IMMUNOCHEMICAL DETERMINATION OF SERUM β_{1-g}-GLOBULIN IN PATIENTS WITH CHORIONEPITHELIOMA

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A β_{1-g}-globulin belonging, evidently, to a protein of the "pregnancy zone," was identified in the blood serum of patients with a trophoblastic tumor and a chorionepithelioma of the uterus. After surgical and/or chemotherapeutic treatment the test for the β_{1-g}-globulin as a rule became negative. It is postulated that the immunochemical test for β_{1-g}-globulin may not only be of diagnostic importance, but it may also prove useful in evaluating the results of treatment of trophoblastic tumors in general and of chorionepithelioma of the uterus in particular.

KEY WORDS: chorionepithelioma; β-globulins; immunodiagnosis.

The writers showed previously [7, 8] that during normal pregnancy a specific β_1-globulin can be identified immunochemically in the blood serum and its concentration falls rapidly in the first two weeks after childbirth. This protein cannot be found in the blood serum of men and nonpregnant women by ordinary immunodiffusion analysis, but by the use of a method of the same sensitivity the β_1-globulin begins to be detectable in the 2nd-4th week of pregnancy [9]. The β_1-globulin evidently is one of the proteins of the "pregnancy zone," where many workers consider [2-4, 6, 11-18] that from 3 to 5 antigenic components may be present.*

This paper gives the results of the immunochemical determination of the β_{1-g}-globulin in the serum of women with various tumors of the uterus and gonads and also at various times during normal pregnancy.

EXPERIMENTAL METHOD

Antisera against β_{1-g}-globulin were obtained by immunizing rabbits either with whole mixed blood serum from pregnant women (30-40 weeks) or with the β_1-globulin fraction isolated from the serum by electrophoresis on agar gel. The scheme of immunization of the animals was described earlier [7, 8]. The resulting antisera were exhausted with mixed donors' serum and with dried human blood plasma. Antisera reacting preferentially with β_{1-g}-globulin were used in the work.

Immunoelectrophoresis was carried out by Grabar's method in a semimicro modification [1]. Immunodiffusion analysis was carried out by Ouchterlony's method, modified by Khramkova and Abelev [10]. The sensitivity of the standard test system in this modification is within the range of 1-3 μg protein/ml.

*To avoid terminological confusion, the name β_{1-g}-globulin is suggested (from the word "graviditas") to describe the β_1-globulin identified previously [7] until its nature is established.

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TABLE 1. Results of Determination of $\beta_{1\text{-}g}$-Globulin in Blood Serum of Some Oncologic Patients and Pregnant Women

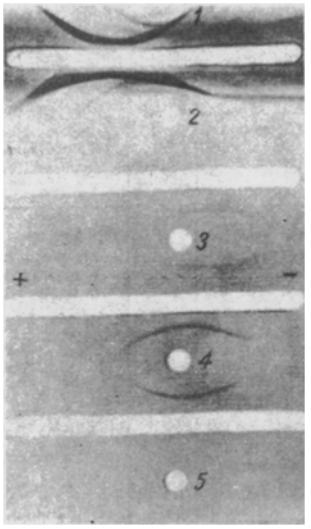
Diagnosis	Number tested	Result of determination of $\beta_{1\text{-}g}$-globulin		
		negative	positive	scatter of titers
Trophoblastic tumor of the uterus	5	2	3	1:1
Chorionepithelioma of the uterus	9	0	9	1:2—1:8
The same, after surgical and (or) chemotherapeutic treatment	19	17	2	1:1—1:2
Teratoblastoma of the ovary with elements of chorionepithelioma and embryonic carcinoma	3	3	0	
The same, with areas of mature teratoma and seminoma	4	4	0	
Fibromyoma of the uterus	38	38	0	
The same, combined with pregnancy of 4-8 weeks	18	0	18	1:2—1:32
Carcinoma of the cervix or body of the uterus	14	14	0	
Carcinoma of the ovaries	23	23	0	
Other gynecological diseases	44	44	0	
Normal pregnancy				
3—5 weeks	66	22	44	1:1—1:2
18—20 "	20	0	20	1:16—1:64
39—40 "	20	0	20	1:64—1:256
Donors:				
women	165	165	0	
men	92	92	0	
Total	540	424	116	

TABLE 2. Comparison of Results of Clinical, Pathohistological, and Immunochemical Analysis of Patients with Trophoblastic Tumors

Case No.	Clinical diagnosis	Pathohistological analysis		Results of determination of $\beta_{1\text{-}g}$-globulin	Remarks
		material	conclusion		
73/5425	Trophoblastic tumor, stage Ib	Scrapings from uterine mucosa	Marked polymorphism of chorionic epithelium, proliferation, atypia	±	Sample of serum taken before chemotherapy
73/4815	"	The same	Elements of chorionic epithelium, endometrium with decidual reaction, foci of necrosis	+	The same
73/4810	"	" "	Atypia of chorionic epithelium, suspected chorionepithelioma of the uterus	+	" "
73/1216		Not carried out		—	" "
73/2076		Not carried out		—	" "
72/5866	Chorionepithelioma of the uterus, stage IIIb	Uterus	Chorionepithelioma of the uterus	+	Sample of serum taken after chemotherapy
73/1073	"	"	Chorionepithelioma of the uterus	+	The same

*Stages of the disease correspond to L. A. Novikova's classification [5].

Altogether 540 individual samples of blood serum were tested, 177 obtained from patients and 363 from the corresponding control group (Table 1). Of the 177 patients 33 had a chorionepithelioma or trophoblastic tumor of the uterus, 100 had various oncologic diseases of the reproductive organs or gonads, and 44 had other gynecological diseases. The control group consisted of 106 women with normal pregnancy and 257 donors (both men and women).



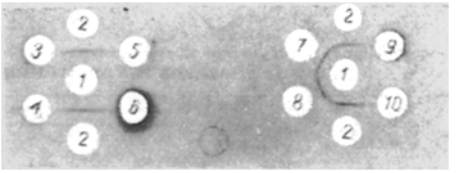


Fig. 1 Fig. 2

Fig. 1. Immunoelectrophoretic analysis of β_{1-g}-globulin in blood serum of patient with chorionepithelioma of the uterus and of a pregnant woman. Sera of: 1, 5) nonpregnant women (donors); 2) patient with carcinoma of the cervix uteri; 3) patient with chorionepithelioma of the uterus; 4) pregnant women, at 40 weeks (not the first pregnancy). Monospecific antiserum against β_{1-g}-globulin (1% solution of Difco agar, veronal–medinal buffer, pH 8.6, ionic strength 0.05; 120 V, 40 mA, duration of test 40 min).

Fig. 2. Immunodiffusion analysis of blood serum of patients with chorionepithelioma of the uterus before and after chemotherapy. Standard test system: 1) antiserum against β_{1-g}-globulin; 2) solution of standard antigen. Sera of patients with: 3, 4) adenocarcinoma of the ovary; 5, 6) carcinoma of the cervix uteri; 7, 8 and 9, 10) chorionepithelioma of the uterus before and after a full course of chemotherapy, respectively.

EXPERIMENTAL RESULTS

It will be clear from Fig. 1 that the blood serum of a patient with chorionepithelioma of the uterus and that of a healthy woman during normal pregnancy (having previously given birth to a child) contained an immunologically similar component with the electrophoretic mobility of β_1-globulins. The concentration of β_{1-g}-globulin in the serum of the patients with chorionepithelioma and trophoblastic tumors of the uterus as a rule corresponded to the level observed in the early stage of pregnancy (3-5 weeks). During the normal course of pregnancy the concentration of β_{1-g}-globulin rose comparatively rapidly as pregnancy advanced (Table 1). In every case in which pregnancy occurred in a woman with fibromyoma of the uterus the test for β_{1-g}-globulin was positive. However, the development of a fibromyoma of the uterus and also of some other tumors of the uterus (carcinoma of the cervix or body of the uterus) and of the gonads (carcinoma of the ovaries and some forms of teratoblastoma of the ovary)* was not accompanied by the liberation of β_{1-g}-globulin into the blood stream within the limits of sensitivity of the method of immunodiffusion analysis. No β_{1-g}-globulin likewise was found in the blood serum of the donors – either women (165 tests) or men (92 tests).

The results of immunochemical titration of β_{1-g}-globulin in the blood serum of the patients with trophoblastic tumors before chemotherapy and/or surgical treatment are very interesting. As Table 1 shows, the test for β_{1-g}-globulin was positive in all 9 patients with chorionepithelioma of the uterus and in 3 of

*Specimens of blood serum from patients with teratoblastoma of the ovary were generously provided by D. A. Él'gort from the Laboratory of Immunochemistry and Diagnosis of Tumors (Head, Professor G. I. Abelev), N. F. Gamaleys Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR.

the 5 patients with a trophoblastic tumor of the uterus (these diagnoses were confirmed pathohistologically). Yet of the 19 patients examined 2-20 weeks after a combination of hysterectomy and chemotherapy (15) or after chemotherapy alone (4), in 17 the test for β_{1-g}-globulin was negative. Only two patients gave a positive test for β_{1-g}-globulin after treatment, and these were patients whose condition was serious. The results of determination of β_{1-g}-globulin in the serum of patients with a trophoblastic tumor and chorionepithelioma of the uterus, in whom surgical (extirpation of the uterus and adnexa) and chemotherapentic (rubomycin, methotrexate, actinomycin D) treatment was ineffective, are given in Table 2. They show that in the early stages of transition of a trophoblastic tumor into a chorionepithelioma the reaction for β_{1-g}-globulin may be positive and that it can be used for the early diagnosis of this form of tumor.

After extirpation of the uterus for chorionepithelioma without metastases in other organs, the reaction for β_{1-g}- globulin became negative on the 10th-16th day of the postoperative period. After a complete course of successful chemotherapy of chorionepithelioma of the uterus with metastases in other organs, with monitoring of the chorionic gonadotropin level, as a rule a negative reaction for β_{1-g}-globulin also was observed (Fig. 2). Presumably β_{1-g}-globulin is synthesized both in the cells of the primary tumor focus (in the uterus) and in the metastatic nodes of the chorionepithelioma, for if metastases were present extirpation of the uterus and chemotherapy of the chorionepithelioma each led to the same decrease in the β_{1-g}-globulin level, down to a level when it could no longer be detected in the blood serum by the ordinary method of immunodiffusion analysis.

The results of this investigation show that the immunochemical test for β_{1-g}-globulin not only is of diagnostic value, but it may also prove useful in the evaluation of the results of treatment of trophoblastic tumors in general and of chorionepithelioma of the uterus in particular. However, before any final conclusions on the clinical value of the test for β_{1-g}-globulin can be drawn, further investigations are required on a large group of human tumors.

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