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Review Article

Endometrial carcinoma in young women: management options and its review

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ABSTRACT

Endometrial carcinoma is a disease of older postmenopausal women, and is relatively uncommon in patients younger than 40 years. The incidence in young women is 2%-14%. Endometrial carcinomas in this age group may be familial, associated with Lynch syndrome, or sporadic. Patients usually have increased exposure to estrogen. Its treatment includes hysterectomy, bilateral salpingoophorectomy and pelvic lymphadenectomy and in some cases, radiation therapy. Preservation of fertility is a major challenge encountered in such cases. Before deciding on the management of any patient with abnormal bleeding a hysteroscopic examination with biopsy should be performed for all the patients, as hysteroscopy make it easy to visualize the cavity and to obtain the biopsy from the specific site. We have reviewed the literature of endometrial cancer management in young women through a case in a 35-year-old woman with previous 3 cesarean treated for abnormal uterine bleeding. We performed Hysteroscopy which showed adenocarcinoma endometrium on histopathology. Most endometrial carcinomas presenting in this young age are associated with estrogen excess. Pathologically they are usually low-grade endometrioid carcinomas with lower stage and are associated with favourable clinical outcomes. With this review the authors emphasize the need of hysteroscopic endometrial reckoning in young females with abnormal bleeding before starting any medical treatment. Also highlighting the management options in such cases where fertility preservation holds a significant challenge.

Keywords: Adenocarcinoma, Endometrial carcinoma, Management, Risk factor, Young patient

INTRODUCTION

Endometrial cancer is a disease that occurs primarily in postmenopausal women and is increasingly virulent with advancing age. It is relatively uncommon (2%-14%) in patients younger than 40 years.¹⁻⁵ Most of these patients have an identifiable source of excess estrogen, while in a small subset the pathogenesis is related to mismatch repair abnormality and Lynch syndrome. But the definite role of estrogen in the development of most endometrial cancers is established. Bokhman et al have proposed the theory of two pathogenetic types of endometrial cancers.⁶

Type 1 has 75- 85% occurrence in young females who have unopposed estrogen exposure. Pathologically it is well differentiated and has favourable prognosis. PTEN & Catenin gene are implicated in the cause. Type 2 occurs in older post-menopausal women who are thin and non estrogen dependent. It is less differentiated and has poor prognosis. HER2/neu, p53, p16 & LOH genes are implicated in pathogenesis of type 2 cancer.

Abnormal uterine bleeding with histological diagnosis of endometrial hyperplasia can be the sole finding in a case of endometrial malignancy. A spectrum of morphological and biological alterations of the endometrial glands and

stroma, ranging from an exaggerated physiologic state to carcinoma in situ can present as endometrial hyperplasia. Treatment includes hysterectomy, bilateral salpingoophorectomy and pelvic lymphadenectomy and in some cases, radiation therapy. As patients are young and eager to preserve their fertility, in such patients hormonal therapy may be an option. Preservation of fertility is a major challenge encountered in such cases.

CASE SUMMARY

We had a case of 35 year old woman who was treated for abnormal uterine bleeding from 3 years. She presented to us with complaints of intermittent spotting since 3 years and menorrhagia since 6 months. To complicate her problems she had previous 3 cesarean with uterine rupture and twin gestation in previous pregnancies. She was a known case of hypothyroidism for 8 years and also obese (85 kg, BMI 31kg/m²). On per vaginal examination we found enlarged uterus of 8-10 week size. Her ultrasound evaluation showed bulky endometrial polyp occupying most of fundus and upper body of uterus measuring 23x36x27 mm with multiple vascular pedicles arising from the fundus (Figure 1). We did a diagnostic and operative hysteroscopy for her. Hysteroscopy showed enlarged and irregular uterine cavity with a multilobed, friable & vascular polyp of 2.5cm x 3cm in size. It was seen covering the whole fundus, more towards right lateral wall. Dense adhesions were present between previous scar and the polyp. We did polypectomy and adhesiolysis for her and thick fleshy polypoidal tissue was obtained. The hysteroscopic variations seen were indicative of it being malignant (Table 1). Histopathology confirmed our suggestive diagnosis. She had focal well differentiated adenocarcinoma of Endometrioid type in background of complex endometrial hyperplasia with nuclear atypia. Back to back arrangements of glands without intervening stroma and necrosis were also present (Figure 2). Due to poor compliance for follow up and complete family, Patient underwent hysterectomy with bilateral salpingoophorectomy with bilateral pelvic lymphadenectomy. The interesting aspect of age made us review all the possible management options available.

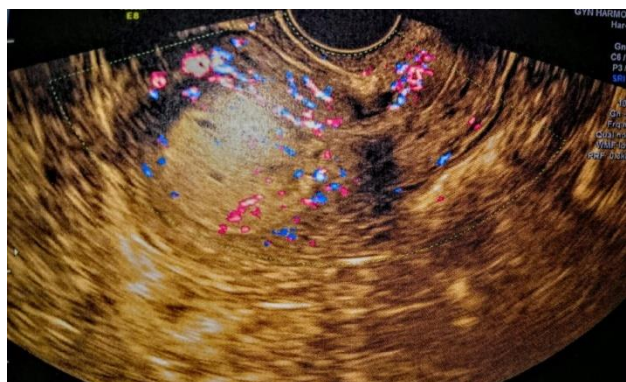


Figure 1: Ultrasound showing vascular endometrial polyp.

Table 1: Variations seen in hysteroscopy due to malignancy.

Finding in hysteroscopy suggestive of cancer
Multilobed
Vascularity
Poor visual field
Friable tissue
Bleeding

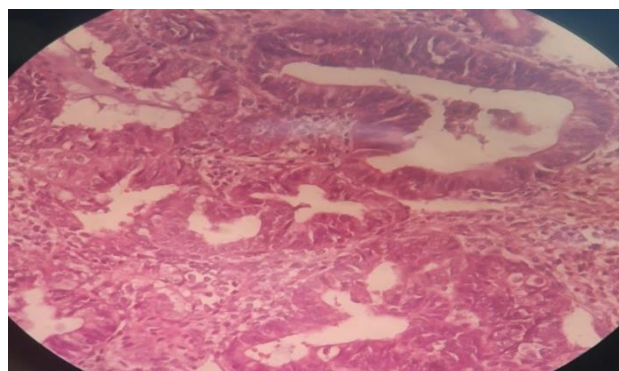


Figure 2: Histopathology showing features of adenocarcinoma endometrium.

REVIEW OF LITERATURE

With the changing trends of diseases it is important to evaluate the young patients also for carcinogenesis. Screening for endometrial cancer cannot be done due to lack of appropriate cost effective and acceptable test. About 90% of women with endometrial carcinoma have abnormal uterine bleeding or discharge as their only presenting symptom.⁷ Any women presenting with these complaints irrespective of the age should be thoroughly evaluated for risk factors and clinical findings. Obesity alone presents as a major risk factor for cancer. It increases the risk by 3 times for women who are 21 to 50 lb over weight and 10 times for women who are more than 50 lb overweight. In our case the patient was 66 lb overweight which increases her risk of having the carcinoma by more than 10 times.

Potischman et al have suggested that insulin may be a relevant factor in explaining the strong associations between body size, adiposity, and risk of endometrial cancer.⁸

Girardi J et al with a case report discussed about obesity causing worse outcome, not only due to medical co morbidities, but also with regards to delayed diagnosis and treatment and progression of disease. As the obesity epidemic worsens, this is likely to occur more commonly.⁹ Therefore it is important to recognize that the work up of abnormal uterine bleeding is thorough and complete. It should include hysteroscopy directed endometrial biopsy even in premenopausal patients as 5 % of them can have cancer.

In endometrial cancer the survival rate is relatively high due to presentation at early stages with symptoms. Definitive surgery is the classic treatment for endometrial cancer. It consists of total hysterectomy and bilateral salpingo-oophorectomy, with a pelvic and aortic lymphadenectomy if required. Chemotherapy and radiotherapy are indicated when there is a high risk of recurrence. The young women affected by endometrial cancer are often nulliparous with a past history of infertility and thus are very anxious to preserve their fertility. This constitutes a dilemma for the patients as well as their physicians.

Shibahara H et al and Shammel DP et al have proposed repeated endometrial curettages or hysteroscopic resection of cancerized polyps; however, most conservative treatments are inspired by the hormone-dependence of endometrial adenocarcinoma.^{10,11} In general, the effect of progestin's is considered to be mediated through progesterone receptor (PR), because the response rate to progestin's in PR-positive carcinoma was higher (70%) compared with PR-negative tumors (16%).^{12,13}

Emons G et al has recently shown that cancer cells express Gn-RH (Gonadotropin-Releasing Hormone) receptors, which implies that progestin's and Gn-RH agonists are the most useful medicines in the framework of conservative treatment of endometrial cancer (Stage I, Grade 1).¹⁴

Masayuki Yasuda, et al reported a case of successful pregnancy after conservative surgery for stage IA endometrial cancer in a 33-year-old woman who was diagnosed with stage IA endometrial cancer and had benefited from conservative surgery with chemotherapy.¹⁵ However, given the risk of recurrence or the development of metastasis and the need for rigorous follow up, our patient has chosen the definitive surgery.

Sodano M et al reported a case, an infertile patient with conservatively treated endometrial cancer (stage 1a grade 1) who conceived and carried a successful pregnancy after IVF treatment. The conservative treatment consisted of hysteroscopic biopsies and oral megestrol acetate 600 mg daily for 3 months. The histological evaluation after delivery showed no evidence of recurrent disease. After the delivery, the woman is healthy and free of the disease. Thus conservative treatment of stage 1a and grade 1 endometrial adenocarcinoma is an available option in young women who wish to preserve their fertility.¹⁶

According to the international literature, it appears that the most important factor for conservative treatment is selecting the "ideal patient" as given by Chiva L et al This is:¹⁷

- A well-differentiated endometrial carcinoma that does not deeply invade the myometrium.
- Absence of suspicious pelvic or pre-aortic nodes.

- Absence of synchronous ovarian tumors.
- No contraindications for medical treatment.
- The patient understands and accepts that this is not a standard treatment.
- The patient should show her desire to complete the follow-up protocol.

So, the authors suggest that before deciding on the management of any patient with abnormal bleeding a hysteroscopic examination with biopsy should be performed for all the patients. As hysteroscopy make it easy to visualize the cavity and to obtain the biopsy from the specific site, hence to diagnose and manage the patient appropriately.

CONCLUSION

Most endometrial carcinomas presenting in this young age are associated with estrogen excess. Pathologically they are usually low-grade endometrioid carcinomas with lower stage and are associated with favourable clinical outcomes. With this case the authors emphasize the need of endometrial reckoning in young females with abnormal bleeding before starting any medical treatment. So the authors suggest that before deciding on the management of any patient with abnormal bleeding a hysteroscopic examination with biopsy should be performed for all the patients. A conservative treatment for endometrial carcinoma at Stage IA with a low histological grade is possible if a complete pre-therapeutic assessment is achieved and if a rigorous follow-up during and after the treatment is pursued. But, it should be kept in mind that every delay in implementing radical treatment can increase the rate of recurrence or the development of metastasis, which will systematically worsen the prognosis. Radical treatment should be indicated as soon as the desire to carry a pregnancy to term is fulfilled.

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