Mature Cystic Teratoma with Well Differentiated Neuroendocrine Tumor: A Case Report

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Abstract

Neuroendocrine neoplasms of the ovary are rare neoplasms constituting 0.1% of all the ovarian neoplasms and less than 5% of all the neuroendocrine neoplasms. We report here such a rare case of neuroendocrine tumor in mature cystic teratoma managed in Khoula hospital, Muscat, Oman. A 41year old lady, G7P6, presented at 9+3 weeks of gestation with vaginal bleeding and pain abdomen. A diagnosis of complete miscarriage was made with an incidental finding of dermoid cyst in the right ovary on ultrasound. Three days later, she presented with features of suspected torsion and underwent emergency laparoscopic right ovarian cystectomy. Histopathological examination of the specimen revealed a mature cystic teratoma with an incidental small focus of a well differentiated neuroendocrine tumour. The patient was referred to the Oncology Centre, where she underwent laparoscopic right salpingo- oophorectomy and left ovarian cystectomy after detailed investigations and multidisciplinary team meeting. Histopathology revealed a well differentiated Dermoid cyst in the left ovary with no evidence of neuroendocrine tumor. There was no residual dermoid cyst or of neuroendocrine tumor in the right salpingo-oophorectomy specimen. The patient did not require any further adjuvant treatment. She is followed up with a 6 monthly clinical review and imaging. Neuroendocrine neoplasms of the gynaecological tract are a heterogenous group of tumours that necessitate involvement of multidisciplinary mode of management. Due to the rarity of the disease and the absence of consensus on the treatment guidelines, proper histopathological grading and referral to experienced centres play an important role in the optimal outcome.

Keywords: Neuroendocrine Neoplasms of The Ovary; Mature Cystic Teratoma; Histopathological Grading; Multidisciplinary Mode of Management.

Introduction

Neuroendocrine neoplasms (NEN) of the ovary are rare neoplasms constituting 0.1% of all the ovarian neoplasms and less than 5% of all the NENs. We report here such a rare case of neuroendocrine tumor (NET) in mature cystic teratoma managed in Khoula hospital, Muscat, Oman.

Case Report

A multiparous lady of 41 years, with previous 6 deliveries, presented with vaginal bleeding and abdominal pain at 9+3 weeks of gestation. She had a previous scan showing intrauterine pregnancy. Transvaginal scan at this presentation showed a thin endometrium, keeping in with the diagnosis of complete miscarriage. There was an incidental finding of 9 x 7 cm size dermoid cyst in the right adnexa. CA 125 was reported as 44 U/ml. CA 19.9, AFP, LDH were normal. A follow up review was planned in the gynecology clinic. However, the lady presented with persistent right sided abdominal pain after 3 days. With a clinical suspicion of ovarian torsion, emergency laparoscopy and right ovarian cystectomy was performed. Histopathological examination of the specimen

revealed a mature cystic teratoma lined by stratified squamous epithelium with underlying skin adnexa [Figure 1]. Other components including adipose tissue, cartilage, smooth muscle, respiratory epithelium, seromucinous glands and thyroid tissue were also present. Focally, there was a small area of infiltrative nests and tubules with stippled nuclei and amphophilic cytoplasm [Figure 2]. There was no mitosis identified and the cells were diffusely positive for neuroendocrine markers CD56 and synaptophysin [Figure 3] as well as focally positive for Chromogranin A. Ki67 (Cell proliferation marker) was positive in less than1% of the cells. The histological findings along with the small size of 3.2 mm, absence of mitosis, low Ki67 index and the immunostain profile was diagnostic of mature cystic teratoma with well differentiated NET, Grade1. The patient never had any symptoms of carcinoid syndrome. She was referred to the Oncology Centre for further evaluation and management by the multidisciplinary team. MRI pelvis showed normal uterus and right ovary. The left ovary was enlarged with evidence of a dermoid cyst. There were no enlarged lymph nodes or ascites. The Ga-68 DOTATOC PET/CT scan did not show any uptake in the right or left adnexa. The histopathology slides were reviewed, which showed mature cystic teratoma with focus of NET that appeared to be completely excised. The panel decided to proceed with removal of the right ovarian remnant and to discuss with the patient the feasibility of left ovarian cystectomy versus left salpingo oophorectomy. The patient decided to proceed with left ovarian cystectomy and agreed for subsequent completion surgery according to the histopathology report. A laparoscopic right salpingo-oophorectomy and left ovarian cystectomy was done. Histopathology revealed a well differentiated Dermoid cyst of 4.2 x 2.7 x 2.2 cm with in the left ovarian cystectomy specimen with no evidence of any NET on immunoprofile. There was no residual dermoid cyst or NET in the right salpingo-oophorectomy specimen. The panel decided that no further adjuvant treatment was required and a 6 monthly clinical follow up with imaging was arranged.

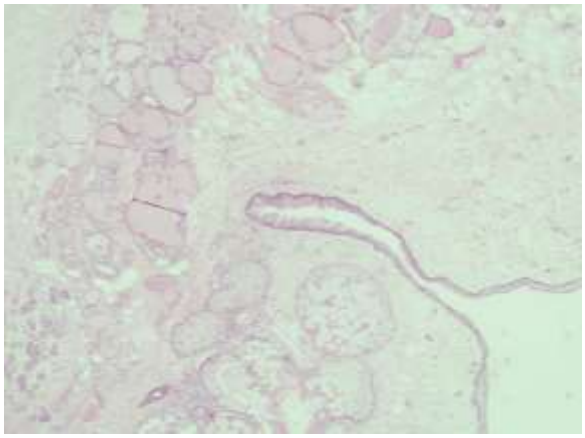

Figure 1: Mature cystic teratoma lined by stratified squamous epithelium with underlying skin adnexa. Thyroid tissue is present.

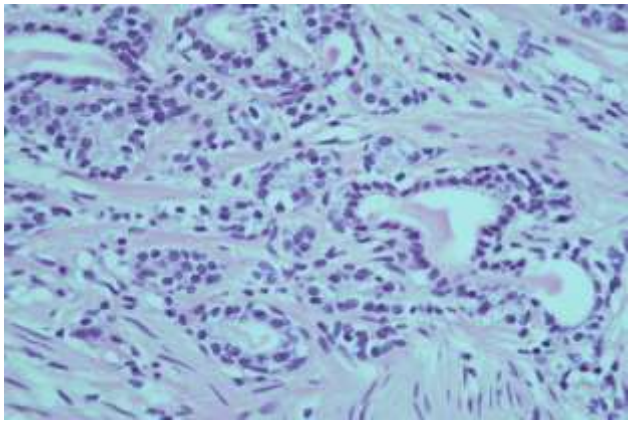

Figure 2: Focus of Neuro Endocrine Tumor.

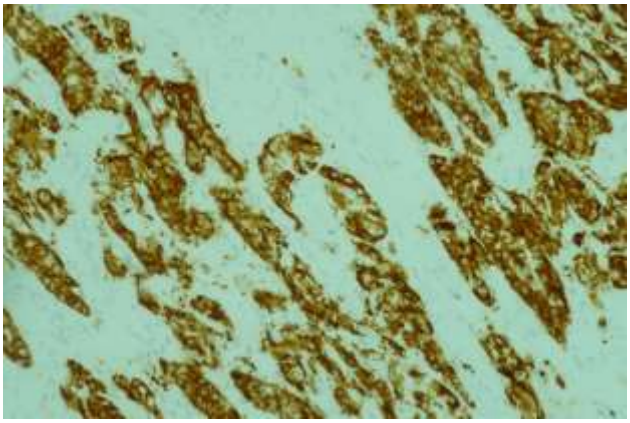

Figure 3: Diffuse positivity for Synaptophysin immunostaining.

Discussion

The reported annual incidence of NENs in the United States is 6.98/100,000, and the prevalence 170,000.[1-3] These heterogenous group of neoplasms arise from the endocrine cells derived from neuroectoderm, neural crest and the endoderm.[4,5] Gastrointestinal and respiratory tracts are the usual locations.[6] In the female reproductive system, cervix and ovaries are the most common locations, however few cases have been described in the uterine corpus. Ovarian NETs are generally uncommon and accounts for around 0.1% of all ovarian neoplasms and less than 5% of all neuroendocrine tumors.[7,8] The median age at diagnosis of primary ovarian NETs have been reported as 50.8(range 16-83 years). The reproductive age group and coincidence of miscarriage makes this case unique.[9] Metastases from the gastrointestinal tract, lungs and thymus should be always excluded, especially when ovaries are involved. Presence of implants outside the ovary, bilateral nature of the tumors, infiltrations into the vessels and the absence of teratoma elements point to the metastatic nature of the tumor. Brenner tumors, Granulosa cell tumor and Sertoli-Leydig cells tumors are the important differential diagnosis for ovarian NEN. A thorough histopathological assessment is essential in these neoplasms to distinguish from other primary ovarian neoplasms.[10] In the present case, the diagnosis was entirely histopathological. The patient never showed any clinical features of carcinoid syndrome. The dermoid cyst was bilateral, with a unilateral small focus of well differentiated NET in the right dermoid cystectomy specimen. A universal definition system for NEN was proposed by WHO in 2022, to standardize nomenclature and to resolve complexity. This classification is based on differentiation and proliferative grading and includes mitotic activity and Ki index as the diagnostic criteria.[11] There are no set treatment guidelines for NEN of the female genital tract due to the rarity of the condition. Literature provides case reports and case series only. Most of the patients with ovarian NEN are treated according to protocols used for epithelial cancers of the ovary. The treatment of choice is surgery. In women with normal contralateral ovary and Ki-67 index that does not exceed 5%, it's possible to have fertility sparing surgery.[10] However, women should be made aware that the information regarding safety of conservative treatment is very limited.[12] Pang et al. mentions that prognostic factors for ovarian NENs are age, stage of the disease, mode of treatment, and histological type.[12]

Younger age, absence of disease at other sites and unilateral small focus of well differentiated tumor in the background of a mature cystic teratoma are the favorable prognostic factors in our patient. Women with advanced stage disease are often treated with debulking surgery followed by adjuvant chemotherapy with carboplatinum and paclitaxel and radiotherapy in line with treatment standards for epithelial ovarian cancer.[12,13]

Conclusion

Neuroendocrine neoplasms of the gynecological tract are a heterogenous group of tumors that necessitate involvement of multidisciplinary mode of management. Due to the rarity of the disease and the absence of consensus on the treatment guidelines, proper histopathological grading and referral to experienced centers play an important role in the outcome.

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Conflicts of interest: The authors report no conflicts of interest.

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