MIXED MESODERMAL TUMORS OF THE FEMALE GENITAL TRACT

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This collection of neoplasms represents the most malignant tumors known to occur in the female genital tract. The terminology in reference to Mixed Tumour as floundered in a maze of confusion. They have been referred to as collision tumours, combination tumours, endometrial sarcoma, homologous tumours and heterologous tumours. The latter two terms have pervaded the recent literature. The homologous tumours (carcinosarcoma) are those that consist of elements normally developing from the mullerian system i.e., glands and stroma. Heterologous (Mixed Mesodermal) tumours contain tissue foreign to the uterus e.g. cartilage, bone and striated muscle cells besides spindle cells.

This group of neoplasms of the female genital tract constitute a familial group that share a common histogenesis. The mixed mesodermal tumors are thought to be derived from a totipotential endometrial stromal cell having the capacity to form both glands and stroma. These lesions are derived from the mesenchyme formed in the area of the genital ridge which surround the mullerian duct. The indifferent epithelial cells are derived from the coelomic epithelium of the mullerian duct (Baggish 1974).

Shaw (1928) has classified these malignant mesodermal tumors according to their site of origin in the body of uterus, the cervix or the vagina. He referred to them as mixed tumours of the uterus and vagina and distinguishes (1) those which arise in the uterus occur usually after the menopause and are polypoidal, papillary or lobulated, (2) those which arise from the cervix which occur in patients from the age of 17 to 52 years and appear typically grape like tumors and, (3) the polypoidal masses of 'Grape-like' structures of the "Sarcoma botryoids" of vagina which occur in the anterior wall, the posterior wall or in the region of hymen. The commonest site of origin is said to be the region of the anterior fornix as described by Willis (1960). The etiology of these tumors has been ascribed to Dysontogenesis by McFarland (1935).

The basic cytologic component of these tumors is a mesenchymal cell derived from the stroma of endometrial, endocervical or vaginal mucosa as emphasized by Sternberg *et al* (1954). All other heterologous mesenchymal elements are presumed to be derived from these multipotential stromal cells. Prognosis is poor irrespective of whether radiation, radical surgery or chemotherapy is used singly or in combination.

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Material and Methods

All the specimens received from the Gynaecologic departments of King George Hospital and Victoria Ghosha Hospital, Visakhapatnam were subjected to thorough gross and histopathological study. All such tumours were subjected to serial sections from the tissues taken from different parts of the tumor. Special studies and stains were made with PTAH and Masson's Trichrome to recognise the foreign tissues like, rhabdomyoblasts. Eight short case reports are given below:

Case 1

B.S., aged 14 years was admitted on 16-12-1964, with the complaint of a mass coming out of introitus and blood stained foul smelling discharge per vaginam since one month. She attained menarche at 13th year. She had regular periods for 9 months, 4-5/30 days. Since 3 months periods were irregular. Her last menstrual period was on 1-12-1964. She was unable to differentiate between the bleeding and the periods since then. A moderately nourished deaf mute thin built young girl, anaemic with leucodermic patches all over the body. Breasts well developed for the age. Other systems—nil abnormal. External genitalia were healthy, normally developed and hymen was intact. There was a congested fleshy polypoidal mass protruding from the introitus. A finger could be insinuated between the mass and vaginal introitus all round. In the upper part the mass was adherent to the vaginal wall. Cervix and body could not be felt The mass was necrotic, friable and bleeding on touch. There was a large mass filling the pouch of Douglas. Parametrium was free on both sides. A diagnosis of Malignant Tumour Vagina/Botryoides sarcoma was made. Biopsy of the small bit from the mass was made: The report was spindle cell sarcoma with giant cells, areas of necrosis, foci of myxomatous degnerated areas, haemorrhage and infection. On 12-1-1965 total abdominal hysterectomy with bilateral salpingo-oophorectomy, colpectomy and excision of the grape like masses was done. Post-operative period was uneventful. Post-operative deep X-ray therapy was planned. After 2 weeks the lower portion of the vagina was again filled with the growth and diathermic excision of the growth was done. The general condition of the patient deteriorated and as the prognosis was very poor, her parents took her home.

Case 2

K.L. 13 years came to O.P. with foul swelling blood stained discharge for the first time. She had not attained menarche, was thin built and anaemic. A polypoidal mass was filling the vaginal cavity and foul swelling discharge was pouring out. Uterus and cervix could not be felt.

On rectal examination a small uterus was felt; gonads were not felt. Parametrium was free. Biopsy material showed spindle cell sarcoma with rhabdomyoblasts in good numbers suggesting heterologous elements. Patient refused operation.

Case 3

A.S., aged 32 years, admitted on 24-3-1965, with the complaints of: (1) offensive leucorrhoea since 8 months, and (2) intermenstrual bleeding since 8 months. Other systems—nil abnormal. She attained menarche in 15th year. Married for 13 years. Separated from her husband since 10 years. Cycles were 3-4/30 days regular, painless and the flow was moderate. Last menstrual period was on 17-3-1965. On vaginal examination necrotic growth protruding from the posterior wall of the vagina and involving the upper 3/4th of left lateral vaginal wall was seen. Cervix was free. Uterus normal in size. Biopsy was taken from the growth. Histopathological report of the biopsy material was spindle cell sarcoma with rhabdomyoblasts suggesting embryonic rhabdomyosarcoma. The complete specimen weighed 150 gm. Uterus measured 3″ x 2½″. There was a bit of vaginal cuff. The growth consisted of a number of grape like structures arising from the upper part of vagina.

Case 4

K.A., 35 years, was admitted on 18-8-1965 with complaint of distension of abdomen and amenorrhoea for 3 months. The patients noticed a small swelling on the right side of the abdomen gradually increasing in size, till the whole of the abdomen was filled up. She noticed marked loss in weight after the onset of these symptoms and was feeling dyspnoeic

for 2 months. Scanty micturition was present. She was thin, emaciated, anaemic with marked distention of abdomen and dilated veins over the abdomen. There were cystic and solid areas in the right iliac fossa with restricted mobility. External genitalia were healthy. The introitus admitted 2 fingers. The cervix was smooth, directed forwards and normal. The body of the uterus was retroverted and normal in size; it felt separate from the tumour. Posterior fornix was ballooned out. On speculum examination cervix and vagina were healthy. On rectal examination a cystic mass was felt bulging out into the rectum. A diagnosis of malignant ovarian tumour was made. X-ray chest:—no secondary deposits. Diaphragm, displaced upwards by a soft tissue shadow in the abdomen. Plain X-ray abdomen-showed soft tissue shadow with calcification. I.V.P.—Normal function of the kidneys. Ovariotomy with salpingectomy only was done as uterus and other adnexae could not be removed being firmly adherent. Rhabdomyosarcoma of the ovary was made.

Case 5

Female, aged 48 years, was admitted on 12-10-1967, with mass in the abdomen of one and a half years duration. Previously, the menstrual cycles were regular with normal flow. Now amenorrhoea was noted. Poor and emaciated. No free fluid in the periotoneal cavity. An irregular, variegated tumour, 34 weeks' size, nodular and mobile from side to side as well as from above downwards, arising from pelvis was palpated. Per vaginam 3rd degree prolapse present; tumour felt through right fornix. Total hysterectomy with bilateral salpingo-oophorectomy was done. Ascites with haemorrhagic fluid and adhesion of colon to tumour mass was found. Diameter of the whole specimen was 24". A well encapsulated lobulated mass about 14" in length (posterior aspect) was arising from the posterior wall of the uterus. The tumour was solid in consistency with cut section showing myxomatous degeneration. In areas there was necrosis. Both the tubes were stretched over the tumour mass; A pathological diagnosis of rhabdomyosarcoma of the corpus uterii was made.

Case 6

K.S. Female 46 years, was admitted on 26-1-1968 for swelling in the lower abdomen since 4 years, bleeding per vaginam on and off since 4 months with piercing type of pain in the lower abdomen. Uterus irregularly enlarged. 20 weeks' size of pregnancy not freely mobile. Blood-stained discharge on pressing the abdomen. Cervix felt to be irregular, moving with the movement of uterus. Os closed. Right fornix normal. Left fornix shallow and a mass felt through left fornix. Tumour mass felt on left side. Left parametrium slightly thickened. Right parametrial thickening felt up to pelvic bone. Cervix irregular. Os closed. Provisional diagnosis cancer of body uterus was made. Endometrial biopsy was done. Necrotic material with hyperchromatic vascularised stromal cells and the mass lined with cuboidal cells in areas. Picture suggests fibroid undergoing sarcomatous change. Total hysterectomy was done, leaving behind the tubes and ovaries. Uterine wall on cutting through was almost gitty and cartilaginous and was thickened to about 2 inches. The uterine cavity was dilated at the fundal portion and from this cavity was projecting a yellowish white polyp-like mass, the tip of which was necrotic and friable. The endometrial surface was nodular with Turkish towel appearance, due to infiltration of sarcomatous cells. Pathological diagnosis of endometrial stromal sarcoma (Homologous type) was made. Patient was well all these years.

Case 7

K.S., 16 years was admitted on 10-8-1968 with foul swelling discharge and mass protruding from the introitus. Biopsy was taken from one of the masses which showed monomorphic spindle cell sarcoma with no Heterologous elements, uniformity of cells, with myxomatous degeneration and no rhabdomyoblasts. Endometrial Biopsy showed proliferative glands. Growth was seen arising from upper part of vagina and cervix, uterus normal size, ovaries not palpable. Total abdominal hysterectomy with bilateral salpingo-oophrectomy and upper cuff of vagina was removed. Patient's general condition was good and she was discharged with no evidence of metastases. Diagnosis of "grape-like sarcoma" with rhabdomyoblasts was made.

Case 8

B.D., 15 years was admitted on 12-6-1975 for blood stained discharge. Young female with well developed secondary sex features. She had menarche at 13th year. 3-4/30 days cycles,

regular, suddenly became irregular since 6 months and noticed small fleshy growths projecting from her vagina, she also passed 1-2 small grape like masses on one occasion.

External genitalia healthy, speculum could not be inserted as plenty of grade-like masses were filling the vagina. Growths were seen arising from upper part of vagina and cervix, uterus small felt per rectum and ovaries just palpable. Parametrium free. Total abdominal hysterectomy and bilateral salpingo-oopahrectomy was performed. Specimen showed typical grape-like sarcoma arising from vagina and cervix. Histologically showed heterologous elements of rhabdomyoblasts with spindle cell sarcoma. Patient is well for nearly 6 months on follow-up.

Microscopic Pathology

All the tumours except the endometrial stromal cell sarcoma, showed the heterologous elements as rhabdomyoblasts in all the tumours plus cartilage in two tumours. The occurrence of striated muscle and cartilage, in a malignant mullerian tumour can be accepted as evidence of heteroplasia. The striated muscle was always present as rhabdomyosarcoma, except in one case in our material.

In 48 malignant mixed mullerian tumours in the Registry of Malignant uterine tumours in the laboratories of Jafferson county, Kentucky, in 15 years, carcinosarcomas were 0.44 per one lakh females of 20 years and older, the corresponding incidence rate for mixed mesodermal tumours was 0.55 per one lakh and combined group was 0.99 per one lakh.

In the 8 tumours studied, 7 showed rhabdomyoblasts and 1 had endometrial stromal sarcoma in the postmenopausal women. Five cases were "grape-like" sarcomas of vagina, 1 of uterus, 1 of ovary and all the 7 showed besides spindle cell sarcoma rhabdomyoblasts confirmed by PTAH stain. One case showed a polypoid mass in the uterus with stromal sarcoma pure, no rhabdomyoblasts could be seen in serial section studied. Thus the real mixed mesodermal tumour i.e., the heterologous tumour carried a much more serious prognosis than the carcinosarcoma i.e., the homologous tumour. However, other authors like Williamson and Christopherson (1972) have found basically the same prognosis for each of the subtypes.

Discussion

Mixed Mesodermal tumours continue to be of interest, chiefly because of the variable end result figures which have been reported and of the uncertainity of the prognosis in relation to the subtypes. The tumours consist of a combination of malignant epithelial and stromal (sarcomatous) elements. The latter forms the dominant part of the lesion. The sarcoma consists of pleomorphic cells with long tails and bulbous heads, containing hyperchromatic nuclei as (strap cells). Giant cells and bizarre mitotic figures are present. Lymphatic and myometrial invasion may be seen in over 80% of the cases. Attempts to correlate prognosis with mitotic activity has been unsuccessful. Heterologous elements that are derived from metaplasia of the indifferent stromal cells may be seen. Rhabdomyoblasts are the most frequently found elements. Norris and Taylor (1966) studied 31 mixed mesodermal tumours and found cartilage in 58%; striated muscle in 55%; and bone in 13%. They considered the finding of cartilage a favourable prognostic sign and of rhabdomyoblasts a portent of death. Others, like Williamson and Christopherson (1972) have been unable to prognosticate on the basis of the type of element found. The extent of the tumour at the time of treatment is probably the most important

single factor affecting prognosis (Bartisich *et al* 1967; Chuang *et al* 1970; Norris and Taylor 1966; Norris *et al* 1966; Williamson and Christopherson 1972). There are no statistically significant diffrences in survival based on the presence or absence of heterologous or homologous elements Chuang *et al* (1970) reported 5 years survival of 30% of patients whose tumour was confined to the uterus. No patient whose tumour spread beyond the uterus survived for 5 years (Chuang *et al* 1970). The only treatment consistently associated with survival is surgical removal of the tumour before spread has occurred. The treatment of choice is total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pre-operative or post-operative irradiation does not consistently affect the survival but may be of palliative value (Mendel *et al* 1967; Ober and Tovell 1959). The administration of progestins has no value in either treatment or palliation. Vincristine has been advocated recently.

Summary

1. Seven cases of mixed mesodermal tumours (Heterologous type) were recorded in this paper of whcih 5 were "grape like" sarcomas, 1 rhabdomyosarcoma of uterus and 1 of ovary. Only 1 was endometrial stromal sarcoma of homologous type.

2. The prognosis was bad in all except the homologous type and "grape like sarcoma early case of cervical origin in an elderly woman.

3. All the 7 showed rhabdomyoblasts and prognosis did not vary in any one of them and all died ultimately.

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See Figs. on Art Paper V-VI