

Prevalence of primary papillary peritoneal neoplasia in patients with ovarian carcinoma

B. G. LINDEQUE, H. S. CRONJÉ, C. J. C. DEALE

Summary

Primary papillary peritoneal neoplasia (PPPN) is a recently recognized disease entity. Macroscopically it resembles ovarian carcinoma. On microscopic examination it also superficially resembles serous ovarian adenocarcinoma, but in PPPN the epithelial cells are single-layered and well differentiated with very rare mitoses, and numerous psammoma bodies are found.

In a retrospective review of 61 consecutive patients with serous or papillary ovarian adenocarcinoma seen over a 7-year period, 4 patients with PPPN were found (6,5%). One of these patients was in clinical stage I, 2 were in stage II and 1 was in stage III. All had undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy. Two of these patients received additional chemotherapy and 1 radiotherapy. After 3, 3, 8 and 4 years there were no recurrences in these patients, in contrast to a 29,1% 5-year survival rate for the other patients with serous carcinoma. Cytological examination of ascitic fluid specimens performed in 3 of the 4 patients with PPPN demonstrated the presence of highly differentiated serous tufted cells.

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Primary papillary peritoneal neoplasia (PPPN) is a recently described disease entity.¹ Extensive tumour formation takes place on the ovaries and peritoneal surfaces, resembling ovarian carcinoma on macroscopic examination. However, the classic criteria for malignancy are absent on microscopic examination (except for the papillary growth pattern). Patients with PPPN are frequently diagnosed when in clinical stage III, but survival is nevertheless approximately 100%. This is in contrast to the expected 5-year survival rate of 25% in patients with serous adenocarcinoma of the ovary.² It is also better than the expected 5-year survival rate of up to 92% in patients with borderline serous tumours.³⁻⁶ Approximately 25% of patients with borderline tumours do eventually die of advanced disease,⁵ so the long-term prognosis of PPPN is therefore also better.

Division of Gynaecological Oncology, Department of Obstetrics and Gynaecology, and Department of Anatomical Pathology, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP

B. G. LINDEQUE, M.MED. (O. ET G.), F.C.O.G. (S.A.)

H. S. CRONJÉ, M.MED. (O. ET G.), F.C.O.G. (S.A.), M.D. (Present address: Department of Obstetrics and Gynaecology, University of the Orange Free State, Bloemfontein)

C. J. C. DEALE, M.MED. (O. ET G.), F.C.O.G. (S.A.), M.MED. (ANAT. PATH.)

The aim of this study was to determine the prevalence of PPPN in patients with previously diagnosed serous or papillary adenocarcinoma of the ovary at Tygerberg Hospital, and to compare the survival rate of patients with PPPN with that of patients with carcinoma.

Patients and methods

Between January 1976 and December 1982 the histopathological diagnosis of serous or papillary ovarian adenocarcinoma was made in 64 patients at Tygerberg Hospital. The pathology records of these patients were searched for the presence of PPPN. The histopathological criteria used for its diagnosis were those suggested by Genadry *et al.*:¹ (i) the epithelium is not well differentiated enough to be interchangeable with normal tubal epithelium; (ii) the mitotic count is a maximum of 0 - 1 in any high-power field; (iii) there is pseudostratification of epithelial cells in papillary fronds; (iv) there is no individual cell anaplasia; (v) there is no evidence of aggressive tumour growth, i.e. necrosis; and (vi) calcifications or psammoma bodies and/or foreign-body reactions and/or intranuclear clear zones suggestive of viral disease are common (Figs 1-4).

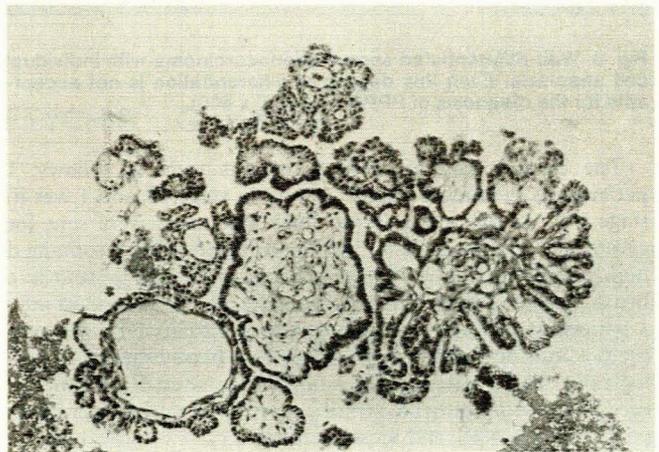


Fig. 1. Papillary growth pattern in PPPN (H and E x 160).

Finally, the records of operative findings, cytological results, treatment and survival of these patients were reviewed.

Results

A total of 64 patients with a previous diagnosis of serous or papillary ovarian adenocarcinoma were reviewed. In 3 cases the pathological records were incomplete and these were excluded from the study. Of the remaining 61 patients, 4 (6,5%) were re-diagnosed as having PPPN.



Fig. 2. Uniform single-layered cells with only pseudostratification in PPPN (H and E x 400).

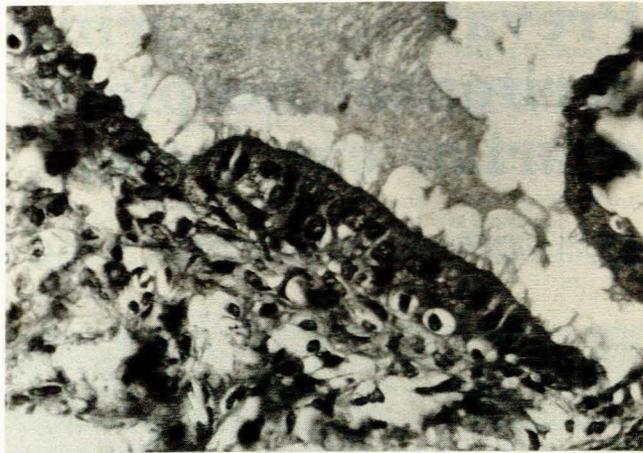


Fig. 4. PPPN — serous columnar epithelium, in single layer, with intraluminal mucin (H and E x 1000).

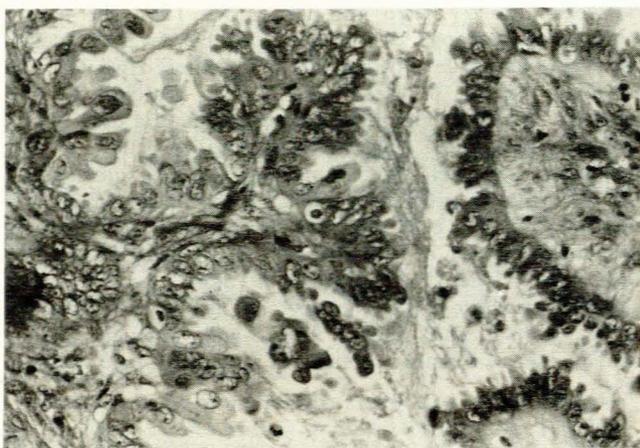


Fig. 3. Well-differentiated serous adenocarcinoma with individual cell anaplasia. Even this degree of differentiation is not acceptable for the diagnosis of PPPN (H and E x 400).

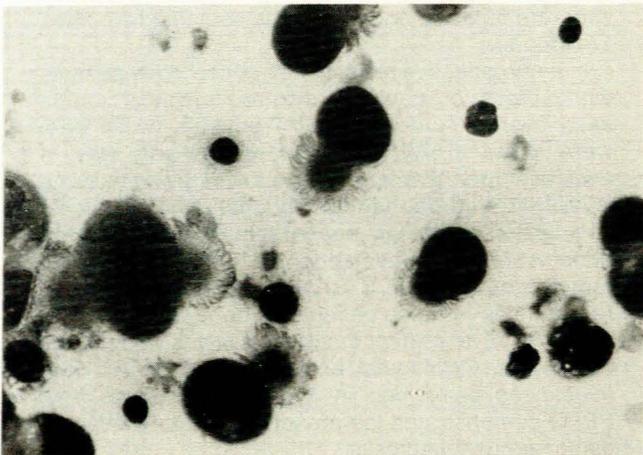


Fig. 5. PPPN — highly differentiated tufted cells in an ascitic fluid specimen (Giemsa x 1 000).

The clinical data of these 4 patients were as follows: 1 patient was in clinical stage I, 2 were in stage II, and 1 was in stage III. At operation ascitic fluid specimens were sent for cytological examination in 3 of the 4 patients; all 3 contained highly differentiated serous tufted cells with cilia present in a brush-border fashion (Fig. 5). Similar cells were found in only 1 patient with ovarian carcinoma out of a total of 37 in whom ascitic fluid or peritoneal washings had been examined cytologically. This patient had a well-differentiated serous adenocarcinoma with epithelial stratification, 1 - 4 mitoses per high-power field (x 400), and focal necrosis.

The histopathological findings were similar to those described by Genadry *et al.*¹ in all 4 patients with PPPN. There were interesting additional findings in 3 of the patients. In 2 patients moderate quantities of intraluminal mucin were found on periodic acid-Schiff and diastasis staining. The third patient's tumour was a 'classic' PPPN except for a single high-power field (x 400) in which 2 mitoses were noticed. In the presence of the overwhelming 'classic' features it was decided to classify this tumour as PPPN.

Treatment in all 4 patients had been primarily surgical, namely total abdominal hysterectomy and bilateral salpingo-oophorectomy. Additional treatment consisted of chemotherapy (2 patients) and radiotherapy (1 patient). The patients had been followed up for 3, 3, 8 and 4 years, with no tumour recurrence in any of them. In contrast, a 5-year survival rate

of 29,1% was found in 24 patients with serous or papillary adenocarcinoma. All but 3 patients in the study group had a minimum follow-up period of 2 years, and the 2-year survival rate was 58,1% in 43 patients. The remaining 3 patients had a follow-up period of at least 20 months, and 2 are still alive. Ten patients with carcinoma were lost to follow-up.

Discussion

Apart from minor differences in emphasis, a number of authors have agreed in general on the histopathological criteria for the diagnosis of serous adenocarcinoma,⁷⁻¹¹ and also of borderline serous tumours.^{3-6,8-10} PPPN must therefore be considered a separate disease entity because the diagnosis is subject to different criteria.¹ The biological behaviour of PPPN is also different from that of borderline and malignant serous tumours, since it is practically a benign disease.

The finding of highly differentiated serous tufted cells on cytological examination of ascitic fluid, previously described in some patients with serous ovarian adenocarcinoma,¹² was in this study indicative of the presence of a well-differentiated tumour. These cells were present in all 3 patients with PPPN who had been examined for them, but in only 1 patient out of 37 with carcinoma who underwent cytological examination of ascitic fluid or peritoneal washings. The presence of these cells

should therefore remind the pathologist to look for the presence of PPPN.

The cause of PPPN is still unknown. Genadry *et al.*¹ regard it as a primary peritoneal tumour induced by a peritoneal irritant. Talc, asbestos or viruses are possible irritants, gaining entry into the peritoneal cavity via the genital canal. The ovaries, pelvic peritoneum and later the whole peritoneum are affected, but PPPN is an *in situ* lesion and can remain in this state for years.

The results of this study indicate that PPPN exists as a disease entity, and forms 6,5% of serous and papillary ovarian adenocarcinomas seen at Tygerberg Hospital. This 6,5% is of importance from the clinician's point of view, because of the very good prognosis. It is also important for research, not only in respect of a search for the causation of ovarian carcinoma but also in the evaluation of survival statistics. Inclusion of these patients in series of patients with ovarian carcinoma might falsely improve the survival rates.

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A comparison of the effects of tobramycin and netilmycin on the functions of human polymorphonuclear leucocytes and lymphocytes *in vitro* and *in vivo*

R. ANDERSON, A. C. FERNANDES, H. A. EFTYCHIS, G. JOONÉ,
A. J. VAN RENSBURG

Summary

The effects of the antimicrobial agents tobramycin and netilmycin on the functions of human polymorphonuclear leucocytes (PMNLs) and on the mitogen-induced transformation of lymphocytes have been investigated both *in vitro* and *in vivo* before and 1 hour after a single intramuscular injection of the antibiotics. Neither antibiotic affected the migratory, phagocytic or antimicrobial capacities of PMNLs or the proliferative responses of lymphocytes to mitogens, at therapeutic concentrations or at 10-100-fold

greater than therapeutic concentrations. Likewise, no alterations in these leucocyte functions accompanied the intramuscular injection of either antibiotic. Neither tobramycin nor netilmycin therefore interferes with host immunodefence mechanisms.

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Division of Immunology, Department of Medical Microbiology, Institute of Pathology, University of Pretoria

R. ANDERSON, PH.D.

A. C. FERNANDES, F.A.S.M.L.T. (S.A.)

H. A. EFTYCHIS, M.SC.

G. JOONÉ, DIP.MED.TECH. (MICROBIOL.) (IMMUNOL.)

A. J. VAN RENSBURG, M.D.

The aminoglycoside antibiotics gentamicin and amikacin at therapeutic concentrations have been reported to inhibit the migration of polymorphonuclear leucocytes (PMNLs) *in vitro*.^{1,2} Administration of these agents to normal healthy adults in therapeutic doses was also found to result in decreased PMNL chemotaxis.³ This decreased PMNL migration was transient, lasting about 24 hours, and followed the intramuscular injection of a single 500 mg dose of amikacin or an intramuscular injection of gentamicin at doses of 1,25 or 2,5 mg/kg. The authors concluded that their findings may be of clinical significance, especially when a patient with altered host defence mechanisms requires antimicrobial chemotherapy.