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CASE REPORT

Mitotically active cellular fibroma of ovary with Meig's syndrome - a rare case report

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ABSTRACT

Fibromas were thought to be benign tumours earlier, however recently described cellular fibromas are considered to be of low malignant potential. The behaviour of these tumours is correlated with mitotic activity and degree of anaplasia. We are reporting a case of mitotically active cellular fibroma with Meigs syndrome for its rarity. A 32 years female patient presented with complaints of irregular menstrual bleeding for 1 year and mass per abdomen for 2 weeks. CEMRI revealed well defined heterogeneous abdomino-pelvic solid lesion measuring 19.2 x 14.1x 9.2cm^3 from Left ovary with mild ascites with bilateral pleural effusion. Histopathology revealed mitotically active cellular fibroma which can be managed conservatively but long-term follow-up is needed due to its rare recurrence. Diagnosis of Meigs syndrome must be kept in mind in cases with solid ovarian mass, ascites and pleural effusion.

Keywords: Mitotically active cellular fibroma, Meigs syndrome, fibroma.

Fibromas are the most common sclerosing stromal cell tumours of ovary which occur primarily in postmenopausal women. They can also occur in the younger age group. Fibromas were taught to be benign tumours earlier. However recently described cellular fibromas are considered to be of low malignant potential. The behaviour of these tumours is correlated with mitotic activity and degree of anaplasia. Meig's syndrome is a triad of ovarian fibromas, ascites, and hydrothorax. This is an uncommon presentation and usually resolves after surgical excision of the fibroma. Ascites with a solid ovarian tumour in young patients put the surgeon in a dilemma while opting for a conservative procedure. Hence we are reporting a case of MACF (mitotically active cellular fibroma) with Meig's syndrome.

Case

32 years old P2L2, a female patient came with the complaints of irregular menstrual bleeding since 1 year and a mass in the abdomen for 2 weeks. No history of any malignancies in the family. On general examination, lower abdomen was distended, sterilization scar was present. A large mass of 20×15cm^2 occupying left and right iliac, supra pubic and right lumbar regions which is non-tender, mobile, firm to hard in consistency was noted. Lower border was well defined. No obvious free fluid was noted. No hepato-splenomegaly. Bimanual examination revealed a healthy cervix, mobile anteverted uterus with exact size not made out. A large 15×20cm^2, firm to hard, mobile mass felt high up in anterior and left fornices. Investigations revealed CA125-8.9 U/ml, CEA-2.71ng/ml, and LDH-218U/liter. USG abdomen and pelvis showed a well-defined heteroechoic lesion 16.8×11.4×17.3 cm^3 with cystic degeneration probably arising from left adnexa. No significant vascularity was noted within the tumour. The uterus and right ovary were normal. Free fluid was noted in the pelvis. Impression was left broad ligament fibroid/ left ovarian fibroma with mild ascites. The risk malignant index was 17.8. CEMRI pelvis revealed a large well defined heterogeneous abdomino-pelvic lesion predominantly solid

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with few necrotic foci measuring 19.2×14.1×9.2cm^3 probably arising from left ovary. Post-contrast showed enhancement with few non-enhancing areas. Right ovary and uterus were normal. Mild ascites with bilateral pleural effusion were noted. There was no evidence of pelvic lymphadenopathy or omental nodules or caking. The final Impression was left ovarian fibroma, ascites with mild pleural effusion suggestive of Meig's syndrome.

Exploratory laparotomy was performed. Intraoperatively 18×12cm^2 left ovarian solid tumour was noted. Uterus, right fallopian tube, and right ovary were normal. Free fluid of 200 ml noted in abdomen. Left salpingoovariotomy was done and sent for a frozen section which revealed fibroma with unknown malignant potential. We did not proceed with total abdominal hysterectomy (TAH) given the young age and inconclusive histopathology. Omental biopsy was taken. Ascetic fluid was sent for cytology to rule out malignant cells. Supervision of abdominal organs, diaphragm and peritoneum did not reveal any malignant deposits. Histopathology revealed left ovarian mitotically cellular fibroma with mildly enlarged nuclei and mitotic figures (4/10).

Discussion

Fibromas are classified into fibromas, cellular fibromas (CF), mitotically active cellular fibromas (MACF) and fibro sarcomas according to the number of mitosis and nuclear atypia. Malignant fibrosarcomas are characterized by higher mitotic activity and moderate to severe nuclear atypia but cellular fibromas are characterized by < 4 mitotic figures under 10x high powers which are benign. Mitotically active cellular fibromas are considered when histopathology shows ≥4 mitotic figures in 10 HPF with mild or no nuclear atypia. Gynaecologists and pathologists should be able to differentiate between MACF, CF and fibro sarcoma to prevent overdiagnosis and treatment.

Fibromas account for 4% of ovarian tumours, of which cellular fibromas are 10%. Cellular fibromas are unilateral most of the time. Meig's syndrome occurs only in 1% of fibromas. Ascites and hydrothorax are believed to be a result of increased capillary permeability secondary to vascular endothelial growth factor production.11% of cellular fibromas and 13% of MACF were found to have extra ovarian spread at the time of surgery. However, these patients had a benign course during follow-up[1]. Ovarian fibromas are associated with Gorlin syndrome and nevoid basal cell carcinoma syndrome which inherit a predisposition to multisystem abnormalities [2].

WHO classification in 2003 titled ovarian fibromatous tumour with markedly increased cellularity and mitotic activity of ≥4 per 10 HPFs and moderate to severe cytological atypia as fibro sarcoma but tumours with no cytological atypia were not categorized. Clinical courses of both entities remain quite different. In 2006, Irving et al[3] studied 70 cases of ovarian fibromas and defined MACF for the first time. In 2014 WHO classification of tumours of the female genital system acknowledged a separate entity of CF which exhibit high mitotic activity but no diffuse moderate to severe cytological atypia as MACF.

MACF is identified with dense cellular proliferation with intersecting bundles of spindle cells with mitotic activity in histopathology. Sometimes fibroma of usual type, verocay-like, storiform pattern, intracytoplasmic hyaline globules and foci of luteinized cells can be seen along with MASF. Minor sex cord elements and microscopic nests of granulosa cells are present in fewer than 10% of tumours and should not lead to an erroneous diagnosis of a fibromatous adult granulosa cell tumour [4]. Our patient had ovarian mass comprising of intersecting fascicles of spindles with plump nuclei alternating with hypocellular edematous areas. Focal areas show compact hypercellular regions with mildly enlarged nuclei and 4/10 mitotic figures hence concluded as MACF. Irving et al [3] noted mitotic count of between 4 and 9MFs/10 HPF in 34 cases (85%), and between 10 and 19 MFs/10 HPFs in 6 cases (15%).

Focal staining with calretinin is often seen in the immunohistochemical examination. Inhibin is a marker of sex cord-stromal tumours which is often negative or weekly positive in fibromas. Yıldırım et al [5] demonstrated ER, PR, calretinin, inhibin-alfa, WT-1, h-caldesmon and CD10 positivity but pan-cytokeratin, EMA, CD34, desmin, and S-100 were negative, CD56 and actin were focal weakly positive. Proliferative index by DNA flow cytometry and Ki-67 labeling index helps in differentiating cellular fibroma from fibrosarcoma. KAKU et al [6] demonstrated positivity for Ki-67 in 50% of tumour cells in the areas with large numbers of mitotic figures however they diagnosed MACF as nuclear atypia in this component were not severe. We did not do immune histochemistry due to lack of facility.

Our patient presented with menstrual irregularity with mass per abdomen. Intraoperatively she had a freely mobile large tumour with ascites. Ovarian surface adhesions, extra ovarian adhesions and implants similar to ovarian carcinoma have been reported in literature [3]. Monteiro SB and associates[7] reported a case of MACF with ascites in the Pediatric age group. Kulkarni R et al [8] reported a case of

MACF presenting with lower limb swelling due to deep vein thrombosis. Irving et al [3]reported 40 cases of MACF in which the Mean age of presentation is 41 years. Patients commonly present with abdominal pain, mass per abdomen, menstrual irregularities, urinary frequency or incidentally in ultrasound or laparotomy. Ahlem B et al[9] reported a case of mitotically active fibrothecoma in association with sclerous peritonitis who presented to hospital with acute abdominal pain.

Our patient underwent exploratory laparotomy and left salpingo-oophorectomy given her young age and inconclusive frozen section report. Absence of adhesions, intact capsule and absence of difficulty in surgery, favoured benign condition. The patient was informed about the need for second surgery if histopathology reveals malignancy. Kim et al [10] reported 3 cases of M ACF among which 1 underwent TAH with BSO and 2 patients underwent unilateral salpingo-oophorectomy. In the largest case series of MACF [3], TAH with BSO/ unilateral salpingo-oophorectomy performed in 14, unilateral salpingo-oophorectomy in 12 patients. 3 patients had bilateral salpingo oophorectomy and 6 patients underwent conservative excision of the ovarian tumour. Conservative treatment in young patients preserves ovarian function and fertility. Our patient was followed up for a period of 9 months with no evidence of recurrence. Clinical follow-up information of 18 patients among 40 cases of MACF for mean of 4.75 years did not show any evidence of disease or tumour recurrence [3]. Matsuda et al [11] reported a case of rapid growth of MACF where tumor size increased from 6 cm to 10 cm in one year. Recurrence of MACF of the ovary after 5 years of surgery has been reported in literature [12]. Though surgical excision seems to be a curative for MACF, further investigation with large cohorts necessary to establish the nature and clinical outcome of tumor. Long term follow up may be required in view of occasional recurrence of tumor.

Conclusion

This case highlights that, in spite of the high probability of malignancy in cases of solid ovarian mass, ascites with pleural effusion, a differential diagnosis of Meig's syndrome must be kept in mind. Careful histopathological diagnosis prevents misdiagnosis of mitotically active cellular fibromas as malignant fibro sarcomas. Fibromas with increased cellularity and mitotic activity in the absence diffuse moderate to severe dysplasia can be managed conservatively but long-term follow-up is needed in view of rare recurrence.

Conflict of interest: None. **Disclaimer:** Nil.

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