MALIGNANCY ASSOCIATED WITH BENIGN CYSTIC TERATOMAS (DERMOID CYSTS) OF THE OVARY

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SYNOPSIS

Benign cystic teratomas (dermoid cysts) of the ovary are common tumours though malignancy in association with these tumours is rare. When malignancy is associated with dermoids the commonest type is a squamous cell carcinoma. Five cases of malignancy occurring with dermoids, including both squamous cell carcinomas and adenocarcinomas are reported and their management, adjuvant post-operative therapy and outcome are discussed. Features which should arouse suspicion of malignancy in association with dermoids at the time of surgery are highlighted to emphasize the appropriate surgical management of these rare tumours. The types of adjuvant therapies used in these tumours are discussed and the urgent need for further studies to enable a rational choice of appropriate adjuvant therapy is stressed.

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INTRODUCTION

Malignancy in association with benign cystic teratomas (dermoid cysts) of the ovary is rare. Dermoid cysts of the ovary are common ovarian neoplasms and account for 20% of all ovarian tumours(1); dermoids constitute 95% of ovarian tumours of germ cell origin. Malignancy complicates about 1–2% of dermoid cysts and may occur either by malignant transformation from one of the pre-existing benign elements or a malignant lesion may co-exist with the benign teratoma. Peterson(2) in an extensive review of the subject found an incidence of malignancy of 1.8% in 8000 cases of dermoid cysts and this was confirmed in a later report by Kelley and Scully(3) who noted an incidence of 1.7%. Most standard textbooks state that the commonest cancer associated with dermoid cysts is an invasive squamous cell carcinoma and this occurs in about 75%; however, adenocarcinoma is the second commonest malignancy at 6.8% and a variety of other cancers including carcinoids, malignant melanomas and a variety of sarcomas have also been reported(4).

We report our experience of this rare condition with 5 cases of malignancy associated with dermoid cysts to highlight features that should arouse suspicion of malignancy when dermoids are encountered at surgery. This it is hoped will facilitate the choice of an appropriate surgical procedure and ensure that the tumour is accurately staged so that appropriate post-operative adjuvant therapy may be prescribed in an attempt to improve their otherwise poor prognosis.

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METHODS

The records of all patients with ovarian tumours seen in the two institutions between 1978 and 1984 were reviewed. Five patients who had a malignancy associated with dermoid cysts were found, 3 were from Rush-Presbyterian St Luke's Medical Centre and 2 patients were from the Department of Obstetrics and Gynaecology, National University of Singapore. All clinical details, pathology reports and the histological sections were reviewed for the purpose of this study.

RESULTS

Patients' details and pathological features

The details of 5 patients with malignancy in association with dermoid cysts are summarised in Table 1. The patients' ages ranged from 31 to 68 years with a mean of 48 years. Three patients had Stage I disease, in the first patient (LSH) there was a right ovarian mass weighing 135 gms and measuring 13.5 × 6.0 × 5.0 cms. It showed solid and cystic areas (Fig 1A). The largest locule contained hair and the inner surface had an orange discoloration due to previous haemorrhage. The rest of the mass showed a multiloculated area containing gelatinous material and a pale firm portion. Histological examination showed that the largest locule was a mature cystic teratoma (Fig 1B). The rest of the lesion consisted of a mucinous cystadenocarcinoma with borderline, obviously malignant and invasive components (Fig 1C). Evidence of a direct transformation from the mature cystic teratoma was not identified. The second patient (PV) had an obvious dermoid cyst

TABLE 1
SUMMARY OF PATIENTS WITH MALIGNANCY ASSOCIATED WITH BENIGN CYSTIC TERATOMAS

Initials	Age (Yrs)	Malignancy*	Figo Stage	Surgery†	Adjuvant Therapy	Outcome
JV	62	Squamous cell carcinoma-PD	III	THBSO	Cisplatin, Mitomycin C 3 weekly × 5 cycles	Persistent disease at 20 months then lost to follow up
PV	35	Adenocarcinoma (endometriod features)	IA (i)	THBSO	Vincristine, Actinomycin-D & Cyclophosphamide 4 weekly × 4 cycles	Alive, free of disease at 7 years
MS	31	Squamous cell carcinoma-MD	IA (i)	R-Oophorectomy later THLSO	Cisplatin & Doxorubicin × 2 doses§	Dead, 7 months
LSH	68	Mucinous cyst-adenocarcinoma	IC	THBSO	Oral Cyclophosphamide × 12 months	Dead, 2 years
CYY	50	Squamous cell carcinoma-MD	III	THBSO	Pelvic radiation 5000 cGray	Dead, 2 years

* PD = Poorly differentiated, MD = Moderately differentiated
† THBSO = Total hysterectomy with bilateral salpingo-oophorectomy, R = Right, L = Left
§ Chemotherapy for clinically recurrent tumour

measuring 7 cm in diameter which was completely intact but within the cyst there was a soft brownish mass 2 cm in diameter at the region of the mamilla and malignancy was suspected macroscopically. The third patient (MS) with Stage I disease was the youngest in this report, she had a 2.5 cm solid tumour with gross features of a dermoid but without any other suspect features which was found at the time of Caesarean section. Two patients had Stage III disease with obvious pelvic spread of tumor in one of them (CYY) and extra-pelvic intraperitoneal spread of tumour in the other (JV), enabling a clinical diagnosis of malignancy. In the patient (CYY), there was a right ovarian mass weighing 200 gms and measuring 12.0 × 7.5 × 4.5 cms. It was adherent to the posterior wall of the uterus. The mass was partly cystic and partly solid (Fig 2A). The cystic area showed a mamilla, hair and greasy contents. The solid area was pale with foci of necrosis. Histological examination confirmed the presence of a benign cystic teratoma ("dermoid cyst") (Fig 2B). The solid area showed an invasive, moderately differentiated, squamous cell carcinoma (Fig 2C) merging with the benign portion. Therefore of the 5 patients we report 3 had squamous cell carcinoma and 2 patients had adenocarcinoma; the tumour in one of the latter patients (PV) had features of an endometrioid carcinoma whereas the other (LSH) had a mucinous cystadenocarcinoma co-existing with a mature cystic teratoma without evidence of direct transformation from the benign elements of the dermoid (Fig 1C).

Post-operative therapy consisted of cytotoxic chemotherapy in 4 patients; in 3 patients it was used in an adjuvant role but in one patient (MS) it was used for treatment of clinically recurrent tumor. One patient (LSH) received a single cytotoxic drug, cyclophosphamide as adjuvant therapy but three others were given combination cytotoxics. The remaining patient (CYY), received pelvic radiation because there was macroscopic residual tumour (squamous cell carcinoma) after initial surgery. In one patient (PV) a restaging laparotomy was done 4 weeks after the initial operation but was negative for intraperitoneal or retroperitoneal tumour spread. Two patients required reexploration for bowel obstruction following tumour recurrence, in one patient (JV) after combination chemotherapy and in the other (CYY) after pelvic irradiation. A single patient (LSH) following a year of oral cyclophosphamide therapy, had a second-look laparoscopy which revealed no persistent tumour including negative peritoneal cytology but she died a year later from recurrent disease.

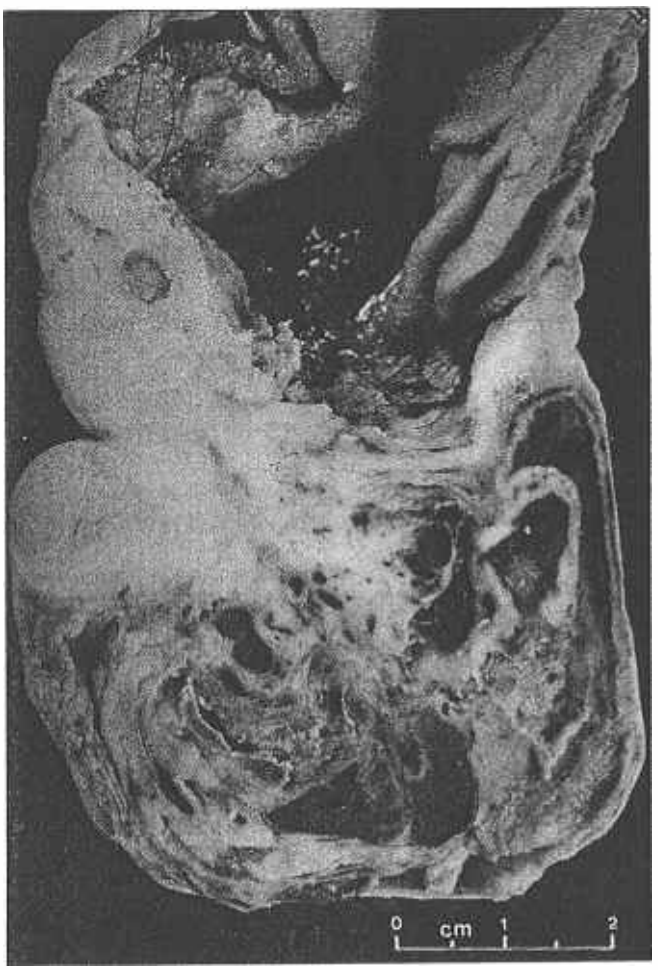

Fig. 1A (Patient LSH). Right ovarian mature cystic teratoma and a mucinous cystadenocarcinoma. Note the hair in the large locule (top) and the more solid pale multiloculated portion (bottom).

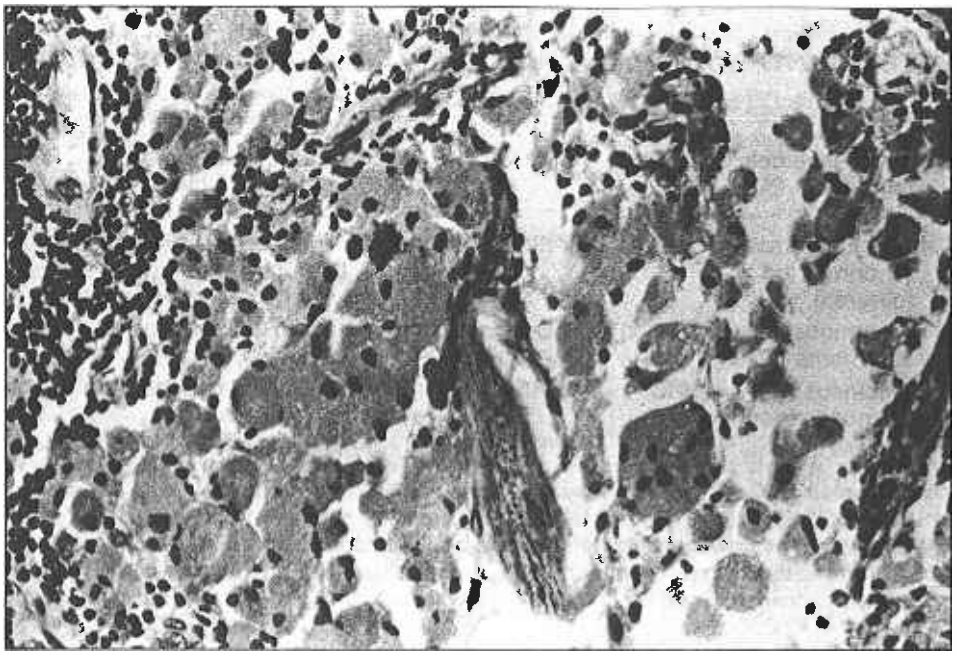

Fig. 1B Note the segment of hair (centre) amidst the inflammatory reaction. (Haematoxylin and eosin, × 350)

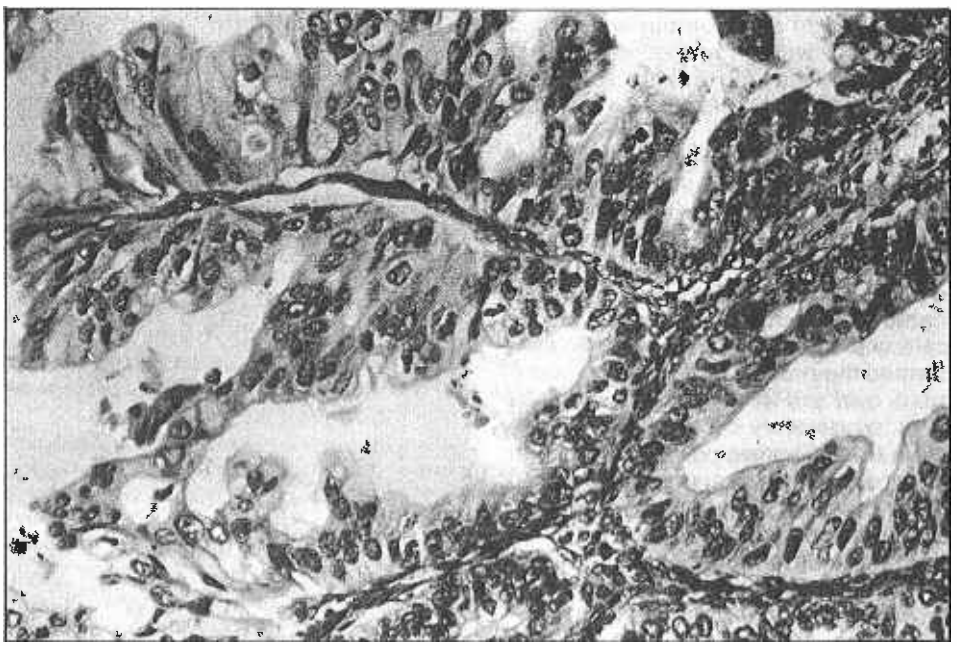

Fig. 1C The locules are lined by malignant mucin-secreting columnar epithelium. (Haematoxylin and eosin, × 250)

DISCUSSION

Dermoid cysts are among the commonest benign ovarian tumours and 80% occur during the reproductive years(1). Dermoid cysts account for the commonest ovarian tumours occurring during pregnancy and malignancy complicated one of the dermoid cysts which was found during pregnancy of the cases we report. This is a rare occurrence since only one instance of malignancy associated with a dermoid during pregnancy was encountered in the exhaustive review by Peterson(2) and none in that of Climie and Heath(4). Dermoids occur less frequently during childhood and the post-menopausal years but they account for 50% of ovarian tumours in the first two decades of life(5). Malignancy in association with dermoids however, occurs only rarely during the first 2 decades and three-quarters of such cases have been detected between the ages of 30–70 years with a peak incidence at 40–70 years(1). Our experience is in agreement with these figures, with the ages of our patients ranging from 31 to 68 years with a mean of 48 years. The youngest patient in our experience was 31 years old and had the tumour discovered during pregnancy.

Dermoid cysts in women above 30 years of age with unusual adherence, suspect solid areas or firm, friable, myxomatous or variegated portions should be suspected to contain malignancy. The presence of

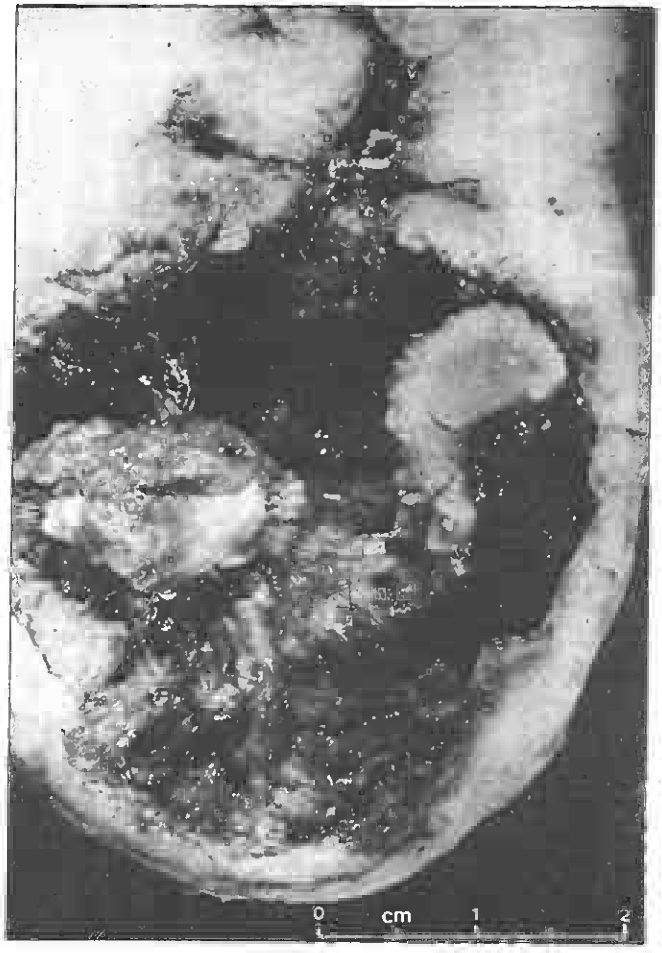

Fig. 2A (Patient CYY). Right ovarian mature cystic teratoma with squamous cell carcinoma. Note the mamilla, hair and greasy contents in the cystic area and pale solid tissue adjacent to the cystic space.

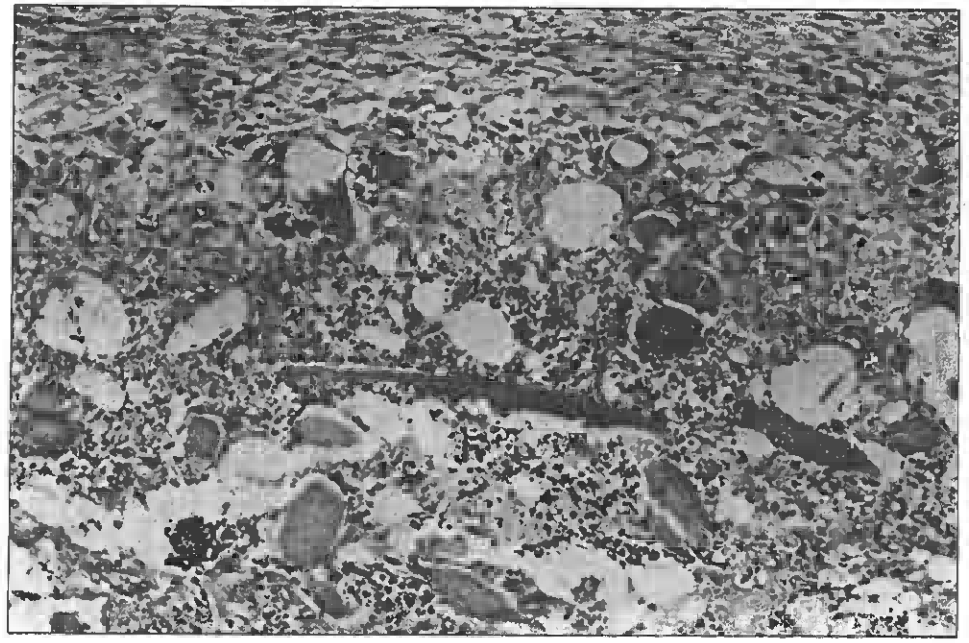

Fig. 2B Segments of hair with an inflammatory reaction within the cystic area. (Haematoxylin and eosin × 140)

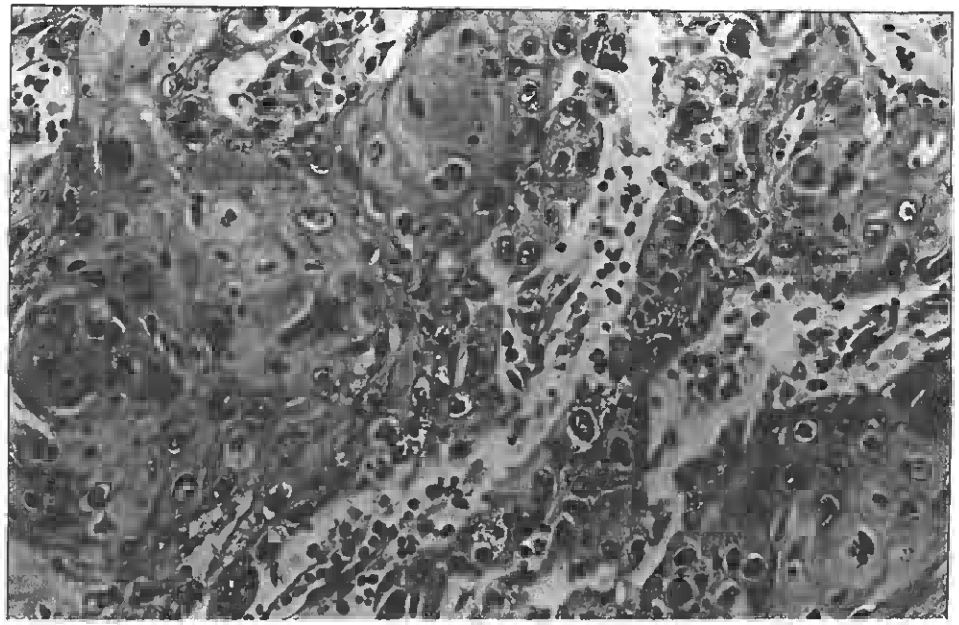

Fig. 2C Moderately differentiated squamous cell carcinoma from the solid portion. (Haematoxylin and eosin, × 250)

nodular, papillary or cauliflower-like growths protruding into the cyst cavity or nodules or plaques in the cyst wall, particularly with areas of capsule penetration are often indicators of malignancy. In all 3 of our patients with Stage I disease, the presence of a solid area or unusual appearance of the cyst contents with myxoid and fibrous features caused malignancy to be suspected and peritoneal cytology was taken but was positive in only one of them. Ascites occurring in association with a dermoid which has not undergone torsion should also arouse suspicion of malignancy and was present in one of our cases; in other instances, like in 2 of our patients with Stage III disease obvious extra-ovarian tumour spread enabled a macroscopic diagnosis of malignancy. Difficulties may occur in cases of benign dermoid cysts with leakage of the sebaceous material from the cyst which elicits a severe peritoneal reaction and this may mimic a macroscopic appearance of intraperitoneal spread of malignancy(6). It is especially important to carefully assess the macroscopic features of surgically removed dermoid cysts which are apparently confined to the ovary or pelvis before completing the surgical procedure, so that if an associated malignancy is suspected the opportunity is taken to request a frozen section examination and to stage the tumour accurately by currently accepted methods. A thorough staging laparotomy should include peritoneal washings for cytology, a complete assessment of the peritoneal, bowel and subdiaphragmatic surfaces including the retroperitoneal pelvic and paraaortic nodes. This would avoid the need for restaging laparotomy which has been found to be necessary in up to 30% of patients with ovarian cancer to accurately stage the tumour prior to adjuvant therapy in other series(7) and in one of our cases.

The surgical treatment of malignancy associated with dermoid cysts generally follows that of primary epithelial carcinomas of the ovary. For tumours confined to one ovary in patients wishing to retain their fertility a salpingo-oophorectomy is adequate surgical treatment but in others, a total hysterectomy and bilateral salpingo-oophorectomy is optimal surgical treatment. Prognosis is dependent more on the extent of tumour at time of diagnosis than the type of operation performed. When only surgical treatment is applied, prognosis is poor when there is tumour spread beyond the ovary with only a 13% salvage rate recorded in one review(2). In squamous carcinomas associated with ovarian dermoids without apparent spillage or cyst rupture, the prognosis is much better and a 5 year salvage rate of 63% is reported(2); there were no survivors in cases of adenocarcinoma associated with dermoids of the cases surveyed in the report.

Adjuvant therapy for malignancy associated with dermoid cysts has not been systematically evaluated in adequate numbers of patients due to their rarity. The efficacy of the different modalities of radiation therapy and various chemotherapeutic agents has therefore not been clearly defined but both modalities have been used on an emperical basis. For adenocarcinomas arising in dermoids, similar chemotherapy as for primary epithelial ovarian carcinoma(8) would seem appropriate adjuvant therapy on an empirical basis but failed in a patient with a stage I adenocarcinoma with positive peritoneal cytology. The other patient with an adenocarcinoma is a confirmed long term survivor but it is difficult to ascribe this to the adjuvant chemotherapy employed which was similar to that used in germ cell tumours(9) since the tumour was completely intact and in such circumstances prognosis is generally good. Whether epithelial tumours arising in or associated with dermoid cysts should be treated with chemotherapy similar to that which is used for malignant ovarian germ cell tumours or the type used for the common epithelial ovarian tumours of coelomic origin is not known and further studies and experience are necessary before chemotherapy can be prescribed on a rational and firm basis.

For squamous cell carcinomas arising in dermoid cysts with tumour spread within the pelvis, pelvic irradiation is recommended(10). However for extrapelvic intraperitoneal spread of squamous cell carcinoma the side effects and complications that would be associated with the required tumoricidal radiation doses delivered to the whole abdomen prohibit its use and therefore chemotherapy known to be effective for squamous cell carcinomas should instead be considered. However in our limited experience with 3 cases of squamous cell carcinomas and extra-ovarian spread, pelvic irradiation was ineffective in a patient who had macroscopic residual disease in the pelvis after surgery and in 2 others combination chemotherapy also failed in both.

It is therefore apparent that more experience is necessary in adjuvant therapy for malignancy associated with dermoid cysts before optimal therapy can be prescribed. Only colloborative studies using uniform therapy in accurately staged and histologically well defined tumours will provide the required information in view of the rarity of these tumours.

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