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Too Much Too Soon- A Case Series on Carcinoma Endometrium in Young Women

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Abstract: *Endometrial carcinoma is predominantly a disease of postmenopausal women .Only 1-6% occur in women under 40 years. Majority of cases are associated with hype- estrogenic states. Younger patients present with clinical challenges as there is loss of fertility and surgical menopause with standard surgical treatment. Young women have an early stage distribution at diagnosis and a good prognosis. This is a retrospective study to emphasize the need for endometrial evaluation in young women presenting with abnormal uterine bleeding .A retrospective case study was carried out at our tertiary health care centre, Sri Ramachandra Medical Centre And Research Institute(2015-2017). A total of 4 cases of carcinoma endometrium less than 30 years were identified and studied. Risk factors, estrogen dependence, common presenting complaints, stage distribution at diagnosis, optimal treatment modality, fertility preservation options and prognosis were studied .Obesity and excess estrogen were Identified as predisposing risk factors . Abnormal vaginal bleeding was the common presenting complaint. Early grade of disease was noted. Hysterectomy with bilateral salphingo-oopherectomy was performed in all three cases. To conclude, in any case of abnormal uterine bleeding, neoplastic endometrial pathology should be excluded irrespective of the age.*

Keyword: *Endometrial carcinoma, prognosis, risk factors, treatment, young women*

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I. Introduction

Endometriod adenocarcinoma is the most common form (nearly 80%) of endometrial carcinoma. These tumors are referred to as 'endometrioid' because they resemble proliferative phase of the endometrium. It is common in post menopausal women (50 years) and presents as abnormal vaginal bleeding [1]. It is relatively rare in the young age group (younger than 40 years old) and accounts only for 2.1–14.4%. Only some cases of younger than 30 years old are published[2-6].Small number of cases have been reported in women under the age of 30 years,the youngest being 15 years. It is unusual in younger age group and can be wrongly diagnosed [7,8]. Majority of patients present with clinical evidence of polycystic ovarian disease but in some reports the patients lacked these features [9]. These patients usually present with estrogen or hormone-related disorders such as nulliparity, obesity, and infertility. In general, endometrial carcinoma arising from young patients tends to be well differentiated and have favorable histologic type, infrequent myometrial invasion, and lack of extrauterine spread [10,11]. Women with endometrial carcinoma may be treated successfully with progestin therapy alone as primary therapy to preserve child bearing potential [11]. There is significantly increasing literature available regarding the management of young women with endometrial cancer, including fertility sparing techniques, such as treatment with progestin based therapies. Conservative treatment is indicated for young women stage I, high-differentiated adenocarcinoma who want to keep child birth potential. The treatment with Medroxyprogesterone acetate is not always a consistent management for every patient [5]. Women under 40 who are not obese are at higher risk of both advanced disease and high-risk histology [6] .With this background we present 4 cases of endometrial carcinoma in woman less than 30 years.

II. Methods

A retrospective case study was carried out at our tertiary health care centre, Sri Ramachandra Medical Centre And Research Institute (2015-2017). A total of 4 cases of carcinoma endometrium less than 30 years were identified and studied. Risk factors, Estrogen Dependence, Common Presenting Complaints, Stage Distribution at Diagnosis, Optimal Treatment Modality, Fertility Preservation Options and Prognosis were studied .The choice on conducting conservative treatment or operation was discussed with the patients. If the patients insisted on hysterectomy, the procedure was carried on. Informed consent was taken from all patients pre operatively. The surgery mode and postoperative treatment was according to the stage and histological type of the tumors.

Table 1 Clinical Profile Of Patients

No.	NAME	PARITY	PRESENTING COMPLAINTS	PAST HISTORY
1	Ms. A, 28 Years	Unmarried	Bleeding per vaginum for 1 month Previous Regular Menstrual Cycles	K/C/O Myotonic Dystrophy
2	Ms. B, 30 Years	Married/ Nulliparous	Amenorrhea for 14 months. h/o Recent Weight Gain Previous Regular Menstrual Cycle	D & C done for Abnormal Uterine Bleeding. Was on Progesterone on & off for 1 year
3	Ms. C, 29 Years	Married/ Nulliparous	Excessive, Irregular Bleeding for 7 Months	Hormonal Rx with Progesterone.
4	Ms. D, 29 Years	Nulliparous/ 1˚ Infertility	Bleeding per Vaginum for 20 days Irregular cycles – 1 year	Curettage showing Complex Hyperplasia without atypia 6 months back. Hormonal Rx

Table 2 Investigations And Imaging Modality

Name	BMI	Investigation	MRI
Ms. A	34	USG Abdomen: • Uterus Bulky • Endometrial Thickness : 2.5 cm • Bilateral Ovaries Normal	◆ Large Endometrial fibroid Polyp of 11 X 7 cm ◆ Endometrial Thickness : 2.5 cm
Ms. B	30	Trans Vaginal Ultrasound of Pelvis: • Polycystic Ovarian Syndrome • Endometrial polyp of 0.5 X 0.2 cm • Endometrial Thickness : 6.7 mm	◆ Small irregular Polypoidal lesion of 5mm in fundal region ◆ Endometrial Thickness : 7 mm
Ms. C	31.6	PET CT : • Heterogeneous hypo dense mass lesion in endometrial cavity 10 x 7 x 6 cm • Aortocaval, Lt. lower Para- aortic, Rt. Common iliac, Rt. Ext iliac, B/L internal iliac lymph node show metastasis	CT Guided Biopsy of right external iliac mass: ◆ Poorly Differentiated Serous Carcinoma of possible Endometrial origin
Ms. D	24	Trans Vaginal Ultrasound of Pelvis: • Endometrial Thickness : 14mm • Endometrial Aspirate showing : Complex Hyperplasia with atypia	◆ Poorly differentiated mass lesion near fundus 2.5 X 2.3 X 3.8 cm ◆ Focal Infiltration involving 60 % of the thickness of Myometrium. ◆ Endometrial Thickness : 15 mm

Table 3 Treatment Modality

	Treatment	Staging	HPE	Chemo Radiation
Ms. A	Posted for Polypectomy TAH with BSO done as frozen section showed Benign endometrial polyp with complex hyperplasia without atypia	FIGO STAGE I A GRADE 1 pT1b pNX cM0	Endometrial Adeno-Carcinoma Margins free of Tumor	No Radiotherapy or Chemotherapy
Ms. B	Endometrial Biopsy – Complex hyperplasia with atypia Counseling given TAH with BSO with Pelvic Lymphadenectomy.	FIGO STAGE I A GRADE1 pT1a pNx cM0	Endometrial Adeno- Carcinoma Margins free of Tumor	No Radiotherapy or Chemotherapy
Ms. C	Staging Laprotomy with Total Abdominal Hystrectomy with Bilateral Salphingo-oopherectomy	FIGO STAGE III C T1b ypN1 cM0	Atypical Pleomorphic Tumor Cells arranged in nests & sheaths with myometrial invasion not involving cervix/adenexa.	Post- Operative Radiotherapy & Chemotherapy
Ms. D	Discussion in Tumor Board TAH with BSO with Bilateral Pelvic Lymphadenectomy	FIGO STAGE I A GRADE 1 pT1a pN0 Cm0	Endometrial Adeno- Carcinoma with <50 % Myometrial Invasion. Margins Free of Tumor	No Radiotherapy or Chemotherapy

III. Results

The patients mentioned in the above case series presented with Bleeding per vaginum as presenting complaint .With three of them being Nulliparous and one being unmarried.With Mean Age at the time of presentation being 29.All patients had previous regular cycles with varying duration of heavy menstrual flow.3 patients were on hormonal treatment for increased bleeding p/v for varying durations.2 patients had history of Curettage being done in the past .One was a known case of PCOS.On examination 3 patients had elevated BMI.The investigations done include TVS Pelvis, Endometrial Curretage, MRI Pelvis.Endometrial thickness ranged between 15 and 25 mm.Surgical treatment was the treatment modality opted in all four cases. Only one case with stage IIIc required post operative Radiotherapy and Chemotherapy.

IV. Discussion

Younger patients with endometrial carcinoma tend to have a history of estrogen use or hormone-related disorders such ovarian dysfunction, chronic anovulation, infertility, obesity and PCOS [12]. Abnormal uterine bleeding was the common presenting complaint. Investigations included complete blood count,biochemical testing, ultrasonogram, hysteroscopy and MRI. Initial staging should be confirmed by enhanced pelvic magnetic resonance imaging (MRI) to exclude myometrial invasion, as well as adnexal or pelvic nodes involvement .Has 90% efficacy.[12]The optimal therapy in young patients with endometrial cancer still remains controversial. The dilemma arises of whether to recommend medical management or definitive surgery.Young women affected by endometrial cancer are often nulliparous with a past history of infertility and thus are very anxious to preserve their fertility. [13]Definitive surgery is theclassic treatment for endometrial cancer. It consists of total hysterectomy and bilateral salpingo-oophorectomy, with a pelvic and aortic lymphadenectomy if required, with a 5-year survival rate of 93%. However it results in a permanent loss of reproductive potential. [13]Most effectively used conservative management includes hormonal therapy alone or combined with hysteroscopic ablation.Most conservative treatments are inspired by the hormone-dependence of endometrial adenocarcinomas Progesterone and Gn-RH agonists are the most useful medicines in the framework of conservative treatment of endometrial cancer (Stage I, Grade 1).[14,15,16]The most important prognostic factors of endometrial adeno-carcinomas are: histological grade, cancer stage, myometrial invasion.Frequency of Grade 1 tumors is higher in young women, reaching 90%. Myometrial invasion rate is much lower in young women in comparison to older women. (24% vs. 49% in older women).The association of endometrial adenocarcinoma with ovarian one seems to be more frequent in younger women than older ones (29% vs.4.6%).[17]Younger women tend to be diagnosed with low grade, early stage disease and have excellent prognosis with 98% 10-year survival rate Given the excellent oncologic outcomes associated with early stage EC in young women, the importance of improving quality of life and preserving fertility while maintaining excellent DFS has been recognized.The

incidence of nulliparity in premenopausal women with EC is 55%.[17]Ideal patient selection is the most important factor for conservative treatment.Factors include 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.[17]For patients undergoing fertility preserving therapy, Medroxy progesterone acetate (400-600 mg/day) or Megestrol acetate (160-320 mg/day) is the recommended treatment. In order to assess response, the following are performed by 6 months following treatment:D&C Hysteroscopy Imaging.Response rate around 75%,recurrence rates are 40%.If no response is achieved after 6 months, standard surgical treatment should be performed .In case of complete response, conception must be encouraged and referral to a fertility clinic is recommended.Maintenance treatment should be considered in responders who wish to delay pregnancy.Patients not undergoing hysterectomy should be re-evaluated clinically every 6 monthsAfter completion of childbearing, hysterectomy and salpingo-oophorectomy should be recommende. The preservation of the ovaries can be considered depending on age and genetic risk factors.[18]

V. Conclusion

The need for high index of suspicion, screening for lynch syndrome in early onset carcinoma,inhibitions involved in carrying out endometrial sampling in young women are areas to be looked upon.In any case of abnormal uterine bleeding in young women there is always a need to suspect and rule out a malignancy ,although uncommon in a women of reproductive age group.

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