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Case Report

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Borderline Mucinous Ovarian Tumour Producing hCG as a Paraneoplastic Tumour Marker

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ABSTRACT

This case highlights an intriguing example of paraneoplastic syndrome associated with borderline ovarian tumors (BOTs), specifically in relation to elevated β-hCG levels. In typical presentations, β-hCG is primarily linked to pregnancy, but in this instance, its elevation in a non-pregnant patient underscores the complex interplay between tumors and hormonal production.

The negative pelvic ultrasound and β-hCG heterophilic antibody testing effectively ruled out common causes of elevated β-hCG, such as pregnancy and phantom hCG. This strengthens the hypothesis that the raised β-hCG levels were indeed related to the tumor itself rather than external factors.

The correlation between the decline in β-hCG and the patient's response to treatment further supports the notion of a paraneoplastic phenomenon. This illustrates how certain tumors can produce hormones or hormone-like substances, leading to clinical symptoms or laboratory abnormalities that may precede the diagnosis of the primary malignancy. In this case, the production of β-hCG by the tumor exemplifies the diverse mechanisms through which neoplasms can influence the body, emphasizing the importance of a thorough investigation in patients with unusual laboratory findings.

Overall, this case adds to the understanding of the clinical implications of paraneoplastic syndromes and highlights the need for clinicians to consider these syndromes when faced with atypical lab results in the context of malignancy.

Introduction

Borderline ovarian tumors (BOTs) are a group of neoplasms with significant potential of malignancy and are histologically defined as nuclear atypia with epithelial proliferation without any recognizable destructive stromal invasion. About 8 % of cancer patients have paraneoplastic syndromes which may appear even prior to the symptoms of the primary tumour itself. Primarily, during pregnancy β-hCG is produced by the placental syncytiotrophoblast cells. However, small amounts can also be found in the testis, liver, lung, colon, and stomach. Henceforth, malignancies in these organs can cause rise in its levels. Here, we have described a case of the patient with borderline mucinous ovarian carcinoma found to have raised beta hCG inconsistent with pregnancy. Intrauterine pregnancy, ectopic pregnancy or phantom hCG were ruled out by normal pelvic ultrasound and negative β-hCG heterophilic antibody testing. Elevated β-hCG in our case was found to be consistent with paraneoplastic syndrome which was reflected in a decline in βhCG correlating with a response to treatment.

Case

A 32 years old P3L3A1 presented with complaints of localized pain in lower abdomen and abdominal mass, increasing in size for 6 months affecting her day to day household work. On abdominal examination, a mass was palpated in suprapubic area of around 20-22 weeks size with smooth surface, firm to cystic in consistency and restricted mobility. However, its lower limit could not be reached. On per vaginal examination, cervix was posterior with uterus felt anteverted, normal size mobile and a cystic mass of approximately 15x 15 cm was palpated obliterating all the fornices. Mass was felt to be cystic with smooth surface, non-tender, restricted mobility and a groove between ovary and

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uterus was felt suggesting its adenexal origin. Patient was further evaluated and routine blood investigations were sent. Ultrasound showed large thin walled unilocular anechoic cystic lesion in midline pelvis measuring ***9.5×10 cm*** with multiple internal echoes. On MRI, a well-defined abdominopelvic cystic mass of 10.7 X 15.5 X 14.7 cm size with irregular wall thickening and multiple papillary projection from the wall without fatty/calcific or hemorrhagic component within suggesting ORADS-4 (Figure 1). Endo-myometrial junction well maintained. ET=6mm. Her tumour markers CA125, AFP, LDH, CEA, CA 19.9 were normal. Only her beta hCG was raised which was 1987mIU/ml.

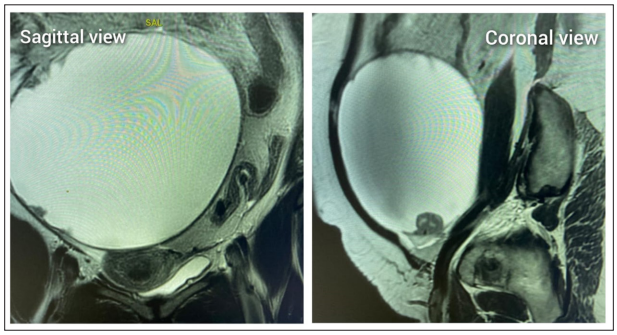

Figure 1: MRI Image (Sagittal and Coronal view) showing large thin walled unilocular anechoic cystic lesion with multiple internal echoes

Patient was planned for Staging laparotomy and frozen section was sent intraop which showed BORDERLINE MUCINOUS TUMOR. However, in view of young age of the patient and HPE report decision for conservative surgery was taken and Left salpingo oopherectomy and right salpingectomy was done (Figure 2). Final HPE report showed Borderline mucinous tumour with microinvasion. Her postoperative beta hCG was 0.33. The further plan of management was discussed and patient was kept on followup with 3 monthly tumour markers and 6 monthly pelvic ultrasound.

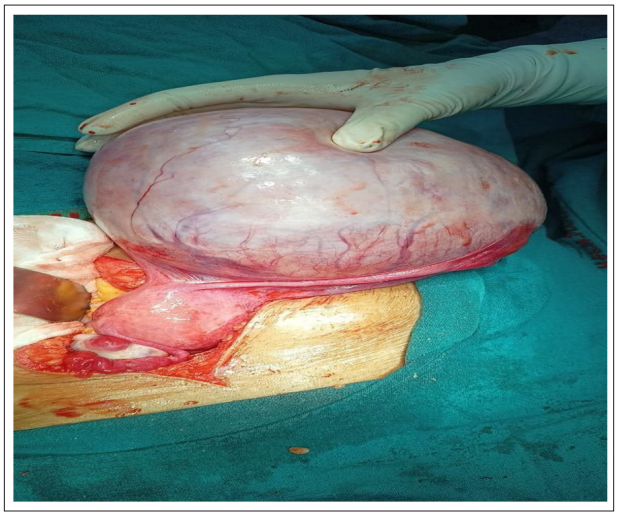

Figure 2: Intraoperative picture of ovarian tumour

Discussion

In the absence of a pregnancy, elevated beta hCG can be seen due to multiple reasons including miscarriage, extrauterine pregnancy, pituitary hCG production, gestational trophoblastic disease, and phantom disease. Other rare causes need to be evaluated after ruling out intrauterine and extrauterine pregnancy. Elevated beta hCG in the setting of an adnexal mass or gynecological tumour in the reproductive age group needs to be evaluated before initiating treatment. In our case, urine pregnancy test and ultrasound pelvis were done to rule out pregnancy. Henceforth, it was believed that the raised beta hCG was due to the patient's tumour, in congruous with a paraneoplastic syndrome. It is critical to keep a high index of suspicion for possible malignancy in young women with adnexal mass with raised beta hCG to avoid surgical spillage which might upstage the malignancy.

Three distinct forms of hCG i.e. regular hCG, hyperglycosylated hCG (hCG-H) and free beta subunit of hCG vary both in form and function. Regular hCG and hCG-H are dimers having both alpha and beta subunit. Alpha subunit of hCG is identical to the alpha subunit of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH), while the beta sub unit is unique to each form. In normal pregnancy, physiological pituitary secretion and non-invasive trophoblastic disease, regular hCG is produced [1]. Extravillous cytotrophoblastic cells produce hCG-H which also promotes invasion involved in invasive trophoblastic disease and choriocarcinoma. In malignancies (gynaecological or non-gynaecological), either the free beta subunit of hCG or its degradations product also known as beta-core fragment is raised which is thought to enhance cellular proliferation, hamper apoptosis leading to tumorigenesis in the ovarian cancers and is thought to be a poor prognostic factor [2,3].

hCG is found in small amounts in testis, lung, liver, colon and stomach. Whenever any malignancy occurs in these organs, the serum levels of beta hCG rises [4]. Most common is the gastric origin ranging from 11-17 % [5]. In the case reported here, the patient had a primary ovarian neoplasm without any metastasis with elevated beta hCG.

As per literature, there has been only two case reports published regarding paraneoplastic hCG production in mucinous ovarian adenocarcinoma and this is the first case of paraneoplastic hCG production in borderline mucinous tumour with intraepithelial carcinoma [6,7]. There has been published literature suggesting overexpression of free hCG in epithelial ovarian cancers playing vital role in tumorigenesis [8]. The study reported that overexpression of hCG was associated with increased cellular proliferation and downregulated apoptosis inducing tumor development. A study by Ind et al. 1997 done on 173 ovarian cancer patients reported 5-year survival as 65% when hCG normal but only 19% with elevated serum hCG ($p < 0.0001$).

Determining the source of elevated beta hCG is essential before starting surgery or chemotherapy. This helps ensure the patient is not pregnant and prevents delays in treatment or the unnecessary initiation of interventions for conditions like ectopic pregnancy or trophoblastic disease. In our case, we identified hCG promptly, allowing for immediate treatment, which was later confirmed by pathological findings. This highlights the importance of accurate diagnosis in directing effective care and minimizing the risk of treatment delays.

Conclusion

This case report underscores the potential significance of elevated beta hCG in patients with borderline mucinous tumors. Clinicians should always consider paraneoplastic syndrome in the differential diagnosis when faced with elevated beta hCG levels in the absence of intra- or extra-uterine pregnancy. Moreover, targeting this hormone and its receptor may pave the way for innovative cancer therapies, enhancing the efficacy and specificity of treatments by directly interacting with beta hCG or its receptor.

The author(s) declare(s) that there is no conflict of interest regarding the publication of this article.

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