Malignant transformations in Ovarian Teratomas: A report of four cases

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Abstract

Mature cystic teratoma (MCT) is a common ovarian neoplasm in young females. A secondary malignant transformation occurs rarely in cystic teratomas at an older age. These secondary malignant neoplasms most commonly are squamous cell carcinomas (SCCs). Various mechanisms are reported, but the exact aetiology is unknown. We report three cases of SCC arising in cystic teratoma and one case of papillary thyroid neoplasm as secondary transformation. The SCCs were arising from the cyst wall, while the papillary thyroid malignancy arose from the normal-looking thyroid epithelium. Histologically, all SCC cases were poorly differentiated. Poor prognostic features for secondary transformations include size more than 10cm, older age and rapid growth. Data is scarce regarding their appropriate treatment. However, surgical debulking is necessary. Platinum-based adjuvant regimens and taxanes are recommended in cases of advanced disease. In this paper we review and share our experience with this rare disorder.

Keywords: Teratoma, Squamous, Papillary, Malignant, Cystic.

Introduction

Mature Cystic Teratoma (MCT) constitutes 20-25% of all ovarian neoplasms, being the most common ovarian tumour of young women.[1] Rarely, secondary malignant transformation of this tumour occurs in women between 40-60 years of age.[2] In cases in which no ovarian malignancy is diagnosed at a younger age, it is thought that the MCT remained undiagnosed and later on presented as secondary malignancy at an older age.[3] Only 1-2% of MCTs undergo this secondary transformation. Squamous Cell Carcinoma (SCC) is the most common (75%) as a secondary malignancy, while other potential neoplasms include Adenocarcinomas, Sarcomas, Basal Cell Carcinomas, Melanomas and rarely Thyroid Neoplasms.[4] We report here four cases of such malignant transformations; three of which were squamous cell, while one was papillary thyroid cancer.

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Case Report

Case-1: A 55-year-old lady presented in May 2010 with two-month history of lower abdominal distention and pain. On clinical examination, a mass was palpable in the lower abdomen occupying the hypogastrium and right iliac region. An ultra-sonogram followed by computed tomography (CT) scanning revealed a mass with a possible origin from the right adnexa. Presumptive diagnosis of an ovarian malignancy was made. Preoperative CA-125, beta human chorionic gonadotropin (B-hCG) and alpha fetoprotein (AFP) were within normal range. She underwent right salpingo-oophorectomy and gross examination revealed an enlarged irregularly surfaced, cystic ovary with an intact capsule. Cut surface showed cheesy material and hairs tuft while the wall of the cyst showed bone and teeth formation. Histo-pathological examination revealed poorly differentiated, p63 positive SCC in a teratomatous ovarian mass. After treatment with two cycles of cisplatin-based chemotherapy, the patient refused further treatment and was in remission when last seen in June 2013.

Case-2: A50-year-old lady presented in January 2013 with one-year history of abdominal pain. Clinical examination revealed a right-sided lower abdominal mass. Imaging, including a sonogram and CT scan, confirmed it to be of ovarian origin. Tumour markers, including CA-125, B-hCG AFP, and Thyroid function tests were within normal range. She underwent total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO). On gross examination there was a complex, cystic 78mm right ovarian mass adherent to the posterior abdominal wall. Histopathological examination revealed cystic walls lined by pseudo-stratified ciliated columnar epithelium. Sub-epithelial stroma showed a tumour arranged in papillary architecture lined by cells showing nuclear grooving, overlapping and clearing. Occasional pseudo-inclusions were also noted. Surrounding the tumour cells, there was normal thyroid parenchyma and a diagnosis of papillary thyroid carcinoma arising in an ovarian teratoma was made. She was offered carboplatin, etoposide, bleomycin (CEB) chemotherapy as she had significant comorbidities and was not a candidate for cisplatin-based regimen of bleomycin, etoposide, and cisplatin. Her disease was in remission when she was seen in clinic in September 2013.

Case 3: A 66-year-old woman presented in October 2012 with six-month history of rapid abdominal distention, pain and constipation. Clinical examination was significant for a palpable huge lower abdominal mass. CT scan confirmed the clinical suspicion of mass of ovarian origin. Pre-operative tumour markers, including CA-125 and germ cell tumour markers, were within normal range. She underwent TAH and BSO. Gross examination of pathological specimen revealed a 30x30cm ovarian mass with intact capsule (Stage I-A). Histopathology of mass showed poorly differentiated SCC in an ovarian teratoma which was p63 positive. Post-operative CT scan was normal. Since she had stage I-A disease, she was kept on observation and was disease-free when last seen in October 2013.

Case 4: A 50-year-old woman presented in November 2012 with 3-month history of abdominal pain, distention and dyspeptic symptoms. Clinical examination showed gross ascites without any palpable mass. Her pre-operative imaging revealed ascites, mesenteric stranding and bilateral tubo-ovarian masses. B-hCG and AFP were within normal range thoughCA-125 was slightly high (74 iu/ml against institutional normal of 21). She was subjected to BSO with TAH. Grossly, she had ruptured ovarian capsule with multiple cysts and involvement of fallopian tubes. Ascitic fluid, as well as omental biopsies, were positive for metastatic deposits. On histopathology, the cysts were lined by stratified squamous epithelium with skin adnexa and hair shafts. Squamous epithelium showed dysplastic changes, giving rise to malignant neoplasm composed of tumour cells showing marked pleomorphism, hyperchromatic nuclei, prominent nucleoli and abundant eosinophilic cytoplasm. The tumour was positive for p63, CK-5 and CK-6 and negative for WT-1. A diagnosis of poorly differentiated SCC in cystic ovarian teratoma was made. Her disease was categorised as stage III-A. After surgery, she was treated with four cycles of bleomycin, etoposide and cisplatin (BEP) chemotherapy which was over in April 2013. Post-treatment imaging showed regression of all disease sites with no measurable disease. Patient was in remission when last seen in October 2013.

Discussion

Secondary malignant transformation in MCTs is quite rare and literature is scarce regarding their proper treatment. These malignant transformations are commonly reported in post-menopausal women, but there are some anecdotal reports that these can also occur at a younger age in the 30s.[5] MCT includes tissues originating from all the three germ cell layers (ectoderm, mesoderm and endoderm), each of which has the potential to undergo

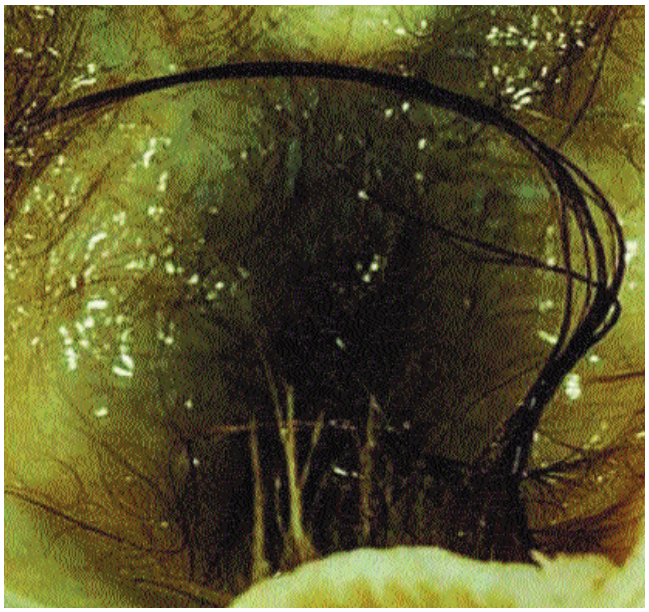

Figure-1: Cystic teratoma showing growth of hair from the cyst wall.

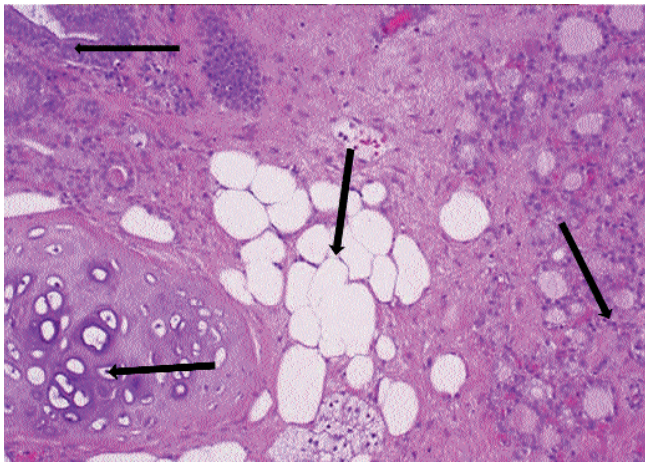

Figure-2: Microscopic image: Cystic teratoma showing adipose tissue (central arrow), cartilage formation (left lower arrow), intestinal epithelium (top left arrow) and thyroid tissue (right arrow).

malignant transformation (Figure-1 and 2). Most common malignancy arising as a secondary tumour is SCC (75%) followed by adenocarcinoma (7%) and sarcomas (7%).[4] Rarely Basal Cell Carcinomas (BCCs), melanomas and even thyroid neoplasms have been reported. As secondary malignancies occurring in MCT are rare, therefore, metastasis from the nearby structures should be excluded like cervical cancer.[6] Our case series is unique in that it also included a case with papillary thyroid neoplasm.

Histologically in our case series all three cases of SCC were

poorly differentiated compared to other literature reports which have shown well to moderately differentiated SCCs. In a study, the dominant histological grade was well to moderately differentiated SCC.[7] Respiratory and epidermal origins for squamous cell neoplasms have been suggested. Some SCCs have originated from respiratory epithelia and histologically may resemble carcinomas of the bronchus. In our case, the SCC was arising from the lining of the cyst wall while the papillary carcinoma was arising from the differentiated thyroid epithelium. The spread of a SCC from a cystic teratoma is principally by direct extension to pelvic structures. Ultra-sonogram has shown a specificity of 80-90% for the diagnosis of MCT, but malignant transformation is usually diagnosed only at histopathology.[8]

Risk factors for malignant neoplasm in MCT include age more than 45 years (mean: 50 years vs. 33 years for benign teratomas), tumour diameter >10cm and rapid growth.[9] Deletion 4 has been shown of some relevance in malignant transformations, but data is very limited and premature. A lot of work is going on in molecular genetics of these malignant transformations, but these are yet not available in Pakistan. Poor prognostic factors after malignant transformation include a higher International Federation of Gynaecology and Obstetrics (FIGO) stage, cyst wall invasion, disseminated disease, tumour rupture, ascites and tumour type other than SCC.[9]

Survival for stage I have been reported to reach a little over 70%, while it is less than 30% for stage II onwards.[10] No clear guidelines exist in the literature regarding proper treatment of stage II or more advanced disease, but surgical cytoreduction followed by platinum or taxane-based chemotherapy is recommended.[10]

Conclusion

Secondary malignant transformation in MCTs is a rare phenomenon with little information about treatment and prognosis. Primary malignancies at other places such as cervix, lung and thyroid should be ruled out before making a diagnosis of secondary transformation.

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