DYSGERMINOMA—A RARE OVARIAN NEOPLASM

by

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Introduction

Dysgerminoma of the ovary is said to be an infrequently occurring primary ovarian neoplasm with certain interesting features. This tumour was identified by Chenot in 1911 and it was found to be identical in histological appearance with a testicular seminoma, first described by Chevassu in 1906. During that period it was thought that this ovarian tumour arose from ovotestis or portion of the ovary, which was quasitesticular, and hence, the name "ovarian seminoma" was prevalent.

Robert Meyer (1918, 1925, 1931) postulated that the tumour arose from indifferent germ cells which could be the earliest recognisable germ cells in the gonad, or cells of the mesenchyme of indifferent phase of the gonad. Novak (1948), Morris and Scully (1958) also thought that such tumours were composed of cells of embryonal type resembling or akin to sexually undifferentiated germ cells of the developing gonad. Hughesdon (1959) was also of the same opinion regarding histogenesis of this neoplasm and believed in the totipotent nature of the tumour.

The clinical features of the tumour, as reported by various authorities (Mueller 1950, Pedowitz 1955, Novak and Novak 1958) are often not very classical. Though this tumour has sometimes been found to be associated with pseudohermaphroditism, it is not in any way responsible for intersexuality (Novak 1958). Sometimes, however, these tumours are associated with precocious puberty (Hain 1949, Pedowitz 1955). In a still rare variety there is a teratomatous variation of this tumour, even with preference for teratomatous elements in it (Neigus, 1955).

The malignant potentiality of the tumour has been found to show some variations (Pedowitz 1955, Novak 1958). At one time the tumour was thought to be less malignant than granulosa-cell carcinoma. Pedowitz *et al* (1955) pointed out that this optimistic view was probably due to inadequate follow up and this author showed that the 5-year survival rate may be as low as 12.5% which is much lower than the figures previously published by Novak and Doderlein (1936).

The histological appearance of the tumour has also been found to be variable. Neigus (1955), Santesson and Marrubini (1957) found that predominance of trophoblastic elements leading to chorionepithelioma may be associated with dysgerminoma. In another malignant form pre-

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sence of adeno-papillary structures resembling Schiller's mesonephroma may be associated with dysgerminoma. In a still more rare variety the teratomatous elements may be embryonal and the tumour cannot be differentiated from embryonal carcinoma. These different histological pictures may be present separately or in continuation with the classical appearance of dysgerminoma and are related to the prognosis of the disease. On the other hand, successful pregnancy in association with dysgerminoma and/or following removal of the tumour has been reported from time to time (Schoemaker *et al* 1947, Mueller *et al* 1950; Misra 1958; Phillips 1965; Chakrabarty 1965).

In order to study the variations of clinical features, endocrine effects, malignant potentiality and outcome of this interesting tumour with varied pathology, a study of clinical and pathological features and results of treatment of 4 cases seen during 1960-1965 in the Department of Obstetrics and Gynaecology, Institute of Post-graduate Medical Education and Research, is being presented with discussion and commentary on the various features.

Results of study

Incidence

In this series, the incidence was 4 out of 12,200 gynaecological cases who attended the outpatients' department during these 6 years (.032 per cent). During this period, there were 375 ovarian tumours; of these, 92 cases were primary ovarian malignant tumours. Incidence of dysgerminoma was 4.3 per cent among primary ovarian malignancy and 1.06 per cent among all ovarian neoplasms.

All the 4 cases were below the age of 30 years. The youngest patient was 9 years of age.

Marital history and parity

Three of the 4 cases were single and one who was married had two children before the disease was diagnosed.

Menstrual history

One of the 4 cases was 9 years old and did not have any menstruation when the diagnosis of the tumour was made. One case had slightly delayed puberty, starting menstruation at the age of 16 years. Two cases started their periods at the age of 13 years; one was having scanty but regular menstruation, while the other used to have more or less normal menstruation. Menstrual irregularity or amenorrhoea was not the primary symptom in any of the cases.

Presenting symptoms

All cases presented with abdominal swelling accompanied by pain and gastro-intestinal disorder. One case was undetected until a routine gynaecological examination was made; she was treated by a general physician for dysentery for four months prior to the detection of the disease. Three cases had visible enlargement of the abdomen and in two cases general weakness was marked. Pain in the abdomen was present in two cases.

Table I shows that none of the cases had any signs of pseudohermaphroditism or masculine type of body

TABLE 1

Physical Examination

Table showing body habitus and stigmata of genital hypoplasia

No.	Age in years	Height in centimeters.	Build.	Nutrition	Body contour	Any stigmata of hypoplasia
1	9	125	Average	Fair	Feminine	Nil
2	17	145	,,	,,	,,	,,
3	20	150	,,	Poor	,,	,,
4	23	147.3	,,	Poor	,,	,,

habitus or facial features. In one case which was diagnosed before puberty, breasts were not developed, axillary and pubic hairs were not present and external genitalia were not formed properly. The other three cases had normal feminine type of features with rounded contour of hips and shoulders and normal carrying angle.

Abdominal examination

Enlargement of the abdomen was noted in all the four cases, varying from 14 weeks to 28 weeks' size of pregnancy. In all cases massess over the lower abdomen were found to be arising from the pelvis and they were relatively less mobile. The feel was solid in three cases and partly cystic in one case. The tumours were firm in consistency and uniform in outline in three cases. In one case, irregularity of the surface was noted. Free fluid in the peritoneal cavity was elicited in all four cases.

Internal examination

The external genitalia were normal in all cases except in one case who had not attained puberty. Three patients were single, and for proper assessment, an examination under anaesthesia had to be performed. In one case who was only 9 years old, a rectal examination under anaesthesia was done. The uterus was hypoplastic in two cases. The tumour was moderately mobile in one case, and more or less impacted in the pelvis in the other three cases.

Operative findings

Ascites was present in all four cases and haemorrhagic fluid was present in three of them. The tumour was unilateral in all cases. Adhesions and infiltration into adjacent structures, like intestines, omentum, back of broad ligament, pouch of Douglas, and sigmoid colon, were present in two cases. Integrity of the capsule was maintained in two cases and was lost in the other two cases.

Regarding its site, the tumour was present on the right side in three cases and on the left side in one.

The surface of the tumour was uniform in two cases and irregular and nodular in the other two cases. Blue-domed cysts were present in two cases indicating presence of haemorrhage within the tumour mass. The size of the tumour varied from 14 to 28 weeks' size of pregnancy.

The external appearance was somewhat dull white and the tumour was surrounded by a rather dense fibrous capsule. The cut surface presented a variegated appearance, being grey-

ish or greyish pink in colour, at places showing a yellowish hue. Haemorrhage was observed in almost all cases.

Type of surgical treatment

Conservative surgery with removal of the diseased appendage was done in two cases where the growth was limited to the ovary. In these cases there was no apparent infiltration of the capsule and no evidence of metastasis was detected at the time of operation.

In the other cases, total hysterectomy with bilateral salpingo-oophorectomy was done as the disease had spread beyond the affected ovary. There were omental involvements along with adhesions to the posterior wall of the uterus and broad ligaments. The liver, spleen, gall bladder and pre-aortic glands were palpated in all cases and were found to be healthy.

Pathological report

Two cases showed the typical tumour cell collections separated by connective tissue stroma. The cells were large and polyhedral with indefinite cell borders and nuclei filling up the cell, hyperchromatic, and mitotic figures were present. The connective tissue elements were variable in amount, disposition and density. Typical lymphocytes were seen in the connective tissue core. (Figs. 1, 2, 3).

One tumour showed partly the structure of dysgerminoma and partly chorionic carcinoma.

In the fourth case, round cells were seen to perforate the capsule and cell emboli could be seen in the lymphatic and venous channels of the ovary indicating dissemination. Part of this tumour showed moderately differentiated papilliferous adenocarcinoma.

Metastases

The variation of metastases was another peculiar feature of the tumour. Perforation of the capsule and ascites were present in two cases. In one case, the other ovary showed evidence of dysgerminoma one year after conservative surgery for dysgerminoma in one ovary. Three cases showed dissemination and distant metastases within one year of the primary surgical procedure.

Deep x-ray therapy

Radiotherapy was used post-operatively in one case where recurrence occurred four months after conservative surgery. Though initially there was improvement of signs and symptoms, patient went downhill rapidly and succumbed.

Role of chemotherapy

Out of four cases, in one case methotrexate was used as there was presence of chorionic carcinoma. Temporary improvement of symptoms was achieved.

Discussion

Dysgerminoma is considered to be a specialised form of ovarian tumour made up of connective tissue and large polyhedral cells with hyperchromatic nuclei probably arising from indifferent germ cells. Mueller *et al* (1950) mentioned that dysgerminoma is found in 4.5 per cent of

cases of primary malignant ovarian tumours and comprises about 1.1 per cent of all neoplasms. In this series, the incidence amongst gynaecological patients was .032 per cent and amongst ovarian neoplasms it was only 1.06 per cent. These four cases were encountered amongst 92 primary ovarian malignancies which are comprising of 4.3 per cent malignant ovarian tumours. These figures are nearly identical and confirm the rarity of the neoplasm. Novak (1948) commented that this tumour was about one-third as frequent as granulosa cell tumour which in turn makes up about 10 per cent of all primary malignant ovarian tumours (Fauvet 1934).

Willis (1948) stated that in his series about 75 per cent of cases were under the age of 30 years. Novak and Novak (1958) presented a series of 17 cases in which the youngest patient was 6 years old and the oldest was 38 years of age, with an average age of 20 years. These four cases also occurred in young adolescent girls and women of early reproductive age. In Mueller's series (1950), 72.35 per cent cases belonged to the 2nd and 3rd decades of life though the oldest patient in his series was 76 years of age. In this series, the youngest patient was 9 years of age. The analysis of marital history and parity showed that in 3 cases patients were single and in 1 case the patient was a mother of two children. As this neoplasm is a disease of young women, patients are often single. There is no correlation of parity and the tumour formation.

In most of the works of Meyer (1918, 1925, 1931 b) great stress was laid upon the frequent occurrence of sexual underdevelopment and/or pseudohermaphroditism associated with this tumour. Stigmata of hypoplasia were not found in any of these four cases except in one case who belonged to the prepubertal age. Pseudo-hermaphroditism was also not encountered. Though the association may occur, it is now realised that dysgerminoma has nothing to do with the development of these sexual abnormalities.

In two cases gastro-intestinal upset was the only symptom; heaviness of lower abdomen was complained of by all patients. The diagnosis was delayed in the younger unmarried group because gynaecological examination was delayed, while medical treatment for intestinal ailments was continued.

The size of the abdominal mass varied from 14 weeks to 28 weeks' size of pregnancy and free fluid could be demonstrated in all these cases. A solid tumour arising from the pelvis in girls of the first and second decades, associated with ascites, should raise the suspicion of dysgerminoma.

Though it is repeatedly stressed that dysgerminoma is a biologically inert tumour and even though pseudo-hermaphroditism is present, reversion to normal sex does not occur after removal of the tumour, yet other endocrine manifestations of the tumour may be encountered from time to time. Pedowitz *et al* (1955), while classifying precocious puberty, mentioned that iso-sexual changes may be present with ovarian dysgerminoma or chorionepithelioma. Scully (1958) discussed the endocrine assays of ovarian dysgerminoma and

found elevated follicle stimulating hormone values in a number of cases and positive pregnancy tests in a few cases. Novak and Novak (1958) discussed a few papers where virilization with dysgerminoma had been reported. These authors commented that such change was related to adrenal hyperplasia rather than to the constituent cells of the ovarian tumour. In this series, chorioncarcinomatous cells were found in one case. A biological test was not performed pre-operatively in this case. Neigus (1955) felt that a positive A-Z test is a poor prognostic sign and mandates radical surgery even in young girls. Pedowitz *et al* (1955), however, noted that in several instances, despite positive bioassays, there was no evidence of chorioncarcinoma along with dysgerminoma. It appears, therefore, that the endocrine aspect of dysgerminoma requires more investigation before the biological inactivity of the growth is decided. All positive bioassays should be confirmed by proper histological study of the tumour to demonstrate trophoblastic elements in the growth.

Operative findings were analysed carefully to evaluate the prognosis of this tumour.

1. Ascites

Mueller (1950) believes that ascites is an important sign, specially when haemorrhagic, and bears a bad prognosis. In this study, there was ascites in all cases; three had haemorrhagic ascites and all of them died within one year.

2. Bilateral involvement

According to Novak (1958) bilateral involvement signifies a bad prognosis because it suggests either multiple primary foci or metastasis in the contralateral ovary and indicates an advanced lesion. In all these four cases in this series, however, unilateral ovarian involvement was detected; three were in the right ovary and one, the left. When unilateral, the right ovary is said to be predominantly affected. Seegers (1962) offered his explanation for the right sided development of the tumour that embryologically the right ovary developed more slowly and to a lesser degree than the left. So, if an undifferentiated tissue remains dormant, the probability of the occurrence of this tumour in the right ovary is greater than in the left.

3. Extent of the growth

Mueller (1950) found a survival rate of only 25.31 per cent in cases where there was evidence of breakage of capsule and metastasis to adjacent structures during operation. The survival rate also varied in cases where the growth involved one or both ovaries.

Table II shows the percentage of survival in different groups of cases in Mueller's series. Pedowitz (1955) observed a 5 year survival rate of only 12.5 per cent amongst 17 cases of dysgerminoma. This author noticed bilateral involvement in 36.4 per cent cases and in these the outcome was far from satisfactory. In the present series, two cases showed breakage of capsule with evidence of infiltration to adjacent structures and both of them expired within six months of the operation. Blue domed haemorrhagic cysts were found in two cases.

TABLE II

Prognostication of the disease based on extent of the growth (Mueller et al 1950)

	No. of cases	Alive 5 years or more	Percentage of survival
(a) Confined to one ovary, capsule intact	49	44	89.79
(b) Bilateral	17	5	29.41
(c) Evidence of metastasis or infiltration at operation	79	20	25.31

This finding indicates haemorrhage within the capsule and is a bad prognostic sign. In this series, although the tumour was unilateral in all cases, evidence of breakage of capsule was demonstrated in two cases.

Though these tumours occur in young women who are desirous to have a family, Pedowitz (1955) stressed the limitation of conservative surgery. In this series, two cases had conservative surgery, and of these one died within six months with multiple metastases and the other had a late recurrence of dysgerminoma in the other ovary within a year of the operation. The girl, however, is still alive and well even one year after the second laparotomy. The remaining two cases who had radical surgery did not survive more than six months. The first case was only 9 years old and showed adenopapillary structures with dysgerminoma and was readmitted within three months for cachexia, ascites and recurrence; she died 15 days after admission. The second patient was a mother of two children and had radical surgery and showed trophoblastic cells along with ovarian dysgerminoma and died 35 days after surgery. The place of conservative surgery is limited in this particular type of neoplasm and requires quite a good judgement during surgery and thorough follow-up afterwards.

Microscopic appearance of the tumour is said to be distinctive. Though large oval or polyhedral cells with hyperchromatic nuclei and mitotic figures are indicative of some amount of anaplasia, no direct correlation has been established between the histological appearance of dysgerminoma and the degree of malignancy (Novak 1958). Sheets of large round cells perforating the capsule and invading the venous and lymphatic channels were found in one case which later proved to be malignant. Combined teratomatous tumours with chorionic carcinoma and/or embryonal carcinoma have been reported by Pedowitz *et al* (1955), Santesson and Marrubini (1957). Out of four cases, one case showed chorionepitheliomatous components of the blastoderm and this case proved to be very malignant. Teilum (1946) described certain dysgerminomas which also showed some adenopapillary structures. In this study one case showed adenopapillary carcinoma along with dysgerminomatous element. Two cases showed the typical picture of dysgerminoma.

Deep x-ray therapy was used in one case with very short lived benefit. Radio-sensitivity of this tumour

(Pedowitz 1955) has been reported from time to time, though radiocurability has been questioned. The effect of chemotherapy in one case of chorion carcinoma was not encouraging.

Dysgerminoma complicating pregnancy is very unusual, and, although reported from time to time it was not found among the four cases studied.

Summary and conclusion

An analysis of four cases of dysgerminoma is presented. The cases were studied and observed at the Institute of Post-graduate Medical Education and Research, Calcutta, during the period of six years from 1960-65. Incidence of the tumour among all gynaecological cases seen during these years was .032 per cent. It represented about 1.06 per cent of all ovarian tumours and 4.3 per cent of all primary ovarian malignancies, suggesting the rarity of the tumour.

All the cases were below the age of 30 years, youngest being 9 years old. This proves that it is a disease of young adolescent girls and women of early reproductive age.

The cases were primarily diagnosed as solid ovarian tumour by clinical methods and corroborated by findings at laparotomy and finally by histological study. Solid tumours arising from the pelvis in young women, associated with ascites, should raise the suspicion of dysgerminoma, although there are no typical manifestations of this tumour.

As regards pseudohermaphroditism and subgonadal growth, in not a single case were these features observed.

Skiagraphy of chest, spines and long bones were taken preoperatively to exclude any distant metastases, but these were not found in any case studied here.

As repards management of the cases, the only line of treatment adopted here was surgery. Conservative surgery was undertaken in two cases where the disease was localised in the ovary, capsule intact, and no evidence of infiltration to adjacent structures or metastases to distant organs, like liver, spleen were noted. Two cases had radical surgery where there was breakage of capsule and adjacent structures had got adherent to the ovarian tumour. Results are rather unsatisfactory and the tumour has proved to be more malignant than previously thought.

Haemorrhagic ascites, breakage of capsule and extent of the growth beyond the ovary suggest a bad prognosis. Association of trophoblastic elements or embryonic structures with dysgerminoma indicate a more malignant nature of the tumour.

Post-operative irradiation was given in one case. Methotrexate was substituted in one case where the histology suggested the presence of chorionic tissue with dysgerminoma. Radiotherapy and anti-cancer drug therapy are not suitable adjuncts to surgery.

Recurrence of dysgerminoma to the other ovary was observed in one case who had conservative surgery, and a second laparotomy, followed by hysterectomy with removal of tumour along with the ovary, was done one year after the first laparo-

tomy. This is the only case who is still alive about one year after the second operation.

The other three cases had recurrence of the growth and expired within one year of the operation.

Not a single case in this series was associated with pregnancy.

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See Figs. on Art Paper III