

IMMUNOAUTORADIOGRAPHIC DETERMINATION
OF β_1 -G-GLOBULIN IN THE BLOOD SERUM
OF PATIENTS WITH TROPHOBLASTIC TUMORS

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The results of determination of β_1 -G-globulin by immunoautoradiographic (IAR) and immunodiffusion (ID) methods in the blood serum of patients with trophoblastic tumors are compared. When negative results were obtained by the ID method, β_1 -G-globulin was found by means of the IAR method in seven of eight tests in chorionepithelioma of the uterus before treatment and in seven of 21 tests of the blood serum from patients of the same group after treatment. In the early stages of development of chorionepithelioma of the uterus (the state after hydatidiform mole, malignant hydatidiform mole) β_1 -G-globulin was found by the IAR method 4.5 times more frequently than by the ID method. This globulin was also found by the IAR method in testicular teratoblastoma with elements of chorionepithelioma. No β -globulin could be found by the IAR method in the blood serum of other oncologic patients or donors.

KEY WORDS: trophoblastic tumors; β_1 -G-globulin; immunoautoradiography; method of diagnosis.

The writers showed previously [2, 3] that a β_1 -G-globulin, one of the specific proteins of the so-called zone of pregnancy [1, 5-8], can be found by immunodiffusion (ID) analysis in the blood serum of patients with trophoblastic tumors (hydatidiform mole, malignant hydatidiform mole, chorionepithelioma of the uterus). The ID method is known to possess relatively low sensitivity and to reveal various antigens present in concentrations of 1-3 μ g protein/ml.

It was considered that an increase in the sensitivity of the method of determining β_1 -G-globulin would enable a more effective diagnosis to be made of trophoblastic tumors in general and of chorionepithelioma of the uterus in particular.

In the investigation described below an attempt was made to determine β_1 -G-globulin in the blood serum of oncologic patients by means of the highly sensitive immunoautoradiographic (IAR) method as previously suggested for the study of α -fetoprotein [4].

EXPERIMENTAL METHOD

Antiserum against β_1 -G-globulin was obtained by immunization of rabbits with the β -globulin fraction of the blood serum from women in childbirth, isolated by preparative electrophoresis or agar gel. The technique of immunochemical identification of β_1 -G-globulin was described previously [1]. The test system,

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TABLE 1. Immunoautoradiographic Determination of β_1 -G-Globulin in Blood Serum of Oncologic Patients (no β_1 -G-globulin could be detected by the ID method)

Diagnosis	Result of Determination*	
	Before treatment	After treatment
Chorionepithelioma of uterus	7/8	7/21
Trophoblastic tumor after hydatidiform mole, malignant hydatidiform mole	12/17	0/3
Teratoblastomas of the testis, seminomas, embryonic carcinoma of the testis	1/7	0/18
Adenocarcinoma of the ovary, carcinoma of the cervix or body of the uterus, fibromyoma, hypernephroma	0/36	Not detected

* Numerator shows number of patients with positive results by IAR method; denominator gives total number of patients.

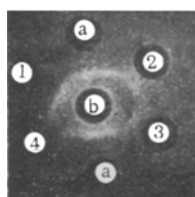


Fig. 1

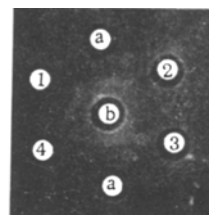


Fig. 2

Fig. 1. IAR determination of β_1 -G-globulin in blood serum in chorionepithelioma of uterus: a) antigen of standard test system in dilution of 1:16; b) antiserum against β_1 -G-globulin in a dilution of 1:16; 1, 2, 3) individual sera of patients with chorionepithelioma of the uterus; 4) blood serum of a woman donor.

Fig. 2. IAR determination of β_1 -G-globulin in blood serum in teratoblastoma of the testis: a) antigen of standard test system in dilution of 1:32; b) antiserum against β_1 -G-globulin in dilution of 1:32; blood sera: 1) of patient with teratoblastoma of testis with elements of chorionepithelioma, 2) of patient with teratoblastoma of testis (embryonic carcinoma), 3) of patient with seminoma, 4) of male blood donor.

consisting of monospecific antiserum against β_1 -G-globulin and a solution of standard antigen, was diluted 8, 16, and 32 times. With these dilutions of the standard test system, precipitation bands during ID analysis became invisible and in order to detect them the agar plates were treated with antibodies against rabbit γ -globulin labeled with radioactive I^{125} . The method of IAR analysis for work with a standard test system was described in detail earlier [4].

The blood sera for investigation were first concentrated by 4 times (Lifogel, lyophilization), with a consequent further increase in the sensitivity of the method of determination of β_1 -G-globulin. It can be taken that for IAR analysis with preliminary concentration of the serum the sensitivity of the method of determination of β_1 -G-globulin was from 64 to 128 times greater than that of the ID method.

Altogether 228 individual samples of blood serum, taken at different stages of the disease from 110 oncologic patients, and 34 sera of blood donors (men and women) were investigated.

TABLE 2. Comparison of Results of Determination of β_1 -G-Globulin by ID and IAR Methods in Blood Serum of Patients with Trophoblastic Tumors of the Uterus

Diagnosis	No. of patients	No. of positive results	
		ID method	IAR method
State after hydatidiform mole	10	1	7
Malignant hydatidiform mole	8	2	7

EXPERIMENTAL RESULTS

The results of determination of β_1 -G-globulin by the IAR method in the blood serum of patients in which this protein could not be detected by the ID method are given in Table 1. The comparatively frequent coincidence between a positive test for β_1 -G-globulin and the diagnosis of chorionepithelioma of the uterus will be noted. Before treatment, in seven of eight patients with chorionepithelioma of the uterus (without metastases in other organs), β_1 -G-globulin was in fact found in their serum (Fig. 1). After surgical (hysterectomy) and chemotherapeutic treatment, the reaction for β_1 -G-globulin remained positive in one-third of the patients (Table 1) with chorionepithelioma of the uterus. This result could point to ineffectiveness of the treatment given.

A high percentage of positive tests on blood sera also was obtained with the group of patients after hydatidiform mole or under observation because of the suspected possible development of chorionepithelioma of the uterus.

In the control group of patients (teratoblastoma of the testis, seminoma, carcinoma of the uterus, adenocarcinoma of the ovaries, etc.), as Table 1 shows, the reaction for β_1 -G-globulin was positive (Fig. 2) in only one of 43 patients (before treatment). In that case a teratoblastoma of the testis was associated with elements of chorionepithelioma. The presence of chorionic elements in the tissue of a trophoblastoma of the testis evidently was responsible for the synthesis of β_1 -G-globulin and its secretion into the blood stream. No β_1 -G-globulin could be detected in the blood serum of clinically healthy subjects (blood donors) by the IAR method.

The development of a chorionepithelioma of the uterus is often preceded by a hydatidiform mole. Observations were made on a group of patients between 2 months and 2 years after removal of a hydatidiform mole, the ID and IAR methods both being used to determine β_1 -G-globulin in the blood serum.

Comparison of the results of the ID and IAR analyses showed (Table 2) that the frequency of discovery of β_1 -G-globulin in the serum in patients with trophoblastic tumors could be increased by more than 4.5 times by means of the IAR method. The development of chorionepithelioma of the uterus can evidently be diagnosed in this way in the early stages of its development. The discovery of β_1 -G-globulin — the specific protein of pregnancy — in the blood serum in teratoblastoma of the testis is also a promising finding for the development of a method of specific diagnosis of teratoblastomas with elements of chorionepithelioma.

The results show that the use of the IAR method for the detection of β_1 -G-globulin can increase the clinical value of the immunochemical test without reducing its specificity for the early diagnosis of trophoblastic tumors.

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