and fetal lever during fetal development. Elevated serum level of AFP is usually associated with germ cell tumor, hepatocellular carcinoma and specific type of gastric carcinoma. Epithelial ovarian cancer had rarely been reported to secrete AFP. Less than 1% of epithelial ovarian cancer is seen in women less than 30 years of age.[1] AFP secreting epithelial tumor at young age is rare occurrence. Here we report a case in a 24 years old woman with mucinous cyst adenocarcinoma and mildly raised AFP but without any germ cell component.

Case Report

A 24 years old woman, G1P1, presented with complaints of pain lower abdomen, abdominal distension & dyspepsia for last 2 months and menstrual irregularity for last 1 month. She had no complaints of fever or vomiting and her bowel habits were normal. She did not have any significant past medical or surgical history. On abdominal examination a 28 weeks size, smooth, cystic, non-tender, mobile lump was palpable. Pelvic examination confirmed the finding as adnexal mass. Routine investigation were within normal

Address for correspondence: Sangam Jha, MD. Department of Obstetrics and Gynecology, AIIMS Patna, Bihar, India
Phone: +91 9827 388001 **E-mail:** sangam.jha78@gmail.com
Submitted Date: July 12, 2020 **Accepted Date:** August 13, 2020 **Available Online Date:** December 01, 2020

limits. USG pelvis showed 17.9x12.7 cm cystic mass with internal echoes & septation (cotton ball appearance) arising from right ovary. Tumor markers CA 125, CEA, CA19−9, LDH, and HCG were within normal limits. Alpha fetoprotein was marginally raised to 21.4 ng/ml (normal range <10ng/ml). A subsequent contrast enhanced computed tomography (CECT) was performed which showed a large well defined cystic attenuating lesion measuring 21x19x20 cm arising from right adnexa with enhancement of septa on post contrast study (Fig. 1 a, b). Based on clinical and radiological findings a provisional diagnosis of malignant ovarian tumor was made and patient was planned for staging laparotomy. Significant operative findings were–minimal peritoneal fluid, 20x19 cm solid cystic mass arising from right adnexa, right fallopian tube was stretched over it, 2700 ml of serous fluid was aspirated from the mass to ease its exteriorization, uterus, left tube and ovary was normal, undersurface of liver and diaphragm were free of tumor deposits. Right salpingoophorectomy along with biopsy from left ovary and multiple peritoneal site had been performed. Pelvic lymph node dissection was omitted as CECT was not suggestive of lymph node involvement. Fertility sparing surgery had been performed as she was desirous of future reproduction. Gross specimen (Fig. 2) submitted for histopathological examination. Histology showed that tumor was mainly comprised of large columnar cells of intestinal type with apical mucin (Fig. 3 a, b). Cells were focally reactive to AFP (Fig. 3g). To further differentiate the cell type reacting to AFP, immunohistochemical staining was used. Cells were diffusely positive for CK7 (Fig. 3c), and strongly positive for CK 20 (Fig. 3d) but negative for WT1 and PLAP (Fig. 3 e, f). Final impression was invasive mucinous carcinoma grade I with FIGO stage of pT1apNx. Patient is under regular follow up and disease free 8 month post treatment.

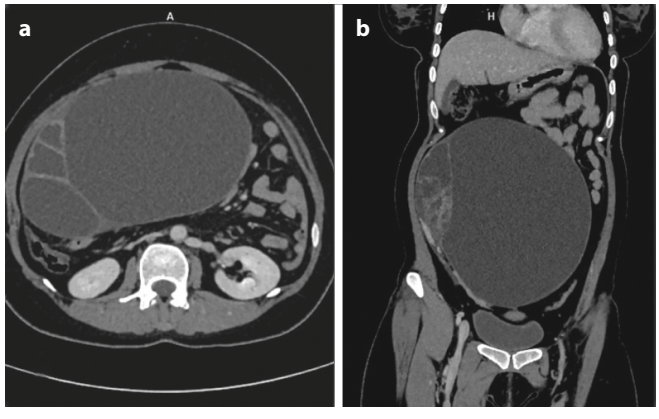

Figure 1. **(a)** Contrast enhanced axial CT image shows cystic component with thick enhancing septa in the abdomen. **(b)** Contrast enhanced coronal CT image shows a large solid cystic abdominopelvic mass.

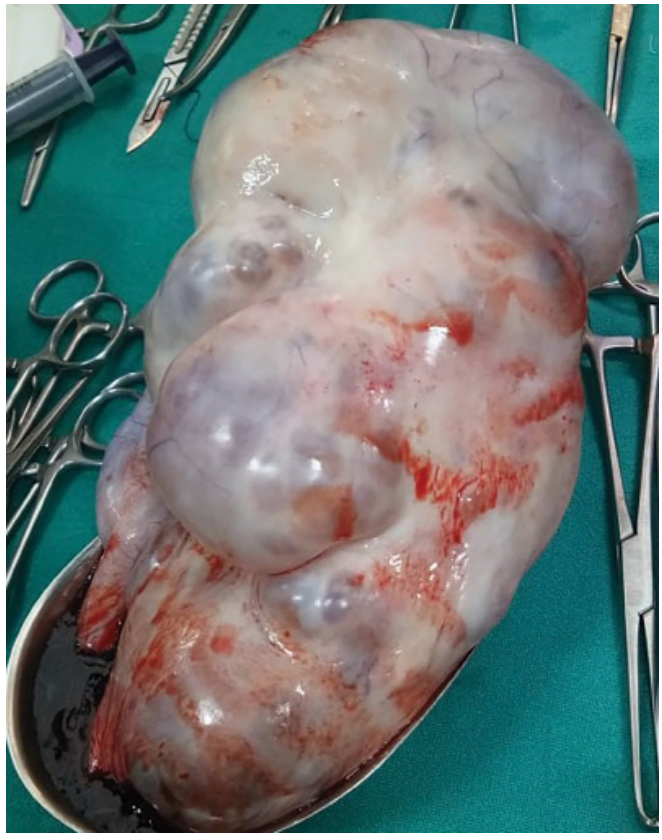

Figure 2. Gross pic of specimen shows right ovary, fallopian tube and solid-cystic mass.

Discussion

Ovarian cancer is the most common cause of death among patients with gynecological malignancy.[2] Yearly incidence of ovarian cancer in Asia is 5 to 7 cases per 100000 women.[3] More than 90% of ovarian cancer are histologically epithelial ovarian cancer and only 3−5% are of mucinous type.[4] AFP is commonly secreted by germ cell tumor and useful for detection and surveillance of the disease.

Ovarian Mass with Raised AFP-Differential Diagnoses

The presence of unilateral mass, in a young patient with raised alpha fetoprotein led to the suspicion of yolk sac tumor primarily as it is the second most common germ cell tumor after dysgerminoma, associated with production of AFP and occurring in second decade of life. But usually they present as the large solid mass which are highly malignant and rapidly spread to distant site, which were absent in the present case making the diagnosis unlikely.

Sometimes Immature teratoma can also present with raised AFP[5] but the absence of solid component containing calcification and foci of fat on imaging making this diagnosis improbable.

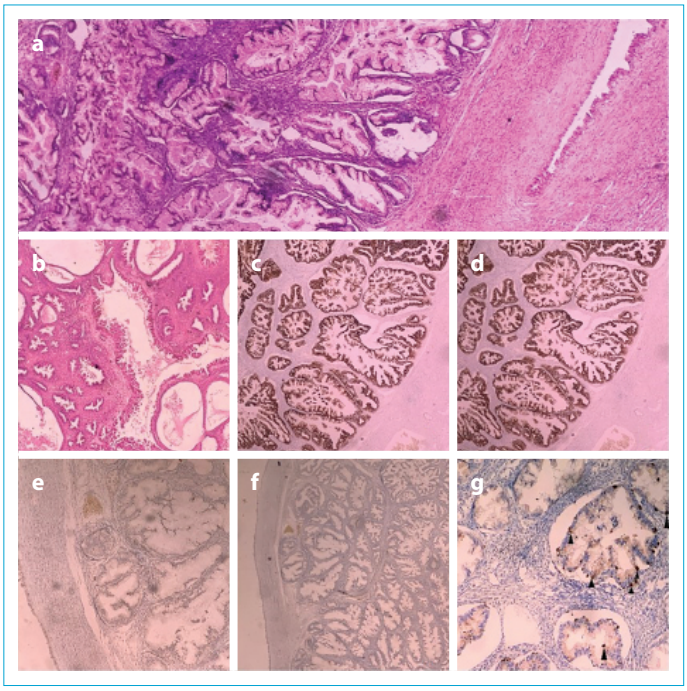

Figure 3. (a) H&E stained section from tumor tissue showing back to back arrangement of varying sized atypical glands lined by tall intestinal type epithelium having pseudo stratified, hyper chromatic, round to oval nucleus and abundant vacuolated cytoplasm rich in mucin. (200x magnification). **(b)** Many Cystically dilated glands with intraluminal mucin and stromal invasion by these glands are seen. (H&E staining, 200x). **(c)** Immunohistochemistry with cytokeratin 7 shows strong diffuse cytoplasmic positivity in the tumor cells. **(d)** Immunohistochemistry with cytokeratin 20 show similar strong diffuse cytoplasmic positivity in the tumor cells. **(e)** WT 1 showed negative immunostaining. **(f)** PLAP showed negative immunostaining. **(g)** Occasional tumor cells of the invasive mucinous glands did show reactivity for AFP IHC antibody (arrowhead).

Non germ cell tumors have also been described to secrete AFP. These include sex cord stromal cell tumor (SCST), epithelial tumor, and metastatic tumors to the ovary.

SCST is an uncommon tumor occurring in young adults presenting as large solid mass with the features of virilization and occasionally associated with elevated AFP level.[6] Clinical and radiological picture of the present case made this diagnosis also less likely.

Clinical and radiological findings excluded the metastatic tumor to the ovary.

Few epithelial ovarian carcinoma (EOC) have been reported to secrete AFP but most of them are reported in the postmenopausal women. The histological variety include clear cell carcinoma, hepatoid carcinoma, serous carcinoma , endometroid carcinoma, undifferentiated carcinoma, mixed mullerian tumors and mucinous adenocarcinoma. Among these only clear cell carcinoma has been reported in under 30 years of age.[7] Clinically it is difficult to rule out these diagnosis. Histology and immunohistochemistry is vital in differentiating these tumors.

On literature review, only three cases of mucinous epithelial ovarian carcinoma (mEOC) with elevated AFP have been reported till date.[8–10] Detailed information of these cases including the present one are briefed in Table 1. All the case reports described previously are in postmenopausal women, with tumor sizes varying from 8 to 14 cm and advanced stage disease. None of them were seen in young patient. So this is the first case of early stage, huge sized mucinous adenocarcinoma occurring in young patient with elevated AFP. AFP producing epithelial tumors can be of two types-with and without the yolk sac component. AFP secretion is ascribed to the foci of yolk cell clusters in few mucinous adenocarcinoma, but present case lacked any germ cell component and source of AFP had been the cuboidal cells. Ectopic tumor marker denote dedifferentiation by indicating autonomous activation of unrelated genes for the given tumor tissue type.

Histopathology and Immunohistochemistry

Malignant mucinous carcinoma of ovary displays characteristics gross and microscopic features. Microscopically these tumors are comprised of glands and stroma, glands are almost always intestinal type with apical mucin. Based on the presence of stromal invasion, it has been divided into two category, intraepithelial (non-invasive) carcinomas and invasive carcinoma. Intra-epithelial carcinoma exhibit marked cellular atypia in the absence of stromal invasion. Invasive carcinoma is characterized by presence of stromal invasion of >5mm. Invasive carcinoma is further subdivided into two type i) expansile (confluent) type-characterized by the presence of confluent glandular growth uninterrupted by normal ovarian parenchyma, ii) infiltrative type which is identified by the presence of small glands or individual cells in the stromal infiltration. Infiltrative carcinoma has more aggressive course compared to expansile variety.[11] The use of selected immunohistochemical markers in conjunction with the microscopic characteristics of individual mucinous tumors is valuable in accurately differentiating atypical mucinous tumors. In the present case, cells were focally reactive to AFP. To further differentiate the cell type reacting to AFP, immunohistochemical staining was performed. Cells were diffusely positive for CK7 and strongly positive for CK 20 but were negative for WT1 and PLAP. Almost 80–100% ovarian mucinous carcinoma stains positive for CK7 whereas CK20 positivity is seen in 40–83% of mucinous adenocarcinoma of ovary.[12] CK20 is not expressed in endometrial adenocarcinomas. WT1 is of significance in differentiating primary serous adenocarcinoma with meta-

Table1. Summary of AFP secreting mucinous adenocarcinoma

Author	Age	Size	FIGO staging	AFP level (ng/dl)	Histology and immunohistochemical staining	Outcome
Konishi et al.[9] 1988	53	14	NA	1120	Mucinous adenoca with solid nest Solid nest CEA(+), AFP(+)	Dead 7 month
Nomura et al.[10] 1992	62	14	NA	4130	Mucinous adenoca with solid proliferating area. Proliferating solid area stained AFP(+)	Dead (posttransfusion)
Arai et al.[11] 1999	71	8	Ic	55.6	Mucinous adenoca with YST, YST stained AFP(+), CEA(+), CA125(-)	Dead 6 month
Present case	24	21	Ia	21.4	Mucinous adenoca, AFP(+),CK7(+) CK20(+), WT(-), PLAP(-)	Alive

NA: Not available; CEA: Carcinoembryogenic antigen; AFP: Alpha fetoprotein; YST: Yolk sac tumor; CA 125: Cancer antigen; CK: Cytokeratin; WT: Wilms' tumor gene; PLAP: Placental like alkaline phosphatase; Stage Ic: tumor limited to one or both ovaries or fallopian tube with either capsule rupture or involvement of outer surface of the ovary or positive washing; Stage Ia: tumor is limited to one ovary with capsule intact.

static endometrial adenocarcinoma and also in typing primary surface epithelial tumor. WT1 is strongly positive in case of serous adenocarcinoma but negative in mucinous carcinoma and metastatic endometrial carcinomas. PLAP is highly sensitive immunohistological marker for malignant germ cell tumor thus helps in differentiating epithelial tumor from germ cell tumor. In the current case diagnosis of mucinous adenocarcinoma without germ cell component was based on these findings.

Keel et al.[13] used primary monolayer culture system of procrine granulosa cell from small ovarian follicle to illustrate the miotogenic effect of AFP. In this study they found that AFP, in dose dependent manner, act synergistically with epidermal growth factor, insulin like growth factor 1 and platelet derived growth factor to induce proliferation of granulosa cells. This study has demonstrated that AFP can function to modulate growth factor mediated cell proliferation during the development of neoplasia.

Management

Optimum debulking surgery is the mainstay of treatment for the mucinous epithelial ovarian carcinoma (mEOC). Different histotypes have different biological behavior and different pattern of sensitivity to chemotherapy. This is particularly true for mEOC. Hess et al.[14] in 2004 reported that woman with advanced stage mucinous adenocarcinoma had worse prognosis compared to other histological type and response rate to platinum based chemotherapy was 26% in stage III/IV mEOC compared to 63% in matched control non mEOC group. Though it has been recognized that platinum based chemotherapy is less efficacious in mEOC than the other EOCs, we lack the proven alternatives. As stated in American Cancer National Comprehensive Cancer Network (NCCN) guidelines 2016, and also highlighted in,[15] adjuvant therapy is not required in mEOC stage I, as survival rate is excellent, while adjuvant therapy should be given for stage III–IV (3–6 cycles of carboplatin/paclitaxel or 5-flourouracile/ oxaliplatin or capecitabine/ oxaliplatin). Due to rarity of AFP secreting mEOC, appropriate chemotherapy regimen is not described. As the patient was young and desirous of fertility, fertility sparing surgery was performed. Tumor marker is helpful in monitoring the disease. AFP fell to normal level following surgery. As she had stage Ia disease, adjuvant chemotherapy was not required and was kept on regular follow up.

Conclusion

This case report highlights the atypical features of mucinous ovarian tumors that is young age, alpha fetoprotein secretion and without any yolk sac component on histology. As the diagnosis would affect the management, it is important for both gynecologist and pathologist to be aware of such cases and its clinicohistological distinction from germ cell tumor. Thus this study along with highlighting the atypical presentation of mucinous adenocarcinoma emphasizes the need for early diagnosis and intervention

in young women presenting with adnexal masses with clinico-radiological suspicious of malignancy.

Disclosures

Ethics Committee Approval: No ethical approval required and the study was performed in accordance with the principles of the declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: There is no conflict of interest.

Financial Support: Authors declare that they have not received funds for this study.

Authorship Contributions: Concept – S.J.; Design – S.J., J.S.; Supervision – S.J.; Materials – S.J., J.S.; Data collection &/or processing – S.J., J.S., S.B.; Analysis and/or interpretation – S.J., S.B.; Literature search – S.J., J.S.; Writing – S.J.; Critical review – S.J., J.S., S.B.

References

1. Chen LM, Berek JS. Ovarian and fallopian tubes. In: Haskell CM, editor. Cancer treatment. 5th ed. Philadelphia, PA: WB Saunders; 2000. p. 55
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10–29. [CrossRef]
3. Takiar R. Status of Ovarian Cancer in India (2012-14). EC Gynaecology 8.5 2019:358–64.
4. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: a review. Cancer Biol Med 2017;14:9–32. [CrossRef]
5. Yamaoka T, Togashi K, Koyama T, Fujiwara T, Higuchi T, Iwasa Y, et al. Immature teratoma of the ovary: correlation of MR imaging and pathologic findings. Eur Radiol 2003;13:313–9. [CrossRef]
6. Jashnani KD, Hegde CV, Munot SP. Alfa-fetoprotein secreting ovarian sex cord-stromal tumor. Indian J Pathol Microbiol 2013;56:54–6. [CrossRef]
7. Bahri I, Boudawara T, Khabir A, Beyrouti MI, Frikha M, Jlidi R. Clear cell carcinoma of the ovary simulating a yolk sac tumor. [Article in French]. Ann Pathol 2003;23:165-8.
8. Konishi I, Fujii S, Kataoka N, Noda Y, Okamura H, Yamabe H, et al. Ovarian mucinous cystadenocarcinoma producing alpha-fetoprotein. Int J Gynecol Pathol 1988;7:182–9. [CrossRef]
9. Nomura K, Miyasaka Y, Murae M, Terashima Y, Aizawa S. Ovarian mucinous cystadenocarcinoma producing alpha-fetoprotein. A case report. Acta Pathol Jpn 1992;42:372–5. [CrossRef]
10. Arai T, Kitayama Y, Koda K. Ovarian mucinous cystadenocarcinoma with yolk sac tumor in a 71-year-old woman. Int J Gynecol Pathol 1999;18:277–80. [CrossRef]
11. Rodríguez IM, Prat J. Mucinous tumors of the ovary: a clinicopathologic analysis of 75 borderline tumors (of intestinal type) and carcinomas. Am J Surg Pathol 2002;26:139–52. [CrossRef]
12. Wauters CC, Smedts F, Gerrits LG, Bosman FT, Ramaekers FC. Keratins 7 and 20 as diagnostic markers of carcinomas metastatic to the ovary. Hum Pathol 1995;26:852–5. [CrossRef]
13. Keel BA, Eddy KB, Cho S, May JV. Synergistic action of purified alpha-fetoprotein and growth factors on the proliferation of porcine granulosa cells in monolayer culture. Endocrinology 1991;129:217–25. [CrossRef]
14. Hess V, A'Hern R, Nasiri N, King DM, Blake PR, Barton DP, et al. Mucinous epithelial ovarian cancer: a separate entity requiring specific treatment. J Clin Oncol 2004;22:1040–4. [CrossRef]
15. Crane EK, Brown J. Early stage mucinous ovarian cancer: A review. Gynecol Oncol 2018;149:598–604. [CrossRef]