Case report

Indian Journal of Obstetrics and Gynecology
Volume 4 Number 2, May - August 2016
DOI: http://dx.doi.org/10.21088/ijog.2321.1636.4216.23

Endometrial Carcinoma in the Young with Leiomyomata – Is it a Coexistence, an Episodic Occurrence or an Existence of a Phenotype?

Bhavya Adla*, Athira Narayanan, Pralhad Kushtagi*****

Abstract

Abnormal uterine bleeding is a common gynecological clinical problem. In premenopausal age uterine leiomyomata are the common cause and among the postmenopausal women the concern is endometrial carcinoma. Ovarian steroidal hormones do stimulate cell proliferation and extracellular matrix accumulation initiating or promoting growth of leiomyocyte. It is known that ovarian hormones are dependent on receptors for exerting their action. Leiomyoma grow even in patients with no increased estrogen. Whereas, endometrial carcinoma is an ovarian hormone dependent tumor with a subtype more often attributed to an unopposed estrogenic stimulation of endometrium. Reported are 4 cases in premenopausal age that were detected to have developed endometrial carcinoma in short time after the myomectomy.

Keywords: Leiomyoma; Endometrial Carcinoma; Premenopausal Women; Nulligravida; Abnormal Uterine Bleeding.

*Junior Resident, **Senior Resident, ***Professor, Department of Obstetrics-Gynecology, Kasturba Medical College, A Constituent of Manipal University, Mangaluru 575001, Karnataka.

Pralhad Kushtagi,
Professor, Department of Obstetrics-Gynecology, Kasturba Medical College, Mangaluru 575001, Karnataka.
E-mail: pralhadkushtagi@hotmail.com

Introduction

Abnormal uterine bleeding (AUB) is the commonly encountered gynecological clinical problem. In premenopausal age uterine leiomyomata are the common cause and among the postmenopausal women the most worried cause of AUB is endometrial carcinoma with median age of presentation 60 yrs.

Leiomyoma are monoclonal tumours of myometrium with chromosomal abnormality in 40% [1,2]. Myometrial cells that develop into leiomyoma have estrogen and progesterone receptors and are hypersensitive to estrogen, but also occur in women with normal estrogen state [3,4]. Whereas, endometrial carcinoma is related to unopposed estrogen stimulation of endometrium [5,6]. It is possible that the presence of leiomyoma with endometrial carcinoma could be correlated as a disease continuum.

Presented are 4 cases where endometrial carcinoma was found along with leiomyoma.

The Cases

Case 1

Nulligravida aged 38 years presented with complaints of heavy menstrual bleeding of 3 years with no other significant history. Vaginal examination suggested a posterior wall fibroid of 6 x 6 cm.

Pelvic ultrasound revealed a bulky uterus with a submucosal fibroid of 7x6 cm.She was posted for myomectomy while awaiting the histopathological report of uterine curettage.

Intraoperatively uterus was of 10 weeks' gravid size and a swelling with no defined capsule on the anterior wall likened to degenerated leiomyoma with cheesy material was removed. Histopathological examination reported well differentiated

©Red Flower Publication Pvt Ltd

endometrial carcinoma with no evidence of leiomyoma.

Later patient underwent total abdominal hysterectomy with bilateral salpingo oophorectomy and pelvic lymph node sampling.

It was a stage 1B well differentiated (Grade 1) endometrial carcinoma extending into the isthmus. She was given adjuvant pelvic radiation.

Case 2

A nulligravida with primary infertility aged 42 years reported with complaints of severe dysmenorrhea and heavy menstrual bleeding of 5 months duration. On examination uterus was 16 weeks gravid size with cervix pushed posteriorly and a mass in pouch of Douglas.

Pelvic ultrasound scan revealed multiple uterine leiomyomata with normal endometrial cavity.

Patient underwent myomectomy. Intra operatively, multiple intramural fibroids were noted in the fundus. Uterine cavity was breeched and was normal.

Postoperatively she was put on intramuscular injections of Depot Medroxy progesterone acetate, 150 mg at monthly intervals. Histopathological examination was confirmative of leiomyoma.

Four months later patient reported with complaints of vaginal discharge, profuse in amount, associated with smell. Speculoscopy showed a friable growth with ulcerated surface seen protruding out of the cervical os, bleeding on touch. The working diagnosis entertained was cervical carcinoma and tissue obtained at vaginal examination was subjected to histopathology.

Ultrasond examination suggested bulky uterus with a heterogenous mass measuring 7*4*5 cm in the lower endometrial cavity filling up endo-cervical canal (Figure 1) and had increased vascularity.

Histopathology of removed friable tissue read endometroid adenocarcinoma.

Extrafascial hysterectomy with bilateral pelvic lymph node sampling was done. Cut section showed a fungating growth measuring 10 cm obliterating the endometrial cavity and cervical canal (Figure 2).

The disease was staged IIIB, Grade 2 endometroid adenocarcinoma. Patient was postoperatively treated with chemotherapy and whole pelvis carcinoradiotherapy.

Case 3

Another nulligravida aged 30 years presented with

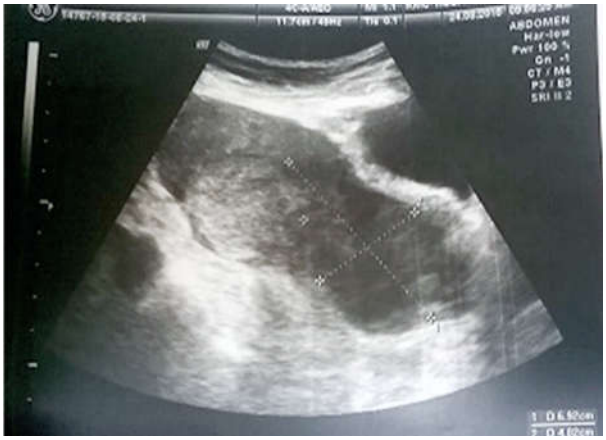

Fig. 1: Ultrasonogaraphic picture showing echogenic mass in the region of isthmus and cervix (marked with cursors)

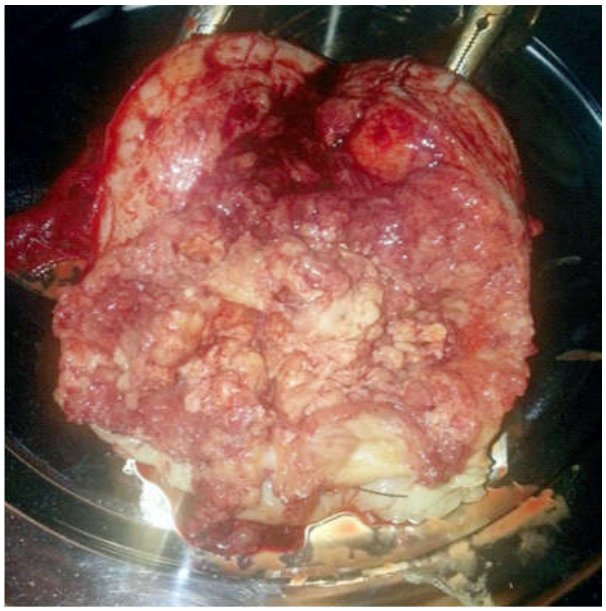

Fig. 2: Cut section of the hysterectomy specimen showing a fungating growth measuring 10 cm obliterating the endometrial cavity and cervical canal; cervix is shown by arrow

complaints of cyclical excessive menstrual blood loss of 6 months duration and abdominal pain since 2 months. Abdominal examination revealed a 16 week gravid size uterus. At vaginal examination, the uterus was felt to be of about 16 week's size and was pushed to the right side.

Ultrasound showed anteriorly pushed uterus with 2 leiomyomas, one in the anterior wall measuring 6.7 * 6 cm and the other posterior to the fundus measuring 5*4.5 cm. Endometrial thickness was 10 mm (Figure 3).

At myomectomy uterus was of 16 week gravid size with an anterior wall leiomyoma measuring 10*10 cm. Uterine cavity was opened to approach the one in posterior wall and cheesy material popped out. Histopathological diagnosis was leiomyoma and

that of the cheesy material was endometroid adenocarcinoma.

Patient was resubmitted to total abdominal hysterectomy with bilateral salpingo oophorectomy. Grossly uterus was enlarged with anterior myomectomy scar. Cut section showed fleshy polypoidal growth infiltrating myometrium and endocervical canal (Figure 4).

The disease was adenomatoid adenocarcinoma of endometrium staged as II B, well differentiated (G1). (Figure 5). Postoperatively the patient received whole pelvis radiotherapy.

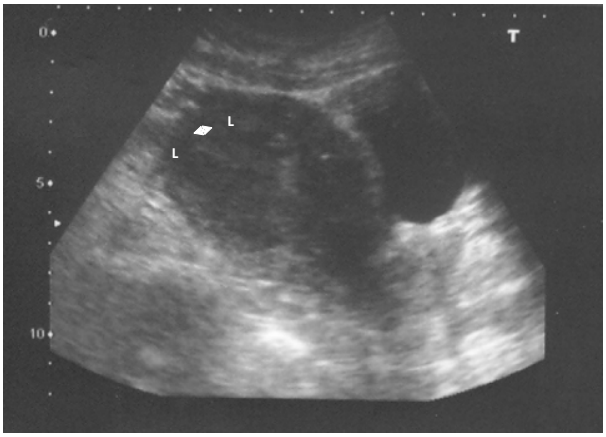

Fig. 3: Ultrasound picture showingleiomyomas(L), one in the anterior wall and the other in posterior wall near to the fundus; endometrial thickness (↔) of 10 mm

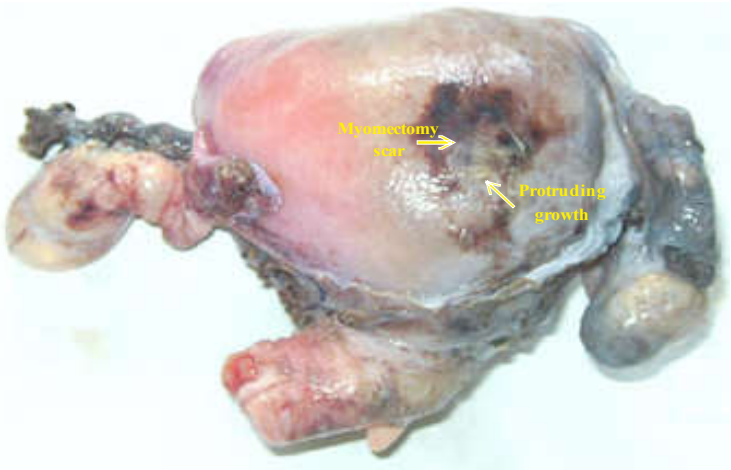

Fig. 4: Hysterectomy specimen showing enlargeduterus with anterior myomectomy scar and protruding growth

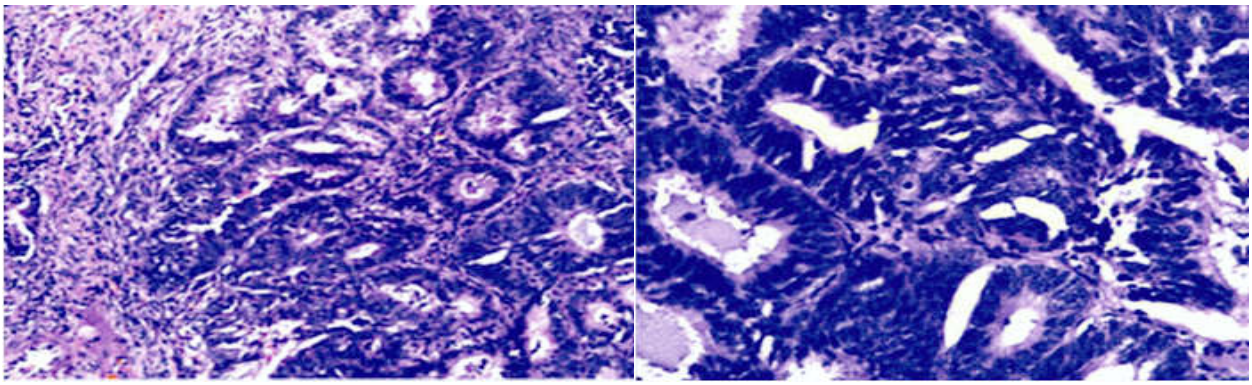

Fig. 5: Microphotograph of tumor histopathology showing well differentiated adenomatoid adeno carcinoma low (A) and high (B) power view

Case 4

Was yet another nulligravida, of 40 years being evaluated for irregular menstrual pattern of 6 months duration. Ultrasound scan showed multiple leiomyoma with bulky uterus. Endometrial biopsy revealed endometrial hyperplasia with nuclear atypia.

Discussion

In the four cases presented above, the common factors were- they were young, premenopausal, nulligravid and had AUB. All of them were clinically

diagnosed to have leiomyoma (although it was proven in three) and finally ended up with endometrial carcinoma barring the last one who was detected with precursor disease.

The questions that arise are: Were both the conditions, leiomyoma and endometrial carcinoma present simultaneously? Did leiomyoma and the hyperestrogenic state lead to the development of endometrial cancer? Should endometrial evaluation be carried out in such subset of patients?

It is known that leiomyoma could be estrogen dependent. They are seen only after menarche and if small, regress after menopause. Their presence coincides with reproductive age when ovarian steroidal hormones, especially estrogen would be continuously present. Leiomyomatous cells have exhibited estrogen and also progesterone receptors.[7] Leiomyomata grow even with physiological changing levels, and grow more if there is hyperestrogenic state [8]. Endometrial carcinoma is an estrogen dependent condition developing in the presence of situations where persistent unopposed estrogenic stimulation is present.

The age at occurrence for both the conditions is widely different. Leiomyomata occur most commonly in reproductive age group and endometrial carcinoma is the disease considered in postmenopausal age group.

In the reported series, all four cases were premenopausal. It is possible that in these cases leiomyomas were associated with increased estrogen state and that ovulatory dysfunction was responsible for nulligravidity and AUB in them. Although unrelated to presence of leiomyoma, the unopposed estrogenic action could have resulted in endometrial hyperplasia, atypia and later malignant change. Studies have noted increased prevalence of leiomyoma in patients with endometrial carcinoma (56.9%, 74 of 130 cases) [9].

In the cases 1 and 3, endometrial carcinoma seems to have been present when intervention for leiomyoma was made. Waiting till the result of uterine curettage would have averted the ignominy of re-surgery at least in the first case. It may be recalled that in patients with pelvic organ prolapse where Fothergill repair is considered, such cases are subjected to uterine curettage at the time of procedure. One of the objectives in these cases is to rule out coexisting endometrial pathology. It is not a prerequisite to have the negative report prior to surgery. In this light, it may be argued that since the possibility of endometrial cancer in a woman of 38 years was remote, the myomectomy alone was contemplated.

In case 2, at myomectomy the uterine cavity was explored and no irregularity was found. The patient was put on depot medroxy progesterone to keep the uterus quiescent for the next 2-3 menstrual cycles so that the strain on sutures of myometrial closure is minimized, as is the practice with the clinical unit. Despite progesterone usage the patient returned with a full blown endometrial cancer in 4 months' time. Uterine curettage when cavity was opened would have helped to pick up the disease, still in an earlier stage.

The fourth case in the hindsight of earlier cases was subjected to uterine curettage, waited for the report and it showed a premalignant change that could be managed without any anxious moments.

In all the three premenopausal cases leiomyomata were intramural, the uterine cavities were not distorted by their presence and endometrial thickness was not more than 10 mm.

This makes one to hypothesize that despite the distinctly different understanding of their oncogenesis, occurrence of subsequent endometrial carcinoma in patients with leiomyoma may suggest an existence of yet another phenotype in the maze of tumorigenesis of these conditions.

Conclusion

It may be deduced that in the nulligravida having leiomyoma and AUB the preoperative work-up protocol should include histopathologic evaluation of the endometrium.

Declaration

The case 3 is taken from the published report by the author (PK) [10] and the case series submitted was presented at the 59th All India Congress of Obstericians and Gyaecologists by one of us (BA).

Conflict of Interests

Authors do not have any conflict of interests to declare.

References

1. Hashimoto K, Azuma C, Kamiura S, Kimura T, Nobunaga T, Kanai T, et al. Clonal determination of uterine leiomyomas by analyzing differential inactivation of the X-chromosome-linked phosphoglycerokinase gene. GynecolObstet Invest

1995; 40: 204-8.

2. Ligon AH, Morton CC. Genetics of uterine leiomyomata. Genes Chromosomes Cancer. 2000; 28: 235-45.
3. KovácsKA, OszterA, GöczePM, KörnyeiJL, SzabóI. Comparative analysis of cyclin D1 and oestrogen receptor (á and â) levels in human leiomyoma and adjacent myometrium," Molecular Human Reproduction. 2001; 7: 1085–91.
4. Kim JJ, SeftonEC.The role of progesterone signaling in the pathogenesis of uterine leiomyoma. Molecular and Cellular Endocrinology. 2011; 358: 223–31.
5. Jabbour HN, Kelly RW, Fraser HM, Critchley HO. Endocrine regulation of menstruation. Endocr Rev. 2006; 27: 17–46.
6. MacMohan B. Risk factors for endometrial cancer. GynecolOncol. 1974: 2: 122-9.
7. Nierth-SimpsonEN, MartinMM, Chiang T, Melnik LI, Rhodes LV, Muir SE, et al.Human uterine smooth muscle and leiomyoma cells differ in their rapid 17/ J-estradiol signaling: implications for proliferation. Endocrinology. 2009; 150: 2436–45.
8. BarbarisiA, PetilloO, Di LietoA,Melone MA, Margarucci S, Cannas M, et al.17-beta estradiol elicits an autocrine leiomyoma cell proliferation: evidence for a stimulation of protein kinase-dependent pathway. Journal of Cellular Physiology. 2001; 186: 414–24.
9. Menczer J, Ben-Shem E, Golan A, Levy T.The effect of coexisting uterine myomas on clinico-pathological variables of endometrial carcinoma. Eur J GynaecolOncol. 2013; 34; 545-7.
10. Bharatnur S, Kushtagi P, Krishnamohan D. Endometrial Carcinoma in a Young Woman – '30 is Not Immune'. J ObstetGynaecol India. 2011; 61: 686-8.