CIRCULATING IMMUNE COMPLEXES IN OVARIAN CANCER

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SUMMARY

Thirty-eight patients of ovarian of cancer were studied for the presence of circulating immune complexes (CIC) before and after treatment. The serial assays were correlated with the tumour burden and outcome of disease in all patients, and with the result of second-look laparotomy in five of these patients. Thirty-six normal women were also studied for the presence of immune complexes, 94.4% of patients with ovarian malignancy showed the presence of CIC compared to 5.6% of normal women. The levels of CIC correlated well with the tumour bulk and the outcome of disease, as well as with the results of second-look laparotomy. Thus, it appears to have a useful role for selecting patients who require more aggressive management and for monitoring the disease process. It may also eliminate the need for the second-look operation in selected cases.

Introduction

Ovarian cancers comprise 25% of all genital maligancies but despite advances in management, the overall cure rate remains 30-35% as most patients are in advanced disease by the time of detection (McGowan, 1973). There is also no method to detect early recurrence in asymptomatic patients.

Though a good correlation has been reported between the levels of circulating immune complexes (CIC) and the prognosis of different forms of cancer e.g. of the cervix (Seth et al, 1979), breast (Hoffken et al, 1977), leukaemia (Carpentier et al, 1977), neuroblastoma (Brandeis et al 1978), results in ovarian malignancy are controversial.

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Material and Methods

Thirty eight patients with malignant ovarian tumours attending the A.I.I.M.S. Hospital were included in the study. Thirty six normal healthy women formed the control group. Both groups were matched for age, marital status and parity. Women with other causes of raised immune complexes like autoimmune disorders, acute and chronic inflammations were excluded from the study.

Five ml. venous blood was collected from every woman before start of treatment (surgery/chemotherapy) and at four - monthly intervals thereafter. The serum was separated and stored at - 20°C. It was tested for immune complexes by the Polyethylene Glycol (PEG) precipitation test by the method of Seth & Srinivas (1981). The result was expressed as PEG index from the formula:-

PEG index = (E 450 with PEG) – (E 450 with BBS) x 1000. Except for two patients, all patients underwent laparotomy and were staged according to the criteria laid down by the International Federation of Gynaecology and Obstetrics in 1975. The diagnosis of ovarian cancer was established by histopathology.

Results

94.4% woman with malignant ovarian tumours were positive for CIC as compared to 5.6% of control (P<0.01).

The mean initial value in the group subsequently found to have complete response was significantly lower (P<0.01) as compared to the group with partial response and those who had progressive disease but no significant difference was noted between the latter two groups - (Table I).

The PEG indices were studied at follow-up with respect to the outcome of disease. In the group with complete response, the decrease of PEG indices at first and second follow-up was statistically significant (P<0.001 and P<0.01 respectively). In the group with partial response, though there was an increase in

TABLE-I
PEG INDEX IN RELATION TO OUTCOME OF DISEASE

Study Group	Number in each group	PEG Index mean ± S.D.	No. +ve for CIC*	% Positive for CIC
Controls	36	25.1 ± 12.5	2	5.6
Malignant Overian Tumours				
Complete response	15	115.1 ± 51.3	13	86.7
Partial response	6	151.8 ± 51.3	6	100.0
Progressive disease	17	171.5 ± 73.4	17	100.0
Total	38	143.6 ± 66.0	36	94.4

* No. + ve for CIC means PEG index value = control mean value + 2 S.D. = 50.1 was taken as cut off point.

TABLE II
PEG INDICES DURING FOLLOW-UP OF OVARIAN CARCINOMA WITH RESPECT TO OUTCOME OF DISEASE

Group	PEG indices during follow-up (mean S.D.)			
	Initial (No.) x ± S.D.	4 Months (No.) x ± S.D.	8 Months (No.) x ± S.D.	12 Months (No.) x ± S.D.
Complete response	(15) 115.151.3	(13) 45.3 32.2	(2)40.5 ±21.5	(1) 24.3 ±10.1
rtial response	(6) 151.8 ± 51.5	(6) 173.5 ±59.3	(2) 176.0 ± 104.7	(1) 166.0
ssive	(17) 171.5 ± 73.4	(8) 174.9 ± 86.2	(2) 181.5 ± 48.8	(1) 354.0

PEG index at first follow-up, it was not statisfically significant. In the group with progressive disease, an increase was noticed in the PEG index, but the increase was not statisfically significant based on the present sample — (Figure I).

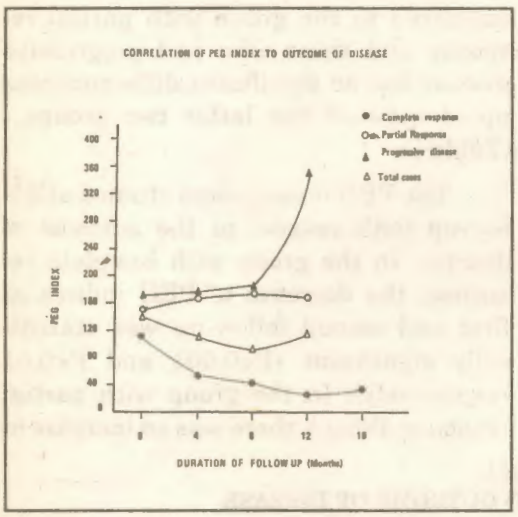

Fig. 1
Correlation of PEG index to outcome of disease

There was a significant difference ($P<0.001$) between the values of PEG index of the cases compared with their controls.

Discussion

Similar results have been found by other authors (Poulton et al, 1978, Clayton et al, 1982, Dodd et al, 1983) using PEG precipitation techniques which have been more useful in ovarian cancer than any other methods of CIC detection, e.g., assays based on complement binding (Teshima et al, 1977, Poulton et al, 1978, Price et al, 1981). This has been shown to be related to differences in solubility of complexes from these patients in comparison with complexes present in non-neoplastic conditions (Mooney et al, 1983 B)

Five patients underwent second-look laparotomy on completion of chemotherapy. Three of these had no evidence of residual disease. In these patients, the PEG index values had already fallen to low levels equivalent to control. Two patients who had high PEG index values were found to have residual disease on second-look laparotomy. Clayton et al, (1982) also found a good correlation between the results of the second-look laparotomy and the PEG index levels. On the other hand, Mooney et al, (1983 a) found no significant difference in CIC levels with minimal residual and no residual disease.

Two patients continued to have high levels of CIC at follow-up, even though there was no evidence of disease. On further follow-up they showed a recurrence at the vaginal vault. This reflects a similarity to the results of Clayton at al, (1982), who clearly demonstrated a rise in serum immune complexes prior to the clinical detection of recurrence. Similar results were seen by Poulton et al (1978), in relapse of ovarian cancer and by Hoffken et al (1977), and Seth and Seth (1984), in breast cancer.

The correlation between tumour load and CIC levels indicates that at least some proportion of the CIC must be formed from antigens shed from the tumour. Efforts are in progress to identify the antigen. Stimson and Farquharson, (1981) have used the technique of monoclonal antibodies for antigen determination. It is hoped that further development in hybridoma technology may help in the identification of the antigen which would make this method more specific.

Meanwhile, this test appears to have good potential for determining the pro

nosis of the disease and monitoring the status of the malignancy on serial samples. It also appears to be of value in forecasting the results of the second-look operation. Therefore, it may help to screen those patients who require more aggressive management at initial presentation and it may do away with the need for second-look laparotomy in selected cases.

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