Original Research Paper

Volume - 11 | Issue - 05 | May - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Obstetrics and Gynecology

UNDIFFERENTIATED ENDOMETRIAL SARCOMA: THERAPEUTIC CHALLENGES DESPITE GOOD SURGICAL RESECTION

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ABSTRACT Undifferentiated endometrial sarcoma is a rare uterine malignancy of mesodermal origin. Only a few cases have been reported in literature. Herein, we describe a 56-year old woman who presented with post-menopausal bleeding of a short duration. Endometrial curettings were suggestive of undifferentiated sarcoma. Computed tomography showed an enlarged uterus with well-defined mass in the endometrial cavity extending down to the cervix. A total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy and omental biopsies were taken. Histological examination revealed a tumour with a permeative growth pattern composed of uniformly high grade round tumour cells with high mitotic activity. However, there was no lymphovascular space invasion. Tumour cells were strongly positive for CD10 signifying high grade endometrial stromal sarcoma (HG-ESS). Post R0 resection, patient is now receiving adjuvant chemotherapy. However, it is seen that most patients have early recurrence following even R0 resection.

KEYWORDS :

INTRODUCTION:

Uterine sarcomas are rare heterogeneous group of tumours with aggressive clinical behavior and usually with poor prognosis. Standard surgical treatment includes total abdominal hysterectomy and bilateral salpingo-oophorectomy [1]. Although pelvic and para-aortic lymphadenectomy has an established role in carcinosarcoma, classical literature denies its importance in leiomyosarcoma and undifferentiated endometrial sarcoma. Some recent studies on low number of patients with endometrial sarcoma appear to show a higher incidence of nodal involvement than was previously expected, thus suggesting a role for lymph node sampling in these group of patients also [2].

Case Report:

We describe the case of a 56-year-old female who presented with post-menopausal bleeding for past 2 months. She had a smooth menopausal transition 6 years back. She had five vaginal deliveries and was tubectomized 20 years back. Upon presentation at our hospital, she was pale. There was no obvious pelvic mass. A bimanual examination revealed a small exophytic growth through the cervical orifice and a 10 to 12 cm firm, non-tender uterine mass. An ultrasound of pelvis showed a large heterogenous echogenic lesion in the endometrial cavity (around 95*58*76 mm) causing its distension with thinning out of adjacent myometrium but no parametrial invasion. There was internal vascularity with few small areas of cystic changes. Lesion seemed to extend upto internal os. Haematoxylin-eosin stained (H&E) slides of endometrial biopsy specimen revealed a histology of round tumour cells with scattering foci and vascular architecture mixed with endometrial glands, suggesting a likely possibility of Undifferentiated Endometrial Sarcoma.

A contrast-enhanced CT of abdomen and pelvis was suggestive of a T2 heterogenous well defined mass of above mentioned dimensions, extending down to the cervical canal. However, parametrium, adnexae and vagina appeared to be free. Pelvic and para-aortic lymph nodes were not significantly enlarged. Disease seemed to be localized to uterus.

A plan for surgical staging was made. Pre-operative blood investigations were all within normal range. Chest X ray showed normal bronchovascular markings. 2D-echocardiography showed no evidence of emboli or any ventricular dysfunction. Serum CA-125 level was 55 U/ml. Intra-operative, uterus was bulky, about 10*12 cm. No growth was visible externally. Bilateral adnexae were also normal in morphology. A staging laparotomy followed by total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection and omental biopsies were obtained.

On gross examination of the uterus, a well-defined polypoidal growth of 7*7*6 cm was identified in the endometrial cavity pushing it to one side. On microscopic examination, numerous mitoses (30-35/10 hpf) were seen in the proliferative growth arising from the endometrium. Uterine serosa and parametrium were free of tumour cells. There was no lymphovascular space invasion. Bilateral tubes and ovaries were free of tumour. Both right and left pelvic and para-aortic lymph nodes were negative for tumour cells. Omentum was not involved. On immunocytochemistry, tumour cells were positive for CD10 but negative for smooth muscle actin and calretinin. There was ER and PR focal positivity. Thus, possibility of high grade endometrial stromal sarcoma, FIGO Stage IB was considered. Post R0 surgical resection, she is now receiving 6 cycles of adjuvant chemotherapy with paclitaxel and carboplatin and is clinically doing well.

DISCUSSION:

The World Health Organization defined undifferentiated uterine sarcoma as a rare tumour arising in the endometrium or myometrium, with no resemblance to proliferative phase endometrium and having a high grade cytological dysplasia [3]. It constitutes less than 1% of uterine malignancies. The mean age at diagnosis is around 60 years [3]. With an aggressive clinical progression, majority of patients succumb to death within three to five years [4]. Typical presentation includes post-menopausal bleeding as was evident in index case also. Approximately 65-70% patients present with an advanced stage disease, detected during surgery [5].

Non-low grade endometrial stromal sarcoma is a new terminology for the classically ever-known undifferentiated uterine sarcoma. Based on nuclear pleomorphism, they are now divided into 2 groups: Undifferentiated Endometrial Sarcoma with nuclear Pleomorphism (UES-P) and Undifferentiated Endometrial Sarcoma with nuclear Uniformity (UES-U). Index case has UES-P, being poorer in prognosis. CD10 remains the most sensitive marker till date and was positive in index case too [6]. High grade ESS typically harbours t(10;17)(q22;p13) resulting in YWHAE-FAM22 genetic fusion [7]. Cyclin D1 has been proposed to be a sensitive diagnostic immunomarker for the said mutation [8]. Due to financial constraints, however, we regret getting cyclin D1 immucytochemistry in the index case.

These tumours are notoriously known to have local and distant recurrences with a high mortality within the first 2 years of primary

surgery [6]. Prognostic factors negatively associated with survival include patients' age, tumour size, pathological status of resection margins, nodal metastasis, omission of lymphadenectomy, etc. Overall prognosis remains poor as majority of these patients usually present with recurrent disease later on during or post adjuvant chemotherapy.

CONCLUSION:

Undifferentiated uterine stromal sarcomas have an aggressive clinical course with advanced stage at initial presentation. Despite good surgical resection, most patients rapidly develop distant metastasis. Role of pelvic and para-aortic lymphadenectomy still remains a dilemma to the gynecologic oncology fraternity. Adjuvant therapy did not show to improve patient survival. Large scale comprehensive systematic reviews and meta-analysis need to be done before laying down concrete guidelines on the management aspects of these rare tumour entities.

Ethical approval
Not applicable

Funding
No funding was received for this manuscript

Declaration of Competing Interest
The authors report no conflict of interest

Acknowledgement
None

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