Predicting Malignancy in Dermoid Cyst: A Case Report and Literature Review

Abstract
Benign mature cystic teratoma is being seen through all ages of a women’s age. It has varied presentations. Malignant transformation in teratoma though rare is usually seen in postmenopausal women. Malignant transformation is usually detected postoperatively in the histopathology. We are reporting a case in which a postmenopausal lady was operated and squamous cell carcinoma in a dermoid cyst was detected postoperatively. Certain signs on the imaging can help to diagnose this in the preoperative period so that the proper counselling and treatment can be given to the patient.

Keywords: Dermoid; Mature cystic teratoma; Malignant transformation; Squamous cell carcinoma

Introduction
Benign Mature Cystic Teratomas (MCT) of ovary are usually termed dermoid cyst as they have abundance of skin elements [1]. It consists of well differentiated derivatives of the three germ layers. Approximately 2% of the cases of malignant transformation is reported which is rare incidence [2]. Of all the malignant transformations, 75- 85% are squamous cell carcinomas [3]. Other transformations are adenocarcinoma (7%), sarcomas (7%), melanomas (<1%), basal cell carcinomas (<1%), anaplastic carcinoma (<1%) [4].

Malignant Transformation (MT) is rare and difficult to diagnose preoperatively. Mostly postoperative diagnosis is made after histopathological examination. Preoperative diagnosis is difficult due to rarity of this malignant transformation and its similarity to MCT [5]. Postoperative histopathological examination makes the final diagnosis of malignancy. The case is being reported for some retrospective insight of features that could help suspect malignant transformation.

Case Report
A 57-year-old unmarried postmenopausal woman reported with vague lower abdominal pain. She carried with herself an ultrasound showing a left adnexal complex cyst (10 cm × 6 cm with a 2.8 cm solid nodule) with no free fluid, suggestive of dermoid cyst. CA125 was 32 IU units and CEA was 2.3 units. There was no history of loss of weight, appetite, or abdominal distension. No family history of ovarian and breast carcinoma.

Clinically vitals were normal with no supraclavicular or inguinal lymphadenopathy. On abdominal examination no ascites or mass was detected. Being unmarried, patient refused per speculum and bimanual examinations. Preoperative workup was within normal limits. While awaiting MRI patient required intervention as a semi-emergency condition for acute abdominal pain and suspected torsion.

Intra-operatively, left ovary was replaced by a cyst measuring 8 cm × 6.5 cm in diameter. The cyst had smooth surface, no papillary excrescences and had undergone torsion by one and a half turns. Peritoneal fluid for cytology was taken. Cyst was adherent to the sigmoid colon. There were no other deposits in the abdominal and pelvic cavity. While separating the cyst, it got accidentally ruptured. It was filled with hair and pultaceous material and a focal solid area measuring 3 cm in maximum diameter was identified, but frozen section could not be arranged due to technical reasons. Total abdominal hysterectomy with bilateral salpingo-oophrectomy was done and multiple omental biopsies were undertaken. Peritoneal fluid was free of malignant cells.

Histopathology confirmed stratified squamous epithelium lining the cyst wall showing full thickness dysplasia and keratinous material in the lumen (Figures 1 and 2). Biopsy from solid area showed presence of an invasive tumour with moderately anaplastic squamous cells arranged in islands, nests, sheets, and evidence of intracellular keratinisation. Intervening stroma show moderate lymphomono-nuclear cell infiltrate. Post-operative

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RMI index is CA125 value × ultrasound findings × menopausal status.

On ultrasound, presence of any feature out of the following is given a score of 1- multilocular cyst, solid areas, bilateral lesions, ascites, intra-abdominal metastases. Premenopausal status is given a score of 1 and postmenopausal a score of 3. RMI values greater than 200 were associated with higher risk of malignancy and these patients needed referral to a gynecologic oncologist.

In a typical suspected case of dermoid on USG, CA-125 may not be even routinely being ordered thus making RMI index irrelevant. Our patient was a clinically suspect case of dermoid cyst preoperatively and intraoperatively but with RMI score of 96 (CA125 × U × M, that is, 32 × 1 × 3), she would command to be treated as malignancy. MT should be suspected in mature cystic teratoma if these criteria are to be met -age>50 years, tumours >10 cm, high levels of squamous-cell-carcinoma antigen and cancer antigen CA125 [2].

CA-125 levels are also measured before chemotherapy or for follow up to subsequent five years [11]. Significance of tumor markers like Serum cancer antigen 125 (CA125), Serum SCC when more than 1.5 ng/ml, Serum carbohydrate antigen 19-9 (CA19-9) and Carcinoembryonic antigen (CEA) levels have been comprehended for positivity and adverse outcomes [12].

Colour Doppler sonography also helps to differentiate between the malignant and benign ovarian masses. Fleischer et al. showed the positive and negative predictive value of colour Doppler sonography as 98% and 83% respectively. Presence of torsion and metabolic activity in benign masses may give false results [13].

Suspecting malignancy preoperatively would help decide the mode of surgery between laparotomy vs. laparoscopic removal. Open surgery is believed to decrease or prevent chances of spillage and peritoneal dissemination of the tumour and up staging of tumour, as laparoscopic removal of adherent MCTs would frequently cause spillage. Intraoperative spillage of the tumour contents is also significant as it leads to expedient postoperative progression [14].

Another study attempted to co-relate HPV infection with MT in MCT of the ovary as HPV is implicated as a causative factor in squamous cell carcinoma of the cervix. By demonstrating HPV capsid and HPV16/18 E6 proteins in the SCC-MCT tissue, cervix, and adjacent reproductive organ tissues including pelvic and para-aortic lymph nodes in 95% cases, the possibility of ascending route of infection of viral particles from the cervix, endometrium, fallopian tubes and then to the ovaries has been suggested suggesting a causal factor relationship between HPV and MT of ovarian MCT into SCC [15].

In his series Black et al. [16], highlighted 100% detection of malignant components within MCTs in frozen sections. This is a significant finding as this helps prevent a second laparotomy [16]. On MRI, MCT reveals high signal intensities and presence of fat fluid levels, whereas on the other hand MT shows solid or necrotic contrast enhancing areas which may extend transmurally. Also in MT ovarian tumour will be adherent to surrounding structures.

Discussion

MCT is commonest ovarian tumour in females of reproductive age and accounts for 10% to 25% of ovarian neoplasms [1]. Malignancy was found in association with MCT in 0.5% to 2% of cases [2]. However, in a retrospective study conducted by Bal et al. [6] the incidence of MT in MCT was much higher, being 6.67%.

SCC of the ovary is usually found in postmenopausal women with mean age of 55.2 years as compared 37.5 years in benign dermoid tumour [7]. Our patient was 57-year-old post-menopausal woman. Mostly patients present with lower abdominal pain, abdominal mass, and abdominal distension as in our case [7]. Mean tumour size of MCT- 64 mm and of MT is 92 mm-152 mm [7] which is like our ultrasound report which may have macroscopically been undersized because of rupture and extrusion of material. They can present with features suggestive of torsion as in our patient [8].

Due to its rarity pre-operative diagnosis of SCC in MCT is difficult to make [9]. The RMI (risk of malignancy index) based on CA125 value, menopausal status and ultrasound parameters helps categorize patients with ovarian mass into various risk groups with a sensitivity of 85.4% and specificity of 96.9% [10].
Radiological features of malignancy consist of solid component, soft tissue protuberance (rokitansky protuberance or dermoid nipple), capsular penetration or direct invasion of adjacent structures (reflecting supervening SCC).

Fat-suppression techniques in magnetic resonance imaging arising from fat present in the dermoid cyst have also been suggested to help in the preoperatively suspecting MT [17]. Prognosis of MCT depend on associated prognostic factors like stage of tumour, tumour metastasis, cyst wall invasion, ascites, spontaneous or accidental rupture, adhesions, type of malignant transformation other than squamous carcinoma and usually poor in advanced stages.

Treatment is multimodal therapy including surgery followed chemotherapy or radiotherapy. Chemotherapy is usually cisplatin-based combination (BEP) therapy. The benefits of radiotherapy and chemotherapy remain doubtful. However, it can be considered in women at high risk of relapse, postoperative radical pelvic radiotherapy [3]. Compared to primary epithelial ovarian tumours chemotherapy is less effective in MCT. Many studies have advocated simultaneous chemoradiation as it is used for cervical squamous cell carcinomas, with varying results [1,8]. The secondary debulking surgery is suggested where long lasting remissions are obtained after recurrence. It is usually performed if it is a single site relapse which is completely resectable.

Conclusion
Malignant transformation in mature cystic teratoma is a rare entity. But it is associated poor prognosis. In advanced ages or large sized ovarian masses complete preoperative work up with all tumour markers and imaging techniques should be availed to substantiate suspicion. Open surgery should be preferred with prior intimation for frozen section and consent for complete surgery. Post-operative follows up and treatment depending on stage should be offered as per institute policy. In view of rarity consensus on ideal treatment is lacking.

References