Malignant transformation of mature cystic teratoma: An uncommon encounter

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SUMMARY

Malignant transformation in a mature cystic teratoma (MT-MCT) of the ovary is a rare condition which poses a great challenge to diagnose it preoperatively and hence, a hindrance to proper treatment planning. In most cases, definitive diagnosis is achieved postoperatively via histological examination of the specimen. Here we report a case of MT-MCT to squamous cell carcinoma (SCC) with intra-abdominal keratin flake seeding.

INTRODUCTION

The most frequent ovarian germ cell tumours are mature cystic teratoma (MCTs), comprising 10 to 25% of all ovarian neoplasms. MT-MCT of the ovary is rare and has been reported to occur in 0.17 to 2% of MCT,[1] predominantly in women in their fifties.[2] SCC is the most common transformation.[3]

CASE PRESENTATION

A 53-year-old, parity 5, post-menopausal housewife presented with abdominal distension and constitutional symptoms with altered bowel habits for 2 weeks. She denied pain, bowel or urinary symptoms. Family history was insignificant and there was no past surgical history. Physical examination revealed a 20-week size non-tender, immobile pelvic mass. Breast, speculum and digital bimanual vaginal examinations were unremarkable.

An abdominal ultrasound assessment revealed a complex multiseptated solid-cystic ovarian mass of 14 × 10 × 14 cm with minimal ascites. The uterus and cervix were normal in appearance and size with endometrial thickness of 24 mm. Both kidneys showed no hydronephrosis.

A contrast-enhanced computed tomography of thorax, abdomen and pelvis (CTTAP) showed a multiloculated cystic enhancing mass in the pelvis measuring 12.5 × 10.7 × 15.8 cm, with septations and calcification within the mass with thickened wall in some areas (Figure 1B). Normal ovaries were not seen while the normal uterus was anteverted and displaced to the right side due to the mass. The urinary bladder and rectum were also displaced to the right with a clear fat plane.

Diffuse enhancing heterogenous fat-containing soft tissue mass was seen at the anterior lower abdomen, suggestive of omental caking measuring 2 × 18 × 13 cm with enhancement of peritoneal lining (Figure 1A). Moderate ascites with enhancing peritoneal lining were noted in the lower abdomen.

There were sub-centimetre mesenteric nodes and an enhancing peritoneal nodule at the left hypochondrium measuring 1 cm. There was also prominent left renal pelvis with mildly dilated proximal and mid ureter.

The overall features were suggestive of advanced ovarian malignancy.

Patient underwent pigtail insertion for drainage of ascites and ultrasound guided omental biopsy. The peritoneal fluid cytology showed no malignant cells.

Histological examination of the omental biopsy showed granulomatous inflammation with foreign body reaction and presence of keratin materials (Ziehl-Neelsen (ZN), Periodic acid-Schiff (PAS) and Congo red stains were negative). There was no immature teratomatous element.

Her cancer antigen-125(CA125) was 377.2U/ml while serum carcinoembryogenic antigen (CEA) was 82.5 U/ml. Her alpha fetoprotein was < 1.3 ng/ml while her beta-human chorionic gonadotropin (beta-hCG) was < 2 mIU/ml. Her infective screening was negative while the erythrocyte sedimentation rate (ESR) was 86, with normal chest X-ray, liver and renal profiles.

A second repeated laparoscopic biopsy of the peritoneal nodules and omentum was done. Intraoperative findings revealed a pelvic mass with minimal ascites, omental caking, extensive peritumour adhesions resulting in inadequate visualisation of the uterus and lower pelvis. The peritoneum fluid cytology taken also showed no malignant cells.

Histological examination of the peritoneal nodules and omentum biopsies were similar to previous biopsies.

GeneXpert and mycobacterium tuberculosis polymerase chain reaction tests were not performed as all the specimens were preserved in formalin solution. Pulmonary tuberculosis was deemed unlikely after assessment and workup by a physician.

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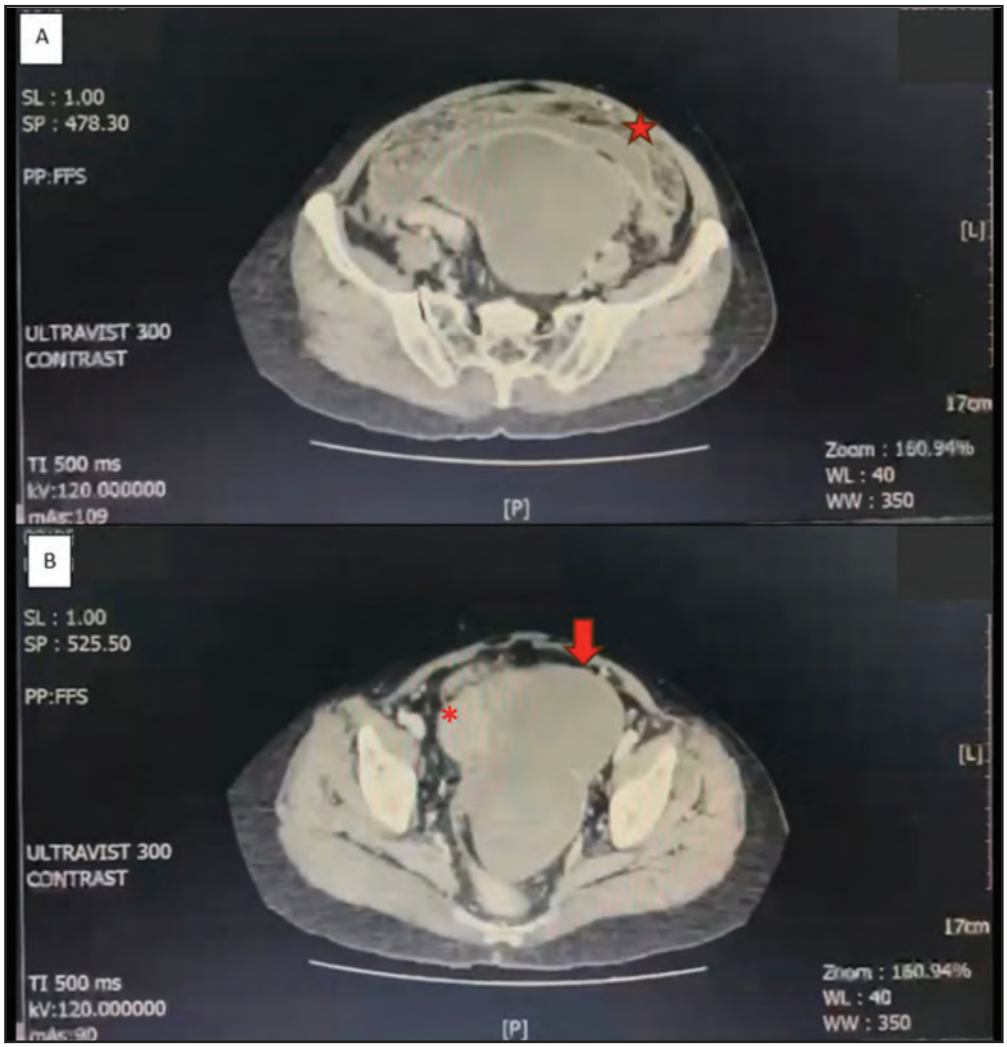

Fig. 1: A: CT of abdomen showing feature (star) suggestive of omental caking with moderate ascites and enhancing peritoneal nodules. B: CT of pelvis showing large multiloculated ovarian cystic enhancing mass (arrow) with septations and calcifications. Uterus (*) was anteverted and displaced to the right side

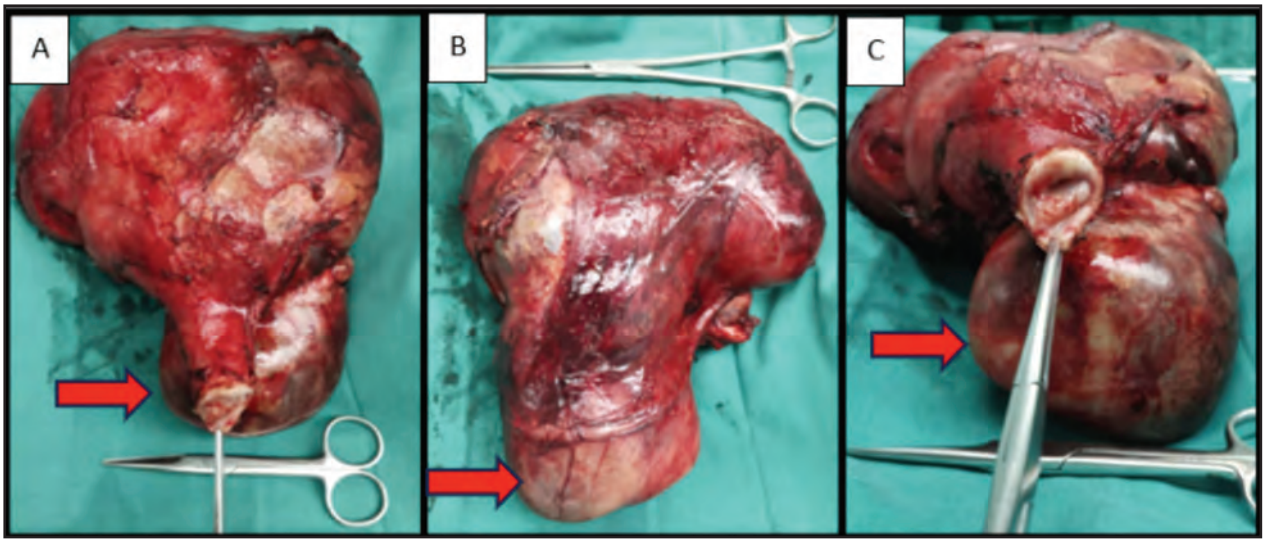

Fig. 2: A: Anterior view; B: Posterior view; C: Inferior view of the specimen. Red arrow: left ovarian mass

Patient then underwent primary debulking surgery (midline supraumbilical staging laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic, para-aortic lymph node dissection, appendicectomy and omentectomy). Intraoperatively, the left ovarian tumour was adhered to the pararectal space and posteriorly to the pouch of Douglas. Right ovary appeared unaffected. Multiple nodules exceeding 2 cm were noted on the omentum and few smaller nodules approximately 2 to 3 mm on the peritoneal surface.

Pathological assessment showed that the left ovarian tumour (18 × 17 × 10 cm) was intact, multiloculated, with thickened cyst wall, patchy plaque at the inner surface and Rokitansky protuberans (2 × 1.5 × 0.8 cm). Histologic examination showed ovarian stroma containing all three embryonic layers, ectoderm (skin and appendages, nerve and glial tissue), mesoderm (fat, cartilage, bone and muscle) and endoderm (glandular and ciliated epithelium). The left ovary showed non-keratinising SCC arising from mature cystic teratoma, in which the malignant cells showed moderate to marked pleomorphic vesicular nuclei with prominent nucleoli. Occasional intercellular bridges were noted with absence of keratin pearls. Capsule was intact. Foci of lymphovascular invasion were seen at the right fallopian tube and left ovary. Sections from cervix, omentum and nodules from various sites (small bowel surface, small bowel mesenteric, pararectal, peritoneum) showed foreign body granulomatous inflammation. Omentum, peritoneal and small bowel serosal nodules showed malignant cells with foreign body granuloma. Malignant cells were also seen at appendiceal serosa. Malignant cells were highlighted by CK 5/6, p63 (diffuse), GATA 3 and CAM5.2 (patchy). Right ovary was normal. Bilateral pelvic and para-aortic lymph nodes were negative for malignancy.

Patient was staged as stage 3C (FIGO staging 2014) in view of presence of tumour exceeding 2 cm on the omentum as well as involvement of the bowel serosa surface.

Patient was treated with adjuvant chemotherapy 8 weeks post-surgery consisting of carboplatin and paclitaxel for six cycles in which she completed without issues.

Her tumour markers showed a decline in values compared to the values prior to surgery. Her CEA reduced to 15.3 U/mL from 82.5 U/ml, while her CA125 showed a reduction from 377 U/ml to 32 U/ml. However, CTTAP done 2 weeks post adjuvant chemotherapy showed multiple enlarged peritoneal nodules, mesenteric and paracaval lymph nodes. There were also multiple liver lesions suggestive of liver metastasis indicating disease progression.

Patient was then planned for second line chemotherapy.

DISCUSSION

According to Malaysia National Cancer Registry Report 2012 to 2016, ovarian cancer ranked tenth in Malaysia and fourth in females. MCT (also known as dermoid cyst) is the most common benign ovarian tumour, composed exclusively of mature tissues from two or three germ layers (endoderm, mesoderm and/or ectoderm) with MT-MCT has been reported to occur in 0.17 to 2% of MCT.

Preoperative suspicion of malignant transformation is difficult, thus posing a great challenge and dilemma regarding ways of surgical resection and need of adjuvant therapy. It is commonly accepted that potential malignancies should be suspected in all ovarian tumours, until proven otherwise. There were no specific clinical symptoms, but abdominal pain was the most frequent complaint and abdominal swelling placed second.[4] In most cases, definitive diagnosis is achieved postoperatively via histological examination. Risk factors for malignancy in a teratoma include age, tumour size,[2] imaging characteristics and serum tumour marker levels, which concur with the current case. It has been reported that malignant transformation occurs in a relatively older population, predominantly in fifties.[2] According to Kikkawa et al.,[8] tumours more than 9.9 cm in diameter or grow rapidly may be associated with malignant transformation. Presence of a solid component with contrast enhancement, evidence of adherence to surrounding structures, necrosis and haemorrhage are important radiographic parameters to suspect malignant transformation in mature teratoma.[5] Chiang et al.[6] found out that in cases of MCT with malignant transformation to SCC measuring greater than 15 cm in diameter were more aggressive than those measuring less than 15 cm.

The importance of serum tumour markers in the diagnosis of ovarian malignancies has been acknowledged in earlier studies. CEA is the best screening marker, followed by SCC antigen for SCC arising from MCT.[2] A combination of age above 40 years and serum SCC antigen levels above 2.5 ng/ml were 77% sensitive and 96% specific for malignant squamous transformation in a teratoma, therefore is considered a suitable marker for diagnosis.[7] Kikkawa et al.[2] recommend that serum SCC and CEA levels be tested in patients aged 45 years or older and the tumour is more than 99 mm in greatest dimension. However, testing of SCC antigen is not readily available in our setting.

This patient had laparoscopic biopsies done to establish the diagnosis as advanced ovarian malignancy was suspected and initially planned for neo-adjuvant chemotherapy. In view of the presence of multiple miliary-like intra-abdominal nodules seen during the laparoscope and histological report of granulomatous inflammation, extrapulmonary tuberculosis was suspected. However, histological examinations showed foreign body reactions (presence of giant cells engulfing keratin flakes) and presence of keratin materials expressing CKAE1/AE3, negative ZN and PAS stains. These findings further support the differential diagnosis of teratoma with squamous components. Combined with the radiological findings, patient's age and tumour size, advanced ovarian tumour became the most suspected diagnosis. However, the biopsy results were not diagnostic. The patient then underwent primary debulking surgery to stage, obtain definite histopathological diagnosis and to further guide her adjuvant treatment.

In a case series, 83% of MT-MCT had obvious large solid

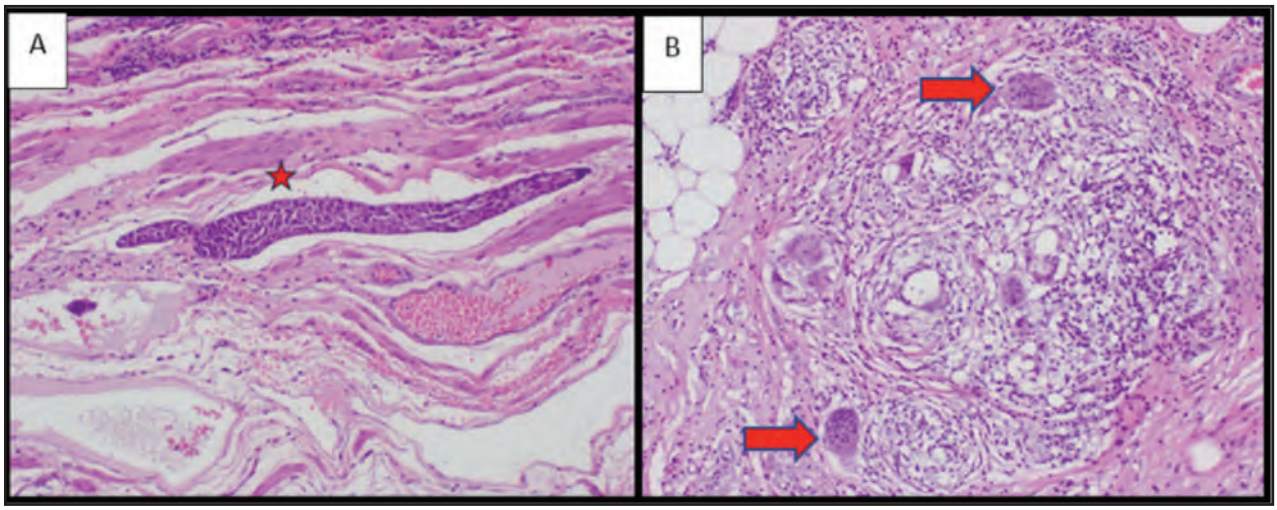

Fig. 3: A: Vascular infiltration by malignant squamous cells (star); B: Foreign body granulomas associated with squames are seen at omentum (arrow)

components in gross pathological examination.[5] However, in this patient, the tumour has no obvious solid component. The malignant component of MCT sometimes exists in only a part of the lesion, causing difficulty in its identification grossly, thus emphasising the importance of careful examination of the MCT specimens.

The occurrence of the keratin flake seeding could be due to focal tearing, localised rupture or penetration of capsule by the tumour, leading to the deposition of keratin debris and/or formation of keratinous nodules in the peritoneal cavity or adjacent organs, and may be easily mistaken for tuberculosis.[9] The diagnosis of MC-MCT is mainly based on the morphology[10] and immunohistochemical (IHC) stains are supportive rather than diagnostic.

Chen et al.[4] revealed that tumour stage, patient age, tumour size, positive preoperative CA 125 and SCC antigens level and optimal debulking affects survival, with tumour stage and optimal debulking being the most significant. They reported that the 5-year survival rates for stages I, II, III and IV were 75.7, 33.8, 20.6 and 0%, respectively. The other factors that may affect prognosis are capsular invasion, ascites, rupture or spillage, adhesions and vascular space invasion.[1] Interestingly, it was reported that patients with increased SCC antigen and CA125 markers had a worse 5-year survival rate, while a high CA125 level is a more reliable prognostic marker than SCC antigen.[4]

Due to the scarcity of literature, adjuvant treatment has yet to be defined, not to mention neoadjuvant therapy. Chen et al.[4] revealed that for stage II-IV cases, instead of radiotherapy, the advanced cases may be better treated with optimal debulking with cisplatin-based chemotherapy.

Pelvic and para-aortic lymph nodes (retroperitoneal lymph nodes) assessment for ovarian carcinoma is recommended and is an important component of staging and debulking, according to the National Comprehensive Cancer Network (NCCN guideline V1.2024). In this patient, pre-operative diagnosis of MT-MCT was not established and there were enlarged pelvic nodes on the CT scan. Hence a full staging for ovarian cancer was performed and no neoadjuvant chemotherapy was able to be given to her.

In general, follow-up for ovarian malignancy is life-long with the interval between follow-ups gradually increasing in correlation with the duration from treatment completion. NCCN recommends every 2 to 3 months with CTTAP every 3 to 4 months in the first year. Unfortunately, in this patient, a follow-up CT scan done 2 weeks after completion of treatment showed disease progression.

CONCLUSION

Malignant transformations of mature teratoma are rare, with squamous cell carcinoma being the most common malignant transformation. With the knowledge of the risk factors, preoperative risk assessments and imaging correlation, teratomas in older women, especially if it is large-sized, should raise clinical suspicion. They should be carefully and adequately sampled to attain accurate diagnosis to decide on appropriate management of the patients.

CONFLICT OF INTEREST

None

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