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# Immature teratoma of the ovary with gliomatosis peritonei

## A case report

J. P. DU TOIT, C. J. C. DEALE, P. M. J. DAVEY

### Summary

Gliomatosis peritonei is a rare complication of immature teratoma of the ovary and should not be confused with metastatic ovarian carcinoma. Treatment depends on the histological grading of the gliomatous lesions. All grades, except grade 0, qualify for adjuvant chemotherapy. Repeated laparotomies for cytological sampling and the removal of tumour are essential. A 16-year-old Ovambo nulligravida presenting with gliomatosis peritonei was apparently cured after 5 laparotomies for removal of tumour and 13 courses of combination chemotherapy.

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Immature teratomata of the ovary occur mostly in young adults and represent approximately 1% of all ovarian teratomata.[1] The malignant potential is determined by the immature component and not by the solid or cystic nature of the tumour. This immature component is mostly of neural origin.[1]

Gliomatosis peritonei is a very rare complication of immature teratomata and should not be confused with metastatic carcinoma. Definitive treatment depends on the grading of the gliomatosis peritonei. Grade 0 disease needs no adjunctive therapy. If, however, it is associated with an immature teratomatous component, repeated surgical removal with combination chemotherapy becomes necessary.

A case of gliomatosis peritonei associated with immature teratoma of the ovary is reported.

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## Case report

On 24 July 1980 a 16-year-old Ovambo nulligravida was admitted to Tygerberg Hospital, having had two laparotomies during the 5 weeks before admission. The first laparotomy was performed at Oshakati Hospital, SWA/Namibia, for a lower abdominal mass and resulted in an unilateral salpingo-oophorectomy. This tumour proved to be a benign cystic teratoma (the pathology could not be reviewed by our laboratory). Within 4 weeks of this procedure she was referred to Windhoek Hospital with a palpable lower abdominal mass and sudden severe loss of weight. On 15 July 1980 at a second laparotomy a total abdominal hysterectomy and removal of the remaining ovary and tube was performed because of a large adnexal mass. The mass was adherent to bowel and at laparotomy enlarged paraaortic glands were palpable. Histological examination revealed an immature teratoma of the ovary.

On examination the patient was emaciated, having a mass of 34,2 kg and a height of 164 cm. The abdomen was slightly distended and tender with a palpable mass in the left iliac fossa. Apart from an erythrocyte sedimentation rate of 83 mm in the 1st hour (Westergren) and a low serum albumin level all other systems and special investigations were normal. Serum $\alpha$-fetoprotein (AFP) and ß-unit of human chorionic gonadotrophin (HCG) estimations were within normal limits.

Histological sections of the second tumour removed at Windhoek were reviewed and revealed a solid tumour consisting predominantly of immature neural tissue, mesenchyme and cartilage. The neural tissue had a neuro-epithelial rosette formation with a high mitotic count (Fig. 1). Three of the 7 sections revealed mature squamous epithelium with keratinization, hair follicles, sweat glands, sebaceous glands and respiratory epithelium. This tumour was considered to be a grade 3 immature solid teratoma of the ovary.[2]

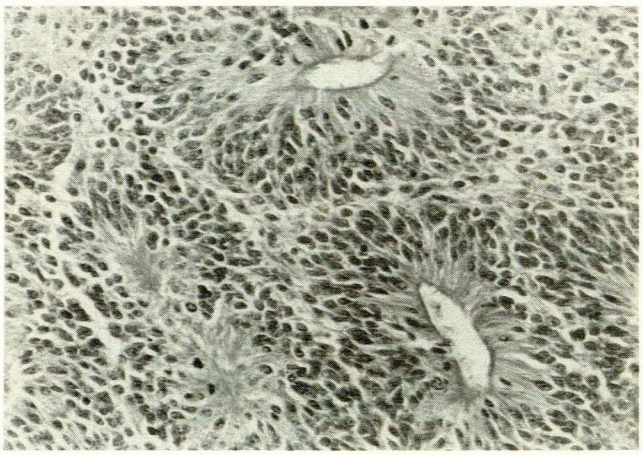

**Fig. 1. Neural tissue with neuro-epithelial rosette formation and high mitotic count (H and E x 400).**

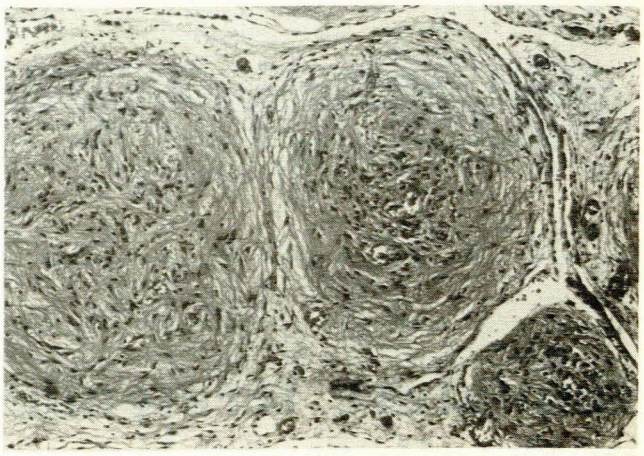

**Fig. 3. Omental nodules with mature glial tissue (H and E x 400).**

Combination chemotherapy with vincristine, actinomycin-D and cyclophosphamide (VAC) was started 7 days after admission and this was repeated at monthly intervals. After completion of the third course of VAC a diagnostic laparotomy was performed on 20 October 1980. At operation multiple solid and partially cystic masses varying from 1 to 3 cm in diameter were found throughout the peritoneal cavity. One large tumour, 8 x 10 cm in diameter and attached to bowel, was also removed. The omentum was infiltrated with numerous solid nodules varying in size from 0,1 to 0,3 cm. A partial omentectomy was performed. A fixed solid mass could be palpated deep in the pelvis but because of adhesions and technical problems could not be surgically removed. Numerous enlarged para-aortic lymph nodes were palpated.

Microscopic examination of the large mass revealed a solid tumour with a few cystic areas, which was a grade 2 immature teratoma.[3] The immature component consisted mainly of neural epithelium with rosette formation and high mitotic activity. Immature cartilage and primitive mesenchyme were present. The cystic areas contained mature squamous epithelium with keratinization and respiratory and intestinal epithelium. Sebaceous gland differentiation was present in the stroma. Cytological examination of imprint smears of the fresh cut surfaces of the preparations revealed mature squamous epithelium with streaks of primitive neural tissue; the latter cells had small nuclei with scanty cytoplasm. The nuclei showed a fine chromatin pattern with some chromocentres (Fig. 2). The nodules in the omentum revealed mature glial tissue with surrounding areas of fibrosis (Fig. 3). The presence of glial tissue was confirmed by staining the glial fibrils with glial fibrillary acidic protein; they could then be classified as grade 0 gliomatosis peritonei.

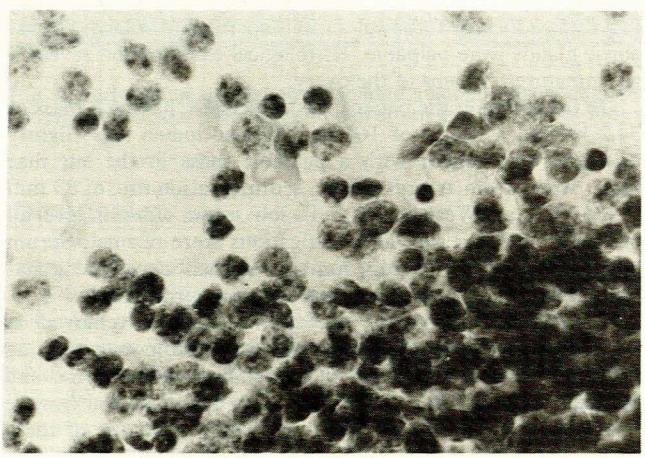

**Fig. 2. Cytological examination of neural tissue showing small nuclei with a fine chromatin pattern and scanty cytoplasm (Papanicolaou staining 1 000 in oil).**

The patient's postoperative course was uneventful, VAC therapy was restarted, and she was transferred back to Windhoek.

At re-examination during February 1981 the only positive finding was the pelvic tumour. At this stage computed tomography (CT) could not demonstrate enlarged para-aortic lymph nodes and it was decided to continue the chemotherapy. A total of 13 courses of VAC therapy was administered to the patient.

In February 1982 the patient was again admitted to Tygerberg Hospital for routine examination and special investigations. Her general condition was greatly improved and the only positive finding was a pelvic tumour extending inferiorly into the rectovaginal space; superiorly it could be palpated suprapubically. CT confirmed the clinical findings. Serum AFP and ß-unit of HCG estimations were normal. A laparotomy performed on 25 February 1982 revealed numerous tumours varying in size from 1 to 15 cm in diameter with small greyish nodules on the peritoneal surface of the bowel and the remaining portion of the omentum. Most of the larger lumps could be removed surgically, but the retroperitoneal pelvic mass was once again considered to be surgically inoperable.

Histologically the tumours were solid and cystic mature teratomas (grade 0),[2] the solid areas consisting almost entirely of brain tissue with choroid plexus formation in some areas (Fig. 4). The cystic teratomas consisted of all the mature components previously mentioned. Cytology of imprint smears revealed squamous epithelial cells, foreign particles and groups of papillary cells suggestive of the choroid plexus. The omental biopsy specimen once again revealed gliomatosis peritonei grade 0. At this stage we decided against any further surgical treatment or chemotherapy.

Exactly 1 year later the patient was admitted complaining of lower abdominal discomfort. Her general condition was better than on the previous admission but the pelvic mass had grown in size. The mass obliterated the pouch of Douglas, and the upper two-thirds of the rectovaginal septum formed part of the mass. On rectal examination the mass almost completely obstructed the rectum but the mucous membrane of the rectum was intact. CT confirmed the pelvic mass but no other intraperitoneal or retroperitoneal masses were observed.

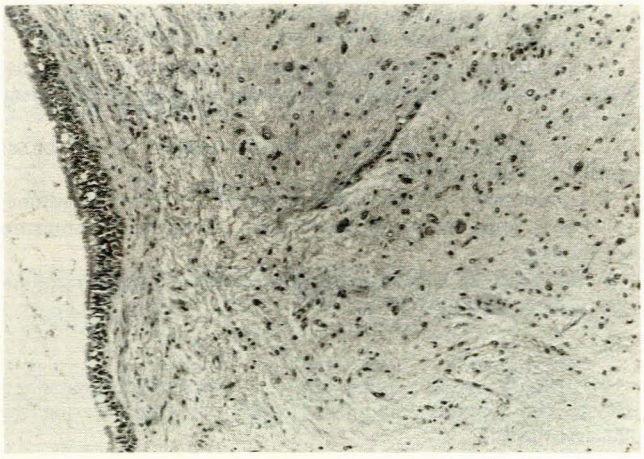

**Fig. 4. Grade 0 tumour with solid areas consisting almost entirely of brain tissue (H and E x 160).**

A fifth laparotomy was performed on 1 March 1983. On entering the peritoneal cavity a peritoneal wash for cytological examination was done. Two tumours ± 2 cm in diameter were removed from the mesentery of the small bowel. Routine appendicectomy was performed because of small greyish growths on the peritoneal surface. No enlarged lymph nodes could be palpated. At this stage we realized that surgical removal of the pelvic mass was imperative. The mass was carefully dissected from the bowel and the pelvic vasculature but it was evident that it could not be completely removed by the abdominal route so the abdominal incision was closed and the operation continued vaginally. The tumour was eventually removed *in toto* via this route. The postoperative course was uneventful but on the third postoperative day the ß-unit of HCG level was 3,6 IU and serum AFP values negative. Subsequent ß-unit of HCG estimations were negative.

Histopathology of the abdominal tumours revealed mature benign cystic teratomata grade 0 with all the components previously mentioned. Gliomatous lesions (grade 0) were present on the peritoneal surface of the appendix and the pelvic mass was a benign cystic teratoma grade 0 with one small focus (smaller than one low power microscopic field) of cytotrophoblastic and syncytiotrophoblastic components with central bleeding and necrosis. Staining of this focus with peroxidase/antiperoxidase HCG staining confirmed the presence of HCG (Fig. 5). The peritoneal washings contained only leucocytes, eosinophils and normal mesothelial cells.

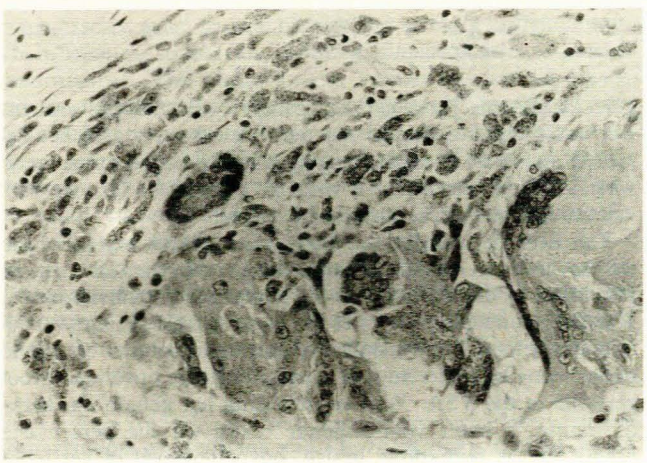

**Fig. 5. Tumour showing cytotrophoblastic and syncytiotrophoblastic components with central bleeding and necrosis (peroxidase/antiperoxidase HCG staining x 160).**

At follow-up examination during June 1983 the patient was in excellent physical condition and results of all clinical and special investigations were normal. The patient was last seen on 20 June 1984 when she was in excellent health without any signs of residual or recurrent disease.

## Discussion

The immature component of a solid or partially cystic teratoma has the potential for local recurrence or metastasis. In approximately one-third of these cases intra-abdominal spread will take place.[3] Histological grading of these tumours is essential for therapeutic and prognostic considerations. Thurlbeck and Scully[4] originally graded these tumours from grade 0 to grade 3 and at a later stage this grading was adapted by Robboy and Scully:[2] grade 0 — only mature tissue with no mitotic activity; grade 1 — isolated areas of abnormal cellular morphology and/or a combination of embryonal and mature tissue, occasional mitosis; grade 2 — moderate amount of embryonal tissue interspaced with mature tissue and moderate mitotic activity; and grade 3 — large areas of embryonal tissue.

The grading of the primary tumour should give a reasonable indication of the chances of secondary tumour formation. The chances are much higher with rupture of the tumour before or during operation.[5] Any tear or adhesion of the tumour wall in the primary lesion may lead to the release of primitive cells. On maturation these cells may eventually lead to either gliomatosis peritonei or a mature or immature teratoma.[2,4,6] The grading of the secondary teratoma also influences future therapy and prognosis.

Gliomatosis peritonei is a very rare complication of an immature teratoma of the ovary, with only 32 reported cases in the literature.[6] However, the incidence of gliomatosis peritonei appears to be as high as 25% in second-look laparotomies after removal of a previous immature teratoma.[6] With the present-day popularity of second-look laparotomies after chemotherapy, this condition may be diagnosed more regularly in future. At laparotomy this condition presents as multiple, widespread, greyish-white nodules (0,1 - 1,1 cm in diameter)[6] on the peritoneal surface. The prognosis for grade 0 gliomatosis peritonei ought to be very good and no further therapy should be necessary.[2] However, the literature reports 3 cases of grade 0[1,5,7] and 1 case of grade 1[5] gliomatosis peritonei with a fatal outcome. It should be stressed that at follow-up laparotomy an adequate incision is essential to facilitate thorough examination of the peritoneal cavity, the taking of samples of ascitic fluid or peritoneal washings for cytology and the taking of adequate biopsy specimens from areas with possible tumour. Cytological imprint smears may also be useful, as in our case. The accurate grading of the lesion at this stage should once again influence the decision on future management and prognosis.

The secondary teratomas are usually larger than 1 cm in diameter. In the present case the size varied from 1,0 to 15,0 cm after removal. These tumours should be thoroughly evaluated microscopically otherwise possible immature tissue, embryonal carcinoma, choriocarcinoma, dysgerminoma or endodermal sinus elements could be overlooked. These combination germ cell tumours differ in their biological behaviour from the true immature teratoma and the management should be adapted accordingly. If a focus larger than one low-power microscopic field of any of the mentioned germ cell elements is present on microscopy, the tumour should not be classified as a true immature teratoma.[5] In this case the choriocarcinoma component was smaller than one low-power field (Fig. 5) and

therefore the tumour was classified as a true immature teratoma. Regular monitoring of serum AFP and the ß-subunit of HCG values could give an early indication of other possible germ cell elements.[6,8] The ß-unit of HCG test was positive on only one occasion and at a very low level and we decided that the small focus of choriocarcinoma in the one tumour should not influence the patient's prognosis.

Because these tumours are more prevalent in young adults, the primary treatment should be by conservative surgery.[5,8] Unilateral salpingo-oophorectomy is preferable to ovarian cystectomy because during the latter procedure the chances of rupture are much higher. Very thorough microscopic examination is essential to exclude other germ cell elements and for proper grading of the lesion. Chemotherapy, preferably VAC, should be instituted if the grading is $\geqslant 1$.[5,6,8-10] Repeat laparotomies should be considered when clinically indicated or on completion of the chemotherapy, and should facilitate proper evaluation and collection of the necessary samples. In our case we stopped repeat laparotomies once the microscopic grading was $< 1$. In a young patient a pregnancy is a possibility after conservative surgery and VAC chemotherapy.[11]

## Conclusions

1. The importance of proper evaluation of the contralateral ovary and the peritoneal cavity at laparotomy for a unilateral adnexal (ovarian) tumour, especially in a young adult, cannot be overstressed.

2. Cytology of peritoneal washings and of imprint smears could be of value in primary and subsequent laparotomies.

3. Adequate sectioning of tumours for microscopic examination at primary and subequent laparotomies, with exclusion of other germ cell elements, is most important.

4. Second-look laparotomy is essential in all patients with a solid or immature teratoma of the ovary to exclude gliomatosis peritonei and malignant metastases.

5. Regular monitoring for ß-unit of HCG and AFP levels will result in earlier detection of other germ cell components.

6. An adequate abdominal incision at subsequent laparotomy is of the utmost importance for proper cytological and tissue sampling.

7. To preserve fertility, primary surgery should be as conservative as is feasible.

8. Combination chemotherapy could be a very useful adjunct to repeat surgery in patients with secondary immature teratomata.

9. To produce a permanent cure extensive repeat surgery should be attempted.

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# News and Comment/Nuus en Kommentaar

## Die rookgewoonte en godsdiens

Een van die veranderlikes wat met epidemiologiese ondersoeke van rookgewoontes dikwels oor die hoof gesien word, is godsdiens. Tog blyk dit uit opnames wat in Holland gemaak is dat kerkbywoning in besliste (omgekeerde) verband tot rook staan (Van Reek, *Medisch Contact* 1984; **39:** 1673). Daar bestaan geen Bybelse verbod teen rook nie omdat tabak destyds onbekend was, maar sekere godsdienstige sektes soos die Sabbatariërs en die Mormone verbied die gebruik daarvan. In Holland is die persentasie rokers onder Protestantse kerkgangers laer as onder Rooms-Katolieke en aansienlik laer as onder persone wat glad nie kerk toe gaan nie. Hierdie verskille kom ook ooreen met verskille wat in 'n opname in die VSA in 1971 aangeteken is.

Hierdie verskil was veral opvallend t.o.v. vrouens. Slegs 18% van vrouens wat gereeld, d.w.s. minstens een maal per week, 'n Protestantse kerk bygewoon het, het gerook teenoor 22% gereelde Rooms-Katolieke kerkgangers, en 48% van vrouens wat nooit kerk toe gegaan het nie, hoewel party gesê het dat hulle Katoliek is. Dieselfde neiging is by VSA-syfers opgemerk, waar 22% van Protestantse vrouens gerook het teenoor 54% van vrouens wat nie kerkbywoners was nie.

Van Reek het gemeen dat die syfers moontlik van provinsie tot provinsie kan verskil. 'n Vergelyking tussen die Calvinistiese provinsies in die noorde met die gemengde provinsies en die Katolieke suidelike provinsies het egter 'n baie geringe verskil in syfers getoon. Die verskille was aansienlik minder opvallend onder mans in Nederland, in teenstelling met opvallend groot verskille in die VSA. Verdere ontleding het getoon dat kerkbywoning 'n beter voorspellende faktor vir die persentasie rokers was as ouderdom, geslag, opvoedingspeil of verstedeliking. Dit lyk dus asof hierdie faktor altyd oorweeg behoort te word by epidemiologiese ondersoeke van rokers en nie-rokers.