The sero-immunological response to antiblastic chemotherapy of cancers of the female genital tract

by
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The natural defence mechanisms against malignant neoplasms are principally of an immunitary type and are brought into action by the formation of antibodies ([1, 2, 3, 4, 5, 6]) and/or cytotoxic lymphocytes ([7, 8, 9]) and the intensity of this immunity response is directly related to the prognosis and metastasization ([10, 11, 12, 13]).

Although patients suffering from gynaecological carcinomas often produce anti-tumour antibodies ([4, 14, 15]) demonstrable in the serum, these circulating antibodies may however be absent in the presence of large tumour masses or in extensive metastasization ([4]). In practice, while initially the host organism reacts to the neoplasia with an immunity response, in subsequent phases it may become incapable of reacting immunologically. This anergy, demonstrable with chemical ([16]) and biological antigens ([17, 18]), may simply be due to cachexia or to substances produced specifically by the tumour ([19, 20]).

In the treatment of gynaecological cancers numerous antiblastic drugs are in use which have at the same time an immunosuppressive action; it is important therefore to study the potential cellular and humoral immunity during chemotherapy for such cancers.

The methods of cytostatic treatment should therefore avoid an excessive lowering of cellular immunity and reduce the seroimmune response which prevents the appearance of blocking antibodies and thus stimulate the lymphocyte action on the neoplastic cells. The extent of the seroimmune response is therefore an important element in defining in each case the efficacy of once chemotherapy, and for the selection of the dosage of the drugs and the most suitable pharmacological combination.

In the present paper we report studies of the variation in humoral immunity as measured by the concentration of immunoglobulins in the serum after antiblastic therapy in patients affected with malignant neoplasms of the female genitalia.

MATERIAL AND METHODS

The changes in the serum immunoglobulins were analyzed in 40 patients suffering from malignant gynaecological tumours demonstrated histologically, viz: 31 cases of carcinoma of the cervix, 2 cases of carcinoma of the vulva, 1 case of chorionepithelioma, 2 cases of ovarian carcinoma and 4 cases of adenocarcinoma of the endometrium. Specimens were taken before and after treatment by intravenous cyclophosphamide in doses of 200 mg/day for 5 days.

Estimations of the serum immunoglobulins were carried out by the technique of radial immunodiffusion on plates, according to Mancini et al. ([21]).

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RESULTS

The results are summarized in the following tables:

Table 1. *Serum immunoglobulins in patients suffering from gynaecological neoplasms (mg per 100 ml).*

	Ig A	Ig G	Ig M.
Average	253.1	1198	67.2
Standard deviation	22.8	244	40.6
Standard error	5.3	57	9.6
P	<0.001	<0.001	<0.001

Table 2. *Serum immunoglobulins after antiblastic chemotherapy (mg per 100 ml).*

	Ig A	Ig G	Ig M.
Average	214.0	1374	183.0
Standard deviation	44.1	360	130.4
Standard error	9.1	69	25.0
P	<0.001	<0.001	<0.001

Examination of the tables shows the large variations in the IgM fraction both before and after treatment. Statistical comparison of the three fractions gives the following results:

Table 3. *Statistical significance of the differences before and after antiblastic chemotherapy.*

	Before	After	Difference	P
Ig A	253.1	214.0	− 39.1	<0.001
Ig G	1198	1374	+ 176	<0.001
Ig M	67.2	183.0	+ 115.8	0.5-0.1

Discussion

The levels of the immunoglobulins in the serum before chemotherapy were all within normal limits except for Ig M's which, though showing wide individual variations, are on average below physiological limits. In this connexion, the data in the literature are rather conflicting. In mammary cancer there may be an increase only in the Ig A fraction while in bronchial carcinoma there can be an increase of both Ig A's and Ig G's ([22]) or an increase of Ig A and a reduction in Ig G ([23]).

In cases of melanoma both Ig M's and Ig G's are usually diminished, especially the former. In our experience, antiblastic chemotherapy, in the somewhat reduced

dosage used, induces a diminution of Ig A's and an increase in Ig M's, which is statistically significant, but there is no variation in Ig G's. In similar clinical conditions, but with greater doses of cyclophosphamide, on the other hand, there is a marked immunosuppressive effect with a reduction especially of the Ig G's, followed by that of the Ig M's and Ig A's ([25]). Similar results have been obtained using triethylenethiophosforamide in cancers of the breast and ovary ([26]).

It is well known that the response of the host organism to a neoplasm also includes blocking humoral factors which protect the tumour cells from cellular immune factors. In other words, antigen-antibody complexes are formed which attack the immunocompetent lymphocytes, thus preventing the destruction of the tumour by the cellular antibodies ([27]) and immunosuppressive drugs may also interfere. The useful effect of antiblastic chemotherapy, apart from its direct cytotoxic action, may occur when it impedes the formation of blocking humoral factors (the depression of which almost always has lethal consequences) without affecting cellular immunity.

In our cases the dosage of antiblastic therapy used only reduces the Ig A fraction, the Ig M's being within normal limits though slightly depressed.

Bearing in mind that the real effect of humoral immunity in the control of tumour growth is practically unknown, in the light of the hypotheses put forward the systematic study of the immunoglobulins during chemotherapy for cancer promises to be a useful parameter in determining the best method of carrying out oncochemotherapy.

SUMMARY

The modifications of the serum immunoglobulins after oncochemotherapy in gynecological cancer have been studied.

Before oncochemotherapy only the IgM are decreased, but IgA and IgG are within the normal range.

After oncochemotherapy IgA are decreased, IgM are increased and IgG are unchanged.

The clinical significance of these variations is discussed.

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Tetrazolium staining in cytology of cancer of the female genitalia

by

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INTRODUCTION

On the basis of previous investigations Ku et al. ([1]) developed a simple cytological technique for the diagnosis of cervical cancer with which they obtained satisfactory results.

The purpose of this paper is to evaluate the diagnostic accuracy of the method in malignant tumors of the female genital organs.

MATERIAL AND METHODS

The analysis comprises 10101 clinic patients, some of whom were hospitalized and others ambulatory ([2]).

The test was performed by the following technique:

a) with the aid of a speculum the upper end of the vagina is visualized and washed several times under high pressure with 8 to 10 ml of the reagent described by Ku et al. The lavage is carried out with an ordinary glass cytology pipette provided with a rubber bulb;

b) the washings from the vaginal voult are collected in a centrifuge tube and kept in a thermostatic bath at 37 to 38 °C for one hour or at room temperature for at least two hours;

c) one drop of the reddish sediment which has formed spontaneously is then placed on a microscopic slide and a coverglass;

d) the sediment is examined microscopically and a search made for cells whose cytoplasm is filled with refrangent granulation of a brilliant orange-red color.

If cells answering to this description, of strawberry-like appearance and at least three times bigger than a leukocyte are detected, the result of the cytochemical test must be regarded as positive for cancer.

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