DYSGERMINOMA OVARY—A CLINICOPATHOLOGIC STUDY OF 11 CASES WITH REVIEW OF LITERATURE

by

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Introduction

Dysgerminoma of the ovary is a poorly encapsulated, highly malignant, solid ovarian neoplasm with an insidious growth pattern. 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. Concepts of management have varied greatly in respect to what constitute proper treatment for this tumour. Because reported mortality rates for patients with ovarian dysgerminomas have varied from 27 to 75 per cent (Brody, 1961; Higuchi and Kato, 1958; Koller and Gjonnes, 1964; Thoney *et al*, 1961) and because of the rarity of these tumours has precluded accumulation of extensive experience. In as much as dysgerminomas occur primarily in young women and children, there is a natural desire to be conservative in management, if this is possible without jeopardizing the patient's chance of being cured. There is no unanimity of opinion about the best form of treatment. One major drawback for a conservative therapy is the incidence of clinically undetectable spread to or development in the contralateral so called healthy ovary. A clinicopathologic study was undertaken of dysgerminomas on file at the Department of pathology, Medical College, Aurangabad.

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Material and Method

A total of 11 cases of dysgerminoma out of 320 ovarian tumours were reviewed from 1964 to 1971 and the approach was purely from a clinicopathological point of view. The patients ranged in age from 13 to 60 years, the majority of them being 20 to 30 years old with an average age of 25. Gravidity varied from 0 to 2; all but 1 were nulliparous. A past history of significant pelvic irradiation was not encountered in any patient.

Three of the 11 subjects were asymptomatic. However, abnormal bleeding and pelvic pain were conspicuous by their absence. Abdominal masses were present in 5 patients, while 3 had gastrointestinal complaints. The duration of symptoms was less than 4 weeks in every instance. Physical findings were very uniform.

Laboratory data were inconclusive. There was no increase in the serum calcium or phosphorous level, and no endocrine abnormalities were encountered. All patients were initially subjected to laparotomy. The operative findings were quite characteristic. An average of 5 tissue sections from each tumour were available for pathologic study.

Pathologic Observations
Gross Examination

The tumours ranged in diameter from 10 to 50 cm., with a median diameter of 15 cm. The configuration of the tumours varied from homogenous to lobate (Fig. 1). Most tumours were solid, although a few had cystic foci. Visible haemorrhage or necrosis occurred in 5 out of 11 cases. The tumours varied in colour from pink to grayish-pink and from yellow to tan. Although the lesions were occasionally soft, more often they were firm or rubbery with smooth surfaces. The right ovary was involved in 4 patients, the left in 6 and both in only one patient.

Microscopic Study

The tumours characteristically infiltrated and replaced the ovary, leaving only occasional uninvolved graffian follicle as recognizable structure, although in a few instances small lesions had rather sharply delineated margins that tended to compress the adjacent ovarian tissue. The histologic pattern varied considerably from tumour to tumour and within different areas of the same lesion. The most frequent finding was the formation of aggregates of tumour cells into solid or alveolar arrangements, incompletely separated by delicate fibrous septums (Fig. 2). A less common pattern in which tumour cells were engaged in cords or strands in an edematous or fibrous stroma. Regardless of the growth pattern, the appearance of individual dysgerminoma cells was quite uniform and distinctive. The cells were large and polygonal, they generally had distinct cell borders, and the cytoplasm ranged from optically clear to granular and slightly basophilic. The nuclei were rounded or ovoid with irregularly clumped chromatin and with one or two large, prominent nucleoli. Multinucleated tumour cells were not identified. Areas of necrosis and haemorrhages were often present in large tumours. Some degree of lymphocytic infiltration was present in 3 cases (Fig. 3).

Age

The highest incidence occurs during the second and third decades of life. Mueller *et al,* (1950) noted that 72 per cent of the tumours occurred at this time. Their youngest patient was 2 years old and oldest 76 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 of 20 years. Theoney *et al* (1961) observed that 85 per cent of the dysgerminomas occur within the first 3 decades and 48 per cent within first 2 decades. Brody (1961) reported a 77 per cent incidence before the age of 30, his youngest patient was 8 years old and oldest being 44. Wider and O'Leary (1968) reported that 50 per cent of their cases were less than 30 years of age and only one was postmenopausal. Kapas (1969) reported that all his cases were below the age of 30 years, the youngest was 9 years old and the oldest being 23. Palaniappan (1971) reported all his cases within 2nd and 3rd decades of life except one above 45 years and the youngest 11 years old. Jagadeshwari (1972) found the youngest 14 years old and the oldest 40 years with an average of 26 years.

Review of Literature

TABLE I

Shows the Incidence of Dysgerminoma as Reported by Several Workers

S. No.	Authors	Years	Percentage incidence amongst malignant tumours	Percentage incidence among total ovarian tumours
1.	Santesson	1917	-	3.7
2.	Meyer	1931	3.1	-
3.	Novak and Gray	1938	3.0	-
4.	Sjovall	1943	-	0.7
5.	Novak	1948	10.0	-
6.	Munnell and Taylor	1949	1.5	-
7.	Mueller et al	1950	4.7	1.1
8.	Hertig et al	1961	5.0	-
9.	Kawahara	1962	5.0	-
10.	Novak and Woodruff	1967	10.0	-
11.	Debrux	1968	5.7	-
12.	Kapas	1969	4.3	1.06
13.	Vora and Bhargava	1969	9.5	-
14.	Palaniappan	1971	-	2.9
15.	Jagadeshwari	1972	9.4	3.4
16.	Present series	1972	10.0	3.4

Symptoms

Pedowitz and Grayzel (1951) found 5 per cent of the patients to be asymptomatic, whereas Wider and O'Leary (1968) reported 20 per cent of their patients asymptomatic. Abdominal mass was reported in 74 per cent (Theony *et al*, 1961); 45 per cent (Pedowitz and Grayzel, 1951); 60 per cent (Wider and O' Leary, 1968). Kapas (1969) described that all the 4 cases presented with abdominopelvic swellings. Association of dysgerminoma and genital maldevelopment was reported by several workers (Meyer, 1931; Novak and Gray, 1938; Brody, 1961). An association with pseudohermaphroditism has been observed by few (Jackson, 1960; Theony *et al*, 1961). Pregnancy has frequently been reported in conjunction with this tumour (Mueller *et al*, 1950; Posner, 1955; Jackson, 1960; Brody, 1961; Kawahara, 1962; Pece, 1964; Chakraborty, 1965; Phillips, 1965; Krishna, 1969). Unusual presenting signs, such as an incarcerated inguinal hernia and cervical adenopathy have been reported (Axeldorf, 1960; Feinberg, 1960).

Operative Findings

Bilateral ovarian tumours were found in 14.6 per cent (Mueller *et al*, 1950 14-17 per cent); (Pedowitz and Grayzel, 1951); and 11 per cent (Brody, 1961) of the patients studied. In addition, 30 per cent of the patients exhibited local extension of the tumours at laparotomy. Tumour size was variable, but some were quite large (Royalty *et al*, 1961). Wider and O'Leary (1968) found a unilateral neoplasm in 9 cases out of 10. Kapas (1069), however, described unilateralness of the tumour in all his 4 cases, 3 were in the right ovary and one in the left.

Prognostic Factors

Authors vary considerably in their evaluation of prognosis. Mueller *et al* (1950)

in their analysis of 427 cases noted that in 49, where tumour was confined to one ovary with an intact capsule, there was 89.76 per cent five year survival. Of 17 cases with bilateral tumours, a 29.4 per cent five year survival and of 78 cases with evidence of metastases or infiltration at operation, a 25.3 per cent survival. The 5 year survival rate in the young patient (15-39 years) was 60 per cent (Wider and O'Leary, 1968) compared with 27.1 per cent for all patients (Pedowitz *et al*, 1955). Similar rates have been observed by Brody (1961) and Jackson (1960).

Treatment

Despite of the aggressive nature of dysgerminomas as evidenced by local infiltration, early recurrences and metastases, there is no unanimity of opinion in regard either to the degree of malignancy or suitable treatment. Most authors recommend total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by postoperative irradiation (Wider and O'Leary, 1968). Jackson (1960) and Mueller *et al* (1950) do not advise irradiation until there is recurrence or local extension of the tumour is demonstrated. Theony and his group (1961) advise routine irradiation following operation.

The management of the unilateral encapsulated tumour in a young woman is a matter of controversy. Pedowitz *et al* (1963); Ayerst and Johnson (1959) and Theony *et al* (1961) continue to advise extensive extirpative procedures plus postoperative irradiation. A total of 17 of 47 patients undergoing unilateral oophorectomy in the Pedowitz series (1963) developed recurrence within 2 years. The combination of conservative operation followed by external radiation (Brody, 1961) has found very few proponents and appears to have fallen into disrepute. Kapas (1969) suggested that a radical treatment of total hysterectomy with bilateral salpingo-oophorectomy followed by routine deep x-ray therapy in all cases irrespective of age, parity and extent of the growth should be undertaken as a challenge against this malignant disease.

Discussion

Some Pathologists (Pedowitz and Grayzel, 1951) are of the opinion that dysgerminoma evolves from undifferentiated mesenchymal cells of the ovarian parenchyma. Moreover, the mesenchymal theory of derivation neither adequately explains why on infrequent occasions chorion-like elements are formed in dysgerminoma, nor why, with the exception of the rare pineal and mediastinal teratoid growths in which dysgerminomatous tissue is differentiated, dysgerminoma arises only in the gonad. Further, this hypothesis does not account for the fact that a dysgerminoma arises so seldom in a postmenopausal ovary.

Meyer's thesis (1931), the most widely accepted theory of the histogenesis of dysgerminoma, postulated that 'neutral' or 'dysgerminal' are the sources of this tumour. Such cells are imagined to have existed in the ovary since the indifferent phase of gonadogenesis and at an early stage to have lost their capacity for male or female sexual differentiation due, in Schiller's (1942) opinion, to an aberration of the chromosomes. The gonadal origin and age incidence of dysgerminoma, the infrequent elaboration of chorion-epitheliomatous elements in such a tumour, together with the not too distant relationship of this neoplasm to teratomas, are all interpretable on the basis of a germ cell theory of genesis.

All authors comment on the young age

at which these tumours occur. The clinical features of the patients reported here were particularly fitted to the diagnosis and consistent with those reported by previous authors. In general the subjects were young; 50 per cent were less than 30 years of age. The symptoms were very similar to those of other ovarian carcinomas and were related to the locally invasive and incidious growth pattern, highly malignant potential, and poor encapsulation of the tumour. All of the tumours were correctly diagnosed only after exploratory laparotomy. Mention is made in standard text books about the marked incidence of pseudo-hermaphroditism coexisting with this tumour (Novak and Woodruff, 1967). This is in persuance of Robert Meyers' (1931) paper that reported 27 such cases. The evaluation of techniques of nuclear chromatin and chromosomes studies have opened new gates of thought whereby we are able to recognise a tumour in the phenotypic female with XY chromosome to be seminoma rather than dysgerminoma as the earlier authors considered (Theiss *et al*, 1960; Asadourian & Taylor, 1069). This series of cases adds to the increasing evidence that dysgerminoma occurs in sexually normal females.

It is interesting to note that in recent years, an increasing number of articles are appearing simultaneously stressing the recognition of higher malignancy potential of ovarian dysgerminoma on the one hand and encouraging end results of conservative management on the other. In the present series one case had unilateral salpingo-oophorectomy because of her young age. Remaining cases had bilateral oophorectomy with hysterectomies. Amongst them, 2 cases had deep x-ray therapy and chemotherapy in addition but both of these cases died within 2 months of the treatment. In the remaining cases follow-up has not been possible.

No single histologic feature was of particular prognostic significance, although tumours with a marked lymphocytic or granulomatous stromal response had a high favourable outlook (Asadourian and Taylor, 1969). Such observation was not observed in the present series.

Very few recorded large series has been mentioned in the Indian literature. Those recorded series, are at considerable variance in regard to the basic information about dysgerminomas.

Summary

Clinicopathological study of 11 cases of dysgerminoma met with in 8 years in the Medical College and Hospital, Aurangabad, was made and the literature is reviewed.

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See Figs. on Art Paper III