CLEAR CELL CARCINOMA OF THE ENDOMETRIUM

(Report of 7 Cases)

by

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The term 'clear cell carcinoma' (mesonephroma) was first coined by Schiller (1939) to a group of ovarian tumours having histomorphological resemblance with mesonephroma of the kidney. Teilum (1959) put these mesonephromas into 2 groups: one, the more malignant tumour usually seen in children and young females and referred to them as embryonal rhabdomyosarcoma, endodermal sinus tumour or yolk sac tumour. The other, being less malignant, is recorded in older age group and histologically consisting of clear cell or hob-nail cells.

Earlier, the tumours were recorded from ovaries but later on cases were also seen from the cervix, vagina, broad ligament and corpus uteri (Villa-Santa, 1964; Scully and Barlow, 1967; Silverberg and Degiorgi, 1973; Lahiri *et al*, 1978). But the involvement of endometrium is very rare and there are very few well documented reports available in the literature (Key, 1957; Rutledge, 1964; Gompel, 1971; and Kurman and Scully, 1976). The findings of 7 cases are being reported.

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Material and Methods

Seventy-nine cases of carcinoma of the endometrium were recorded from 1960 to 1977 in the Postgraduate Department of Pathology and Bacteriology, S.N. Medical College and Hospital, Agra. These constitute less than 0.1% of all malignant tumours of female genital tract.

All the 7 cases under report were reviewed critically and wherever indicated special stains including PAS, with or without diastase and mucicarmine were done.

Observations

The clinical data is summarised in Table I.

The cases 3 and 5 were hypertensive, while 7th case was diabetic. Cases 1 and 4 had received hormonal (estrogen) therapy for 7 and 5 months respectively.

TABLE I

Clinical Features of 7 Cases of Clear Cell Carcinoma of the Endometrium

S. No.	Age (Yrs.)	Parity	Duration of Symptoms (Months)	Age of Menopause	Symptoms				Clinical diagnosis	Follow-up (Months)
					Spotting bleeding	Profuse bleeding	Lower Pain Abd.	Discharge		
1.	38	3	12	—	+	+	—	+	F.U.B.	11
2.	49	2	36	43	+	+	+	+	Ca. Body	15
3.	56	5	30	45	+	—	+	+	Ca. Body	—
4.	41	4	24	—	+	—	—	+	F.U.B.	—
5.	47	3	36	46	+	+	+	+	Ca. Body	—
6.	54	4	34	—	+	+	—	+	Ca. Body	—
7.	51	3	42	44	+	+	—	+	Ca. Body	17

Age of the patients varied from 38 years to 56 years with mean age of 45 years. The parity ranged from 2nd to 5th. Menopause was recorded in 5 cases and 2 were still menstruating at the time of diagnosis. The most common presenting symptoms were bleeding per vaginum and foul smelling discharge. Clinical diagnosis of carcinoma body of the uterus was made in 5 cases and F.U.B. in 2 cases. A routine vaginal cytology revealed presence of malignant cells in 4 cases. A total hysterectomy with bilateral salpingo-oophorectomy was done in all cases with postoperative irradiation in 3 cases.

Cases 1, 2 and 7 were healthy with no clinical or radiological evidence of metastases upto 11, 15 and 17 months. Cases 3 and 5 died during postoperative period. Cases 4 and 6 were lost to follow-up.

Gross Pathology: In all cases the tumours were in the fundus and confined to upper 1/3rd of body of uterus. The involvement of myometrium was only upto 2-3 mm. Rest of the myometrium, endocervical canal, cervix, and ovaries did not reveal any abnormality.

In remaining 2 cases, though whole of endometrium was involved, tumours did not extend upto endocervical canal. The myometrium was involved from 0.4 mm to 1.5 mm. But in none of the cases serosa was involved macroscopically. In 2 cases both side ovaries were also involved.

The tumour was yellowish white, mucoid, soft in consistency with areas of haemorrhage and necrosis.

Microscopic

The tumour cells were oval or polygonal in shape with well-defined cellular outline. The cytoplasm was clear or vacuolated with prominent nuclei. These cells were arranged in solid sheets,

tubular or acinar pattern (Fig. 1). Most tumours showed more than one pattern. The tubular pattern was predominant in 4 cases. Though the papillary projections were also noted, psammoma bodies were not seen, acinar pattern was seen in one case, solid sheets in one case and hob-nail type in 1 case.

The combination of tubular and acinar pattern is seen in 2 cases and tubules with solid sheets in 2 cases. Tubular with hob-nail like cells were seen in 1 case.

A combination of clear cell and non-clear cell type was seen in 1 case (Fig. 2).

Nuclear abnormal mitotic figures were very scanty (2 to 5 per high power field in 2 cases only). These cases were having infiltration in the deeper myometrium.

Strikingly the mononuclear cell infiltration was marked at the junction of tumour and normal tissue and it was noted in 5 cases.

PAS positive material was seen in scanty amount in 3 cases. Out of these 3 cases, 2 cases were having involvement of ovaries.

Discussion

The incidence of clear cell carcinoma, a recently reported entity, is rapidly increasing in female genital tract, specially in women who had been exposed to stilbesterol, diethyl stilbesterol; or related synthetic hormone either in their intrauterine life or as a part of hormonal treatment (Silverberg and Degiorgi, 1973). But definite sequence of events are still to be pointed out.

The age group of clear cell carcinoma of the endometrium has been reported from 25 to 89 years with an average of 68 years (Silverberg and Degiorgi, 1973; Kurman and Scully, 1976). But in the present study the age group is lower. In general endometrial carcinoma in India has lower age group as compared to the reports from Western countries.

In the present study only 2 cases received exogenous hormone that too only for 7 and 5 months. They were still menstruating at the time of diagnosis of disease. Rest of the 5 cases had not received any hormone and were post-menopausal. The other cases also have been reported where there is no history of exogenous hormonal exposure specially in post-menopausal women (Gray *et al*, 1970; Silverberg and Degiorgi, 1973 and Kurman and Scully, 1976). Therefore, it can be concluded that only exogenous hormone can not be considered as causative agent for clear cell carcinoma but it may also be due to imbalance of endogenous hormone or there may be still unsuspected factor contributing to the genesis of the lesion.

Histogenesis: Initially, the tumour was thought to be of Wolffian duct origin because of its histological pattern and distribution of lesion corresponding to Wolffian duct remanant (Schiller, 1939). Later, the cases were also reported at the sites where duct remanants were not seen, favouring the genesis to Mullerian duct origin. The following points favour this view.

(a) Tumour occurring at the sites other than Wolffian duct remanants specially endometrium, cervix and vagina (superficially) to benign endometrial.

(b) Even in endometrium only confined polypoid mass or polyp.

(c) High incidence of association of clear cell carcinoma with pelvic or ovarian endometriosis and sometimes it may arise from endometrial cyst.

(d) Histochemical and ultrastructural studies favour Mullerian duct origin.

Clinico-Pathological Correlation

The clear cell carcinoma had a poor survival rate (20.6%) in the series of Silverberg and Degiorgi (1973) and 55.6% in the series of Kurman and Scully (1976) as compared to adenocarcinoma of endometrium which ranges from 66% to 75% (Shah and Green, 1972 and Keller *et al*, 1974).

In the present study Cases 1, 2 and 7 who had only superficial invasion, had no evidence of recurrence or metastases even after 11, 15 and 17 months respectively. This observation differs from that of Silverberg and Digiorgi (1973) and Kurman and Scully (1976) who had reported poor survival rate. Therefore, it can be concluded that it is not the type of the tumour but invasion in myometrium effects the prognosis.

Summary

The clear cell carcinoma of the endometrium is a recently developing new clinical entity. Seven such cases have been reported for the first time in Indian literature. Histomorphologically, solid, acinar, tubular pattern alone or a combination of any of them may be seen in a single case. There is no definite correlation with exogenous hormone with oncogenesis. Histogenesis favours Mullerian duct origin. Prognosis depends upon extent of invasion and not on type of lesion.

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See Figs. on Art Paper IX