OVARIAN TUMOURS IN CHILDHOOD

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Ovarian tumours occur less frequently in children than in adults, but while rare in childhood, they are definitely not scientific curiosities. A review of the literature by Witzberger and Agerty,[26] in 1937, showed that at that time only 186 cases had been reported in children up to 10 years of age. Five percent of all ovarian tumours are said to occur in the pre-pubertal age-group.

Steel[23] states that an ovarian tumour may be brought to the attention of parents or physician in one or more of the following ways:

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1. An abdominal mass
2. Sexual precocity
3. Pressure effects on adjacent viscera
4. Complications such as torsion of the pedicle with local circulatory disturbances and possible rupture.

We wish to present 3 cases of ovarian neoplasms in children between the ages of 6 and 8 years, all admitted to the Baragwanath Non-European Hospital department of paediatric surgery between April and June 1965. The first was a highly malignant epithelial tumour of embryonal type presenting with isosexual female precocity; the second, a dysgerminoma, far less malignant; and the third, a benign dermoid cyst which was admitted as an acute abdominal emergency following torsion of the pedicle.

CASE REPORT

Case 1

M.K., a Tsoana girl aged 6 years, was transferred from Zeerust Hospital on 26 April 1965. She complained of lower abdominal pain and an abdominal swelling for 'a few months'. The pain was continuous and central in position. There was no previous medical, surgical or gynaecological history of significance. Bladder and bowel function were normal.

Examination revealed an undersized little girl weighing 49½ lb., with obvious malnutritional skin changes. Despite this, her breasts were fully developed and pubic hair was present and of female distribution. The blood pressure was 110/70 mm.Hg, the pulse rate 108/min. and the temperature normal. The heart, lungs and nervous system appeared normal. Urinalysis revealed no abnormality (specific gravity 1·020). The blood count was normal.

Abdominal examination revealed a mass the size of a 28 weeks pregnancy in the lower abdomen, arising from the pelvis and extending to 3 fingerbreadths above the umbilicus. It was central in position, firm, spherical and mobile and was non-tender to palpation. The abdomen was otherwise normal. On rectal examination the mass could just be tipped with the examining finger and was not adherent to the rectal wall. Vaginal examination was not performed. The vulva was inspected and found to be hypertrophied for her age.

Vaginal cytology showed the presence of a moderate but definite oestrin effect, scattered erythrocytes and occasional small atypical cells (superficial cells 38%, intermediate cells 62%, basal cells 0%). The shoulder and elbow regions were X-rayed for bone age, and ossification in these areas was found to be consistent with her chronological age. X-ray of the chest was normal. A 24-hour collection of urine for oestrogens (1,120 ml.) showed the following assay: oestriol 3 μg., oestrone less than 2 μg., oestradiol less than 2 μg.

The 17-ketosteroid level of a 24-hour collection of urine was 1·1 mg. and the total 17-hydroxycorticoid level was 1·7 mg. The haemagglutination-inhibition test for pregnancy revealed a negative result in all dilutions.

Clinically, the mass was thought to be a 'feminizing ovarian tumour', probably a granulosa cell tumour. The differential diagnosis included a large follicular cyst of the ovary and the feminizing tumours—thecoma, luteoma, embryonal tumour, teratocarcinoma or choriocarcinoma.

Laparotomy was performed on 4 May 1965 via a lower left paramedian incision. A large spherical, solid tumour of the right ovary was found, measuring 16 × 14 cm. in 2 diameters. There was early infiltration of the capsule. There were no adhesions and the tumour was freely mobile. The left ovary, both fallopian tubes and the uterus appeared normal. There was no adherence to surrounding viscera and palpation of liver, spleen, kidneys and para-aortic nodes showed no evidence of metastasis. No nodules were found in the pouch of Douglas. The tumour was easily delivered through the incision and a right salpingo-oophorectomy was performed. Haemostasis was secured and the abdomen closed in layers.

The postoperative course was uncomplicated and she was discharged 14 days after operation.

The operation specimen consisted of an oval, smooth-walled mass, which measured 16 × 14 × 9 cm. The cut surface showed a solid tumour with a few haemorrhagic cysts. The tumour was soft, greyish-white and showed an ill-defined lobular structure with small areas of calcification. Microscopic examination of the tumour revealed an anaplastic carcinoma

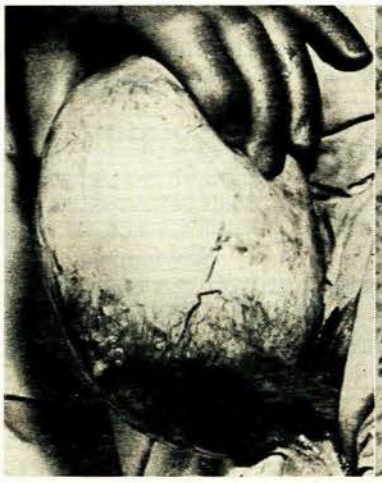

Fig. 1. See text.

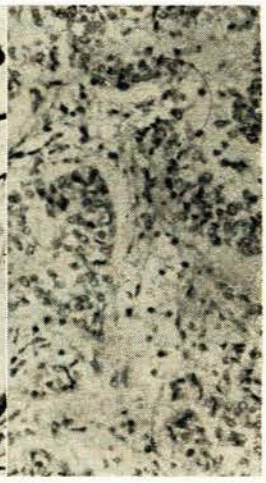

Fig. 2. See text.

with areas of tubule formation. There were also areas of calcification and some psammoma bodies were seen. The stroma surrounding the lobules was composed of highly cellular fibrous tissue in which mitotic figures were frequent. The features were those of an embryonal carcinoma of the ovary (Figs. 1 and 2).

Case 2

K.M., a Zulu girl aged 7 years, was admitted on 15 June 1965, complaining of vague abdominal pain for the previous few months. Her mother had noticed a swelling in the abdomen for 2 weeks. There were no symptoms. Micturition was normal.

She appeared a thin, but otherwise healthy girl, weighing 49 lb. No abnormality was found of the heart, lungs or central nervous system.

On abdominal examination, a large mass was evident, lying to the right of the mid-line and filling the right loin. The mass was hard, irregular and non-tender. It was slightly mobile on palpation and respiration. The liver edge was palpable 1 fingerbreadth below the costal margin and appeared to be attached to the mass. The abdomen was otherwise normal. Rectal examination showed no abnormality; the mass could not be reached with the examining finger. Vaginal examination was not done.

Laboratory investigations showed the following results: Haemoglobin 11·8 G/100 ml., WBC within normal limits. The ESR was 51 mm. in the 1st hour. A mid-stream specimen of urine was normal. The blood urea was 25 mg./100 ml. Serum electrolytes were normal. Total serum bilirubin was 1·3 mg./100 ml. (direct 0·4 mg./100 ml., indirect 0·9 mg./100 ml.). The hydatid complement-fixation test was negative.

A chest X-ray showed clear lung fields and intravenous pyelography was normal.

The differential diagnosis included Burkitt's lymphoma and Wilm's tumour of the right kidney.

Laparotomy. This was performed on 18 June 1965 using a supra-umbilical transverse incision. A large right ovarian tumour was found in the upper abdomen, loosely attached to the under-surface of the liver and to the right edge of the greater omentum. The lymph nodes around the stomach, porta hepatis and some of the para-aortic nodes were enlarged, discrete and firm. The right tube extended as a tenuous connection between the tumour and the uterus in the pelvis

below. The other ovary and tube were normal in appearance and position. There were no metastatic nodules in the pouch of Douglas or peritoneum and the other abdominal organs looked healthy. The tumour was removed together with the attached part of greater omentum and those adjacent lymph nodes that were mobile and accessible.

The specimen consisted of an oval mass 12 × 8 × 6 cm. in size. Stretched fallopian tube and omentum containing enlarged nodes were attached to the surface, which had a nodular appearance. The cut surface was solid, with greyish-white lobulations of rubbery consistency. A few small areas of necrosis were seen.

Sections of the mass showed the presence of numerous large malignant epithelial cells, with large nuclei and prominent nucleoli. The cells were arranged in alveoli, sheets and cords, separated by fibrous trabeculae infiltrated with lymphocytes. In areas the cytoplasmic margins of the cells appeared to have shrunk away from adjacent cells. A few multinucleated giant cells, both foreign-body and Langhans in type, were seen scattered throughout the tumour. This appeared to represent an inflammatory reaction to products of degenerated neoplastic cells. Such cells, together with epithelioid cells, were found at the periphery of 2 of the 10 lymph nodes examined. The above features were typical of an ovarian dysgerminoma (Fig. 3). No evidence of metastatic spread to the lymph nodes examined could be found.

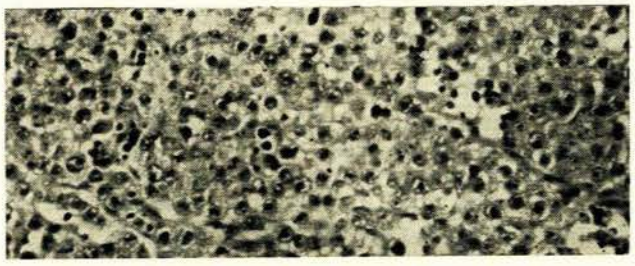

Fig. 3. See text.

Two weeks after laparotomy a radical course of high-voltage X-ray therapy was commenced. This included the whole abdomen and pelvis. Therapy was completed on 9 August 1965, when the patient was discharged. She was seen as an outpatient 3 weeks later and appeared quite normal and well.

Case 3

D.M., a Tsoana girl aged 8 years, was admitted on 16 August 1965 as an emergency case, complaining of severe colicky lower abdominal pain and vomiting for 2 days and burning on micturition for 24 hours. There was no frequency or haematuria, and no previous history of significance.

On examination she was a thin, rather anxious child, weighing 44 lb. The blood pressure was 110/70 mm.Hg, the pulse rate 120/min. and the temperature 99°F. The mucosae were well coloured and there was no abnormality of heart, lungs or nervous system. The blood count was normal, with a haemoglobin level of 12 G/100 ml.

Abdominal examination showed the presence of a very tender, tensely cystic spherical mass, arising out of the pelvis and lying centrally in the lower abdomen. The mass was freely mobile. There was considerable abdominal guarding but no rigidity. Bowel sounds were normal and there was no evidence of intraperitoneal fluid. The kidneys, liver and spleen were not palpably enlarged.

Catheterization produced 50 ml. of clear urine which was normal on ward testing. The specific gravity was 1·030. The character of the abdominal mass was unchanged following this procedure.

On rectal examination the mass was easily palpable and free from the rectal wall.

Pain and vomiting continued on admission and the differential diagnosis appeared to be confined to haemorrhage into or torsion of an ovarian cyst or tumour.

Laparotomy. Examination under anaesthesia was performed before laparotomy, and the vulva, vagina and cervix were found to be normal. The uterus was palpable and of normal size for her age. The mass arose from the right uterine appendages.

The abdomen was opened via a lower left paramedian incision. A right ovarian tumour measuring 8 × 6 × 4 cm. was found. It was markedly congested and oedematous, as was the right fallopian tube which had undergone a 360° torsion at its cornual end (Fig. 4). The uterus, left tube and ovary appeared normal. The omentum adhered to the tumour anteriorly. There was no evidence of infiltration, lymphadenopathy or metastasis. A right salpingo-oophorectomy was performed and the abdomen closed.

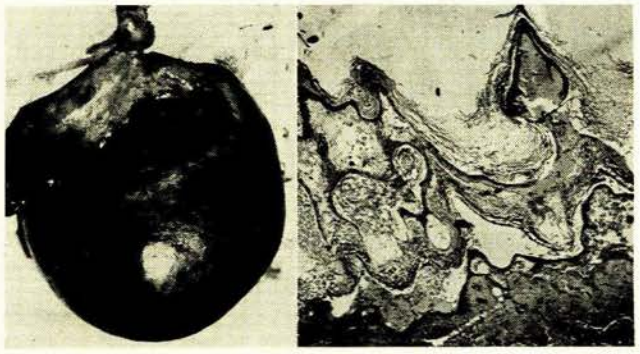

Fig. 4. See text.

Fig. 5. See text.

The specimen of tube and cystic ovary was markedly congested. On section it contained brown fluid and fragments of sebaceous material. Attached to the inner wall of the cyst was a papillomatous mass which appeared to be covered by skin. Histological examination showed the presence of a dermoid cyst and very marked congestion of the tissues consistent with a torsion (Fig. 5).

The patient's postoperative recovery was uneventful and she was discharged 9 days after admission.

DISCUSSION

Gross[12] has stated that if an ovarian tumour in a child is large enough to cause an endocrine disturbance, it can always be felt abdominally or rectally. Thatcher[24] points out that with a palpable ovarian mass in a child over 1 year old, opinion as to possible malignancy should be guarded.

The distribution of the different types of ovarian tumours in children under 14 years of age, in the collected series published since 1937, is demonstrated in Table I (263 cases from 14 series). The over-all malignancy rate was 19% (range from 10 to 44%). The age incidence of the various tumour types showed that all varieties were quite rare in the infant and young child, with an increasing occurrence rate towards puberty.

The first tumour presented is undoubtedly the rarest of the three, and the most interesting. Undue emphasis has been placed on the association of precocious puberty with hormone-producing ovarian tumours, whereas from the point of view of frequency they are probably the least common cause of sexual precocity. In the majority of these cases the aetiology is not known.[16,17,25] Functioning neoplasms of the ovary compared to ovarian tumours in general are relatively infrequent, and only 5% occur before puberty,[17] so that exploratory laparotomy in the absence of a palpable adnexal mass is not warranted in these young

TABLE I. DIFFERENT TYPES OF OVARIAN TUMOURS IN CHILDREN IN COLLECTED SERIES SINCE 1937

	Benign					*Malignant*							
Author	*Benign cystic teratoma*	*Simple follicular cyst*	*Solid teratoma*	*Serous cystadenoma*	*Pseudomucinous cystadenoma*	*Granular cell tumour*	*Adenocarcinoma*	*Dysgerminoma*	*Malignant teratoma*	*Embryonal carcinoma*	*Chorionepithelioma*	*Sarcoma*	*Pseudomucinous cystadenocarcinoma*
Craig (1959)[5]	35	—	—	—	1	—	—	—	—	—	—	—	—
Darte (1960)[8]	19	5	—	5	—	1	2	2	—	—	—	—	—
Gross (1953)[12]	8	3	4	—	1	3	3	1	1	—	—	1	—
Butt (1955)[2]	6	5	8	—	—	1	1	1	—	—	—	1	—
Reis (1962)[21]	10	9	—	—	—	3	—	—	1	—	—	—	—
Costin & Kennedy (1948)[4]	7	7	2	2	1	1	—	1	1	—	—	—	—
Forshall (1960)[9]	12	—	1	1	1	1	3	2	—	—	—	—	—
Dargeon (1949)[6, 7] (1960)	5	2	—	—	1	1	1	—	3	5	1	—	—
Boles *et al.* (1961)[1]	8	6	—	—	—	1	—	—	—	—	—	—	—
Groeber (1963)[11]	6	1	1	2	2	—	—	—	—	—	1	—	—
Garfinkel & Rosenthal (1962)[10]	10	2	1	—	—	—	—	—	—	—	—	—	—
Radman & Korman (1960)[20]	2	2	4	—	—	—	—	—	—	—	—	—	—
Schaefer & Veprovsky (1949)[22]	3	1	—	—	—	1	—	—	—	—	—	—	1
Charache (1959)[3]	—	—	—	—	—	—	2	1	1	1	—	—	—
Total (263)	131	43	21	10	7	13	12	8	7	6	2	2	1
Percentage	50	16	8	4	3	5	5	3	3	2	0·8	0·8	0·4
	81%					19%							

girls. In this case the ovarian mass was obvious, but 2 unusual features were present: The first was the absence of vaginal bleeding, usually the initial presenting sign of the isosexual form of precocious puberty, and the second was the low level of urinary oestrogen secretion, which contrasted markedly with the high percentage of cornified superficial cells due to oestrogen. A possible explanation is that oestrogens other than the 3 usually assayed in the urine were producing the precocious development and vaginal epithelial cornification. Histologically the tumour was highly anaplastic and consisted of sheets of epithelial cells with some attempt at the formation of acini.

It was clearly not a granulosa or theca cell tumour, and there was no microscopic evidence of contamination with chorionepitheliomatous or teratomatous elements. It was thus relegated, on histological grounds, to the very rare embryonal group of tumours of germ cell origin. Embryonal carcinomas are basically teratomatous tumours in which the tumour tissue is extremely undifferentiated and morphologically analogous to the structures present in the earliest stages of embryonic development. This is a highly malignant group of tumours, with a poor prognosis. Neubecker and Breen[15] have shown an 86% mortality rate in 27 patients with this tumour. The average survival time was 13·5 months (41% died within 5 months and 78% within the first 10 months following radical surgery—one-third of the cases having had additional radical deep X-ray therapy). Pedowitz and co-workers[17] had 10 cases of precocious pseudo-puberty associated with embryonal tumours in their series, of which 9 were followed up. Seven patients were dead from metastasis, and only 2 were alive, one less than 2 years and the other more than 10 years postoperatively.

Treatment in this first case, by simple oophorectomy, was based on the assumption that if the tumour had not already spread, the patient would be cured and left with a normal ovary, tube and uterus. If it had spread, the prognosis was so grave as to make further radical surgery pointless. The case for radical hysterectomy plus bilateral salpingo-oophorectomy in every case once the diagnosis has been histologically confirmed, has not yet been established. The advisability of further radical surgery with or without radiotherapy, once the diagnosis had been histologically confirmed was carefully considered. The decision not to proceed was based on the exceedingly unfavourable prognosis of patients with this group of tumours, as mentioned above. This decision is open to criticism.

The degree to which the physical stigmata of sexual precocity regress after excision of the functioning tumour depends upon the expected normal development of the patient at the time of removal. A younger patient, like this one, will exhibit a more obvious, rapid and complete regression than a girl who is closer to the menarche.

The second tumour was a typical dysgerminoma. The histological appearances were quite characteristic, with large cells containing large nuclei lying in sheets and comprising one type of cell population. Interlacing fibrous tissue strands divide the tumour and lymphocytes infiltrating these fibrous strands comprise the second clearly defined cell population. This tumour, also of germ origin, is relatively rare, and occurs about one-third as frequently as the granulosa cell tumour at all ages. Seven percent of dysgerminomas are found in the 1 - 10 year age-group.[13] The pure dysgerminoma, as this one, is non-hormone producing. Those associated with feminizing signs are felt to contain chorionepitheliomatous elements. The mode of presentation is a usually painless, irregular enlarging mass in the pelvis or lower abdomen.

The mass in this patient was in the region of the right kidney and an ovarian tumour was not suspected before laparotomy. Treatment again was by local excision, which is our policy in dealing with these tumours in young children. Frozen sections are not relied upon as the interpretation of ovarian tumours cut by frozen section is notoriously difficult and may be misleading. The potentiality of the tumour to recur or to metastasize is best determined macroscopically at the time of operation. Furthermore, no apparent correlation exists between the histological appearance of a dysgerminoma and its degree of malignancy.

Evidence has recently appeared to show that this tumour is more malignant than has been previously realized. In a review based on 102 cases of dysgerminoma, Pedowitz *et al.*[18] reported a 5-year mortality rate of 72·9%, with a

tendency for rather early recurrence of the tumour as well as 34% involvement of the contralateral ovary. Whether these figures would be improved by reoperation and removal of the other ovary, uterus and omentum in all cases is not yet known. The prevailing opinion is that the course of the disease would not be altered by more thorough and extensive surgery. Moreover, these figures conflict markedly with the prognosis given by Mueller, Topkins and Lapp,[13] as expressed in Table II, showing, as is generally

TABLE II. 5-YEAR SURVIVAL RATE IN CASES OF DYSGERMINOMA[13]

Dysgerminoma	*No. of cases*	*Alive 5 yrs. or more*	*% survival*
Confined to 1 ovary—capsule intact	49	44	89·79
Bilateral	17	5	29·41
Evidence of metastases or infiltration at operation ..	79	20	25·31

felt, that the degree of malignancy of dysgerminoma is usually less than that of most forms of ovarian cancer. Lastly, it should be noted that the tumour is markedly radiosensitive, including metastases or local recurrence, since it is made up of an undifferentiated type of cell.

The third case, the benign cystic teratoma or dermoid cyst, is by far the most common ovarian tumour in children, with an incidence of 50% of all types.[11,12] Thatcher[24] has shown that 81% of these tumours undergo torsion, this susceptibility possibly being a result of their greater weight. Cyclical bouts of abdominal pain and vomiting are characteristic and are probably due to episodes of partial torsion of the pedicle.

The diagnosis, especially from 9 to 13 years, is frequently difficult, for the symptoms may be ascribed to the impending menarche or to recurrent appendicitis. Infarction, resulting from torsion, with massive haemorrhage into the cysts, and necrosis of the solid portions of the tumour, occurs more commonly in children than in adults.[5] The malignancy rate in dermoids is low (0·8 - 1·7%),[16,19] the malignancy occurring in squamous cells. This is in contrast to the solid teratomata containing more primitive elements where the chance of malignancy is higher (25 - 50%).[14] The presenting symptoms of acute abdominal colicky pain with episodes of vomiting, together with the tender, mobile, cystic mass rising out of the pelvis, led to the diagnosis. The mass was palpable bimanually on rectal examination.

Treatment was by removal of the ovary and tube on the affected side, since they were obviously infarcted. Histological diagnosis was simple, the tumour containing a variety of different tissues from the different germ layers, and marked congestion and haemorrhage confirmed the clinical findings of torsion. The prognosis is of course excellent in this child.

CONCLUSIONS

The failure to make the correct diagnosis of an ovarian tumour in a child may be due to the comparative rarity of the condition, the difficulty of examination in the younger children and because the position the tumour may occupy in the abdomen may not suggest any connection with the pelvis (as in our second case). Failure to consider the possibility of such a diagnosis is probably the most common fault.

The usual modes of presentation are: abdominal pain, progressive enlargement of the abdomen or the accidental discovery of a mass by a parent or doctor. Vomiting and abdominal pain together with a tender pelvi-abdominal mass will suggest torsion. Precocious sexual development with vaginal bleeding, breast and vulval hypertrophy and the early appearance of pubic hair in association with a mass palpable in the lower abdomen or *per rectum* will suggest a feminizing ovarian tumour. These symptoms and signs are all well demonstrated in the above 3 cases.

Early diagnosis and prompt management are essential to ensure the best possible prognosis, and where a tumour is palpable, apprehension that it may harbour malignant cells makes prompt laparotomy mandatory.

Gross inspection alone cannot definitely differentiate which ovarian tumour is malignant. A plea for conservative surgery in the first instance at laparotomy is made, as castration with hysterectomy is a serious error to make in a child if the paraffin sections subsequently show the tumour to have been benign. Further radical surgery or radiotherapy or both, may then be employed, where indicated, according to the nature and progress of the tumour.

SUMMARY

Three cases of ovarian neoplasms in children between the ages of 6 and 8 years have been presented, the first a highly malignant epithelial tumour of embryonal type presenting with sexual precocity, the second a dysgerminoma, far less malignant, and the third, a benign dermoid cyst presenting as an acute abdominal emergency. Some of the relevant literature has been reviewed.

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