ROLE OF SERUM IMMUNOGLOBULINS IN THE CLINICAL MANAGEMENT OF CANCER CERVIX

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SUMMARY

Estimation of serum immunoglobulins (IgG, IgM and IgA) has been done in 40 cases of cancer cervix, 10 women were taken as control. The levels of all serum immunoglobulins were found to be significantly raised in the cancer cervix patients. The levels of IgG showed a decreasing trend with the advancement of cancer, while IgM and IgA followed an increasing pattern. After tumour ablation by surgery or radiotherapy on 10th day, IgG and IgA levels decreased significantly while IgM further increased. The levels were found to increase with recurrence.

Introduction

Quantitative analysis of some tumour marker substances has begun to have an impact on the clinical management of cancer cervix patients. It is in this context that we have tried to ascertain the relationship between levels of certain immunoglobulins (IgG, IgM and IgA) in the cancer cervix patients and the severity of the disease. The effect of treatment and recurrence of the tumour on the immunoglobulins concentration has also been studied.

Material and Methods

Forty women having histopathologically proved cancer cervix were selected. Ten healthy women were taken as controls. The cases were properly matched in age, parity and socio-economic status. The test group was further divided according to Broder's (1926) histopathological grading as follows:

Carcinoma in situ—3 patients		7.5%
Squamous cell carcinoma—		
Grade I	5 patients	12.5%
Grade II	21 patients	52.5%
Grade III	11 patients	27.5%

The sera samples of all the subjects were studied before commencement of therapy. Six females were also studied on 10th day after operation and another 6 after complete course of radiotherapy. For collection of sera, we took 5 ml of patient's blood in a clean dry vial, sera were separated at room temperature, centrifuged for better results and stored at 20° C until analysed.

Radial gel immunodiffusion technique of Mancini *et al* (1965) was applied for the estimation of immunoglobulins using tripartigin agar plates supplied by immunodiagnostics. Undiluted sera was

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used for IgM estimation while for IgG and IgA it was diluted with isotonic saline in a ratio of 1:10 and 1:2 respectively. The evaluation of precipitin rings were made after 50 hours for IgG and IgA and after 80 hours for IgM. The readings were obtained by plotting the values on a semilog graph paper with that of controls in different dilutions. The results were analysed statistically.

Results and Discussion

The serum immunoglobulin levels reflect the balance of an interaction between immunoglobulin production and their destruction which occurs throughout the body. The levels of all the 3 immunoglobulins were found to be significantly raised in the cancer cervix patients as compared to the controls. The mean values of serum IgG, IgM and IgA in controls were 1420 ± 61.64 mg/dl, 184.12 ± 52.08 mg/dl and 146.87±33.53 mg/dl respectively while in cancer cervix these were IgG 2123.12 ± 206.49, IgM 360.29 ± 150.99 and IgA 395.8 ± 106.27 (Table I). Statistically the difference in IgG level, when compared with the normal, was found to be highly significant ($p < .001$). The next in order of significance was IgA ($p < .01$). On the other hand the rise in IgM level was not found to be significant statistically. Our observations are in agreement with that of Sinha *et al* (1985). He explained this rise to be due to non-specific antigenic stimulus because of tissue destruction by the tumour. This indicates the protective role of IgG and IgA on female genital organs against carcinogenic agents. It also signifies the immunological surveillance and defence existing in the body of the patient during early stages of cancer cervix.

TABLE I

Serum Immunoglobulin Levels in Control and Different Grades of Cancer Cervix Patients

(mg/dl)

Immunoglobulins		Controls (n = 10)	Cancer Cervix (n = 40)	Cancer-Situ (n = 3)	Grade-I (n = 5)	Grade-II (n = 21)	Grade-III (n = 11)
IgG	Range	1100 1800	1864-2416	2218-2416	2200-2389	2018-2206	1900-2100
	Mean	1420	2123.12***	2284	2291.6	2095.43	2000
	±S.D.	61.84	206.49	93.34	84.40	71.62	26.96
IgM	Range	124.20-287.50	130.70-679.70	130.70-237.90	194.10-237.90	194.10-586.10	220-679.70
	Mean	184.12	360.29*	187.56	267.12	366.80	400.40
	±S.D.	52.08	150.99	44.00	90.73	139.19	105.50
IgA	Range	102.10-202.60	149.40-599.40	149.40-255.50	149.40-255.50	338-555.90	338.40-599.40
	Mean	146.87	395.80**	164.20	197.94	513.64	535.25
	±S.D.	33.63	106.27	61.68	91.96	70.00	103.17

*** $P < .001$ Highly significant. ** $0 < .01$ Highly significant. * $P < .05$ Significant

On estimation of these levels in the different grades of cancer cervix we found significant rise in the concentration of serum IgA with the increasing histological grades of the disease. The difference in the levels of IgA in carcinoma in situ and grade III was found to be highly significant statistically ($p < .01$). Similarly IgM levels also increased but this rise was not significant statistically ($p > .05$). In contrast to this IgG showed an initial rise in its levels but later on with advancement of cancer the values decreased with a highly significant $p < .01$, though the level was still higher than the controls (Table I).

The initial rise in IgG levels could be due to intensive antigenic stimulation and further decline was probably due to exhaustion of the regional lymphatic system denoting knockdown of immunological responses or a block in the B-lymphocyte funcion. It is also seen that with the advancement of cancer there occurs some change in the antigenic nature of the tumour for which the immune system of the body fails to respond. Our findings are in support of Gupta *et al* (1980) and Ramaswamy *et al* (1986). In contrast to this Sharma *et al* (1971) and Chaddha *et al* (1984) reported an increasing pattern in the levels of IgG with the increasing grades of disease.

The increasing levels of serum IgA with the advancement of cancer cervix might be due to increased production of this antibody by the tumour cell itself as the IgA can be demonstrated in the cervical secretion of cancer cervix patients in abundance. It is also seen that there is high incidence of intra uterine infection in the cancer cervix patients. Our findings are consistent with those of Gupta *et al* (1980), Aggarwal *et al* (1985) and Ramaswamy *et al* (1986).

On 10th day after operation or after full course of radiotherapy S. IgG and S. IgA levels decreased. The fall in IgG level was found to be significant ($p < .05$) while that of IgA was not significant ($p > .05$). In contrast to this IgM concentration increased after tumour ablation (Tables II and III). The decrease in IgA and IgG levels after tumour ablation might be due to none or very small amount of tumour tissue left in the body to produce antigenic stimulus which will in turn reflect decline in the antibody formation. The rise in IgM could be due to non-specific effect of surgery or radiotherapy.

Two patients of cancer cervix, 6-8 months after therapy showed again a rise in immunoglobulin levels (Table IV). On further investigation they were found to

TABLE II

Levels of Immunoglobulins in Pre and Post Operative Cases

		IgG	IgM	IgA
Pre-operative				
(n = 6)	Range	2020-2200	237-562.700	480-590
	Mean	2100	374.11	523.33
	±S.D.	74.83	108.18	47.84
Post-operative				
(n = 6)	Range	1700-2000	586.10-737.20	338.40-500
	Mean	1900	642.50	429.46
	±S.D.	34.00	59.55	73.46
		p <.01	<.05	>.05

TABLE III
Levels of Immunoglobulins in Pre and Post Radiation Cases

		IgG	IgM	IgA
Pre-Radiotherapy				
(n = 6)	Range	1900-2100	539.30-697.70	338.40-500
	Mean	2000	570.50	412.80
	±S.D.	81.65	24.90	66.59
Post-Radiotherapy				
(n = 6)	Range	1800-2000	679.70-855.20	300-400
	Mean	1866.66	757.37	346.66
	±S.D.	74.54	73.05	47.40
		p <.05	p <.01	p >.05

be having recurrence of cancer cervix. Thus, we found that the levels of immunoglobulins in the sera of cancer cervix patients correlates well with the severity of disease, with the clinical response to therapy and recurrence.

TABLE IV
Mean Value of S. Igs in Pre-operative, Remission and Relapse States
(n = 2) in mg/dl)

	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)
Pre-Oper.	— 2000	370	520
Remission	— 1900	540	425
Relapse	— 2100	400	500

Conclusion

We observed that the high levels of serum immunoglobulins in cancer patients appear even in the earliest stage of development of the disease. Therefore if estimated, these may help in diagnosing cancer cervix in quite an early stage. This early detection of carcinoma will have a definite impact on the treatment and on the prognosis of the patients. We can also monitor the effects of treatment by estimating serum immunoglobulins in pre and post-treatment cases. It may as well help in diagnosing the recurrences. More elaborate and intensive work is still required in the field of tumour immunology to make it useful in the clinical management of cancer cervix patients.

References

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