GERM CELL TUMOURS IN CHILDHOOD

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ABSTRACT:

Germ cell tumours of children are curable by chemotherapy in almost all patients with virtually no effect on subsequent reproductive function.

KEY WORD:

Tumours in childhood, germ cell tumours.

INTRODUCTION:

Only 2% of ovarian tumours occur in childhood (upto 20 years of age) and about 5% of childhood tumours are ovarian in origin[1], the vast majority being dysgerminomas (sharing many characteristics with seminomas in male) yolk sac tumours, teratomas and granulosa cell tumours. Because of their rarity, even experienced gynaecologists see very few such patients and treat them as they would adults - primarily surgically with sacrifice of reproduction in the interests of survival. This is incorrect as the vast majority can be cured with preservation of reproductive function.

REVIEW OF FERTILITY SPARING SURGERY

Fertility sparing surgery has been carried out at many leading centres in the USA[45, UK[6, Canada[7, Italy[8, Australia[9, and Yugoslavia[10 since the mid 1980's. Those with recent reports of at least 10 year follow ups and reported in sufficient detail reveal the following:

TABLE - 1

<table>
<thead>
<tr>
<th>OUTCOME OF FERTILITY SPARING TREATMENT</th>
<th>NUMBER</th>
<th>EVALUATABLE PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENTS</td>
<td>356</td>
<td>100%</td>
</tr>
<tr>
<td>SURVIVAL</td>
<td>338</td>
<td>94.9%</td>
</tr>
<tr>
<td>RECURRENCE</td>
<td>25 (254)</td>
<td>9.8%</td>
</tr>
<tr>
<td>SECOND PRIMARY</td>
<td>2 (204)</td>
<td>1%</td>
</tr>
<tr>
<td>REGULAR PERIODS OR PREVIOUS PATTERN</td>
<td>99 (111)</td>
<td>92%</td>
</tr>
<tr>
<td>FERTILITY - AT LEAST ONE CHILD</td>
<td>175 (203)</td>
<td>86.2%</td>
</tr>
<tr>
<td>PGY LOSS</td>
<td>9 (138)</td>
<td>8.7%</td>
</tr>
<tr>
<td>FETAL ABNORMALITIES (ALL IN ONE SERIES)</td>
<td>3 (138)</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

MANAGEMENT

1. Diagnosis

The usual presentation is abdominal swelling and pain due to rapid growth. Ultrasonic examination with Doppler is mandatory as a size of > 10cms is invariably malignant - Diffuse vascularization, a Resistance index of <0.4 and a flow rate of 12cm/sec being pathognomonic of malignancy[10]. Except for a fetoprotein in yolk sac tumours and rarely BHCG in teratomas, tumour markers are at present of no use. Chromosomal assay is essential as an XY chromosome constitution demands bilateral oophorectomy.

2. Treatment

The major treatment modality, with proper staging (particularly of Para aortic glands), is tumour debulking and omentectomy. The only difference is that normal ovarian tissue is preserved - the Australians[9] even leave residual tumour for cytotoxic therapy in the interests of future fertility. Splitting of a normal ovary for inspection to find minimal bilaterally is seldom carried out, as ultrasound has replaced this. Because of rapid growth, there are few patients with FIGO stage II disease - either early or late presentation occurs.

Postoperatively 3 to 6 cycles of Bleomycin, etoposide and carboplatin at intervals of 21 days are the most widely used treatment. Slightly different doses have been used by the M.D. Anderson[3] workers.

Prolonged follow up is required for late recurrences or second primary tumours although most recurrences occur within 2-years.

The quality of life experienced by these patients is excellent unlike childhood sarcomas and reproduction is preserved in the vast majority.

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COMMENT

It is clear that the prognosis is excellent with not a single death at Irvine since 1984\(^5\). Most recurrences were treated successfully with second line drugs.

The incidence of second primary tumours is lower than expected in these dysontogenetic ovaries.

Reproductive function is very adequate as measured by return of regular periods or previous pattern of menstruation in over 90%. Failures have been attributed to postmenarchal age at treatment and even older women have a high (over 80%) rate of correction often with a delay of up to 6-months after chemotherapy. Chiarelli\(^7\) considers alkylating agents and the dosage to be important factors, but this was not found by other authors.

Similarly, the take home baby rates were high with over 200 children being born after treatment. Both the miscarriage rate (although as high as 21% in one series)\(^8\) and fetal abnormality rate (confined to one series)\(^8\) were acceptable.

The diagnosis is usually made by a painful abdominal swelling and rapid growth (all tumours over 10cm were malignant)\(^9\). It should be noted that doppler u/s enables a clear differentiation to be made between benign and malignant tumours because of vascularization and blood flow. In this respect, for follow up, it should be noted that unilateral oophorectomy predisposes the other ovary to cyst formation, which may be mistaken for recurrence\(^15\).

Radical surgery has a worse prognosis than fertility sparing surgery\(^8\). It is well known that bilateral adrenalectomy in animals has only a 50% mortality whereas the addition of oophorectomy has a 100% mortality. The reason for this is unclear and may involve immune defences but further predicates less radical surgery in young women even with advanced disease - 8 out of 10 patients with stage III or IV disease in one series delivered full term children subsequently\(^4\).

The standard cytotoxic regimes clearly had minimal effect on subsequent reproduction, in women up to 30 years of age, even with radiotherapy premenarchally on occasion\(^7\). Certainly premenarchally, with inactive ova, no effect was seen as expected because cytotoxics generally act on actively dividing cells.

Young patients also have an advantage in the lack of deleterious effects perhaps due to a lack of comorbidity in these healthy patients. Consequently, fertility sparing surgery should always be recommended for young patients even when extensive disease is present.

It should be emphasized that ovarian tumours in young patients differ from older women in terms of cell type, rapid growth and curability. This is possibly because of post differentiation change or perhaps clonal nature as in childhood tumours with the BCR-ABL fusion protein of the Philadelphia chromosome being the best known example\(^12\). Another possible cause is cytomegalovirus infection in predisposed individuals\(^13\). The ovary, however, may simply be dysontogenetic.

In conclusion, childhood germ cell tumours, although highly malignant are almost all curable by fertility sparing surgery with virtually no impact on subsequent reproduction\(^14\).

REFERENCES

7. M. Chiarelli R.M., Marrett L.D., and Darlington G. Menopause and infertility in Females after Treatment


