ONCOLOGY

CARCINOMAS WITH IDENTICAL AND WITH DIFFERENT SPECIFIC ANTIGENS

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(Received April 8, 1958. Presented by Active Member of the AMN SSSR N. N. Zhukov-Verezhnikov)

The fact, observed by us [1] in 1956, that no single antigen exists which is specific for all carcinomas occurring in man, and that tumors in the same situation may differ qualitatively in their specific antigenic properties, has received further experimental confirmation. It has been shown [2, 3] that there are tumors in which the specific carcinoma antigens are identical, and conversely there are others in which the specific antigens differ. The identity of or difference between the carcinoma antigens does not depend on the location of the tumors, their structure nor on the specificity of the normal antigens contained therein. These investigations have also established that the specific antigenic structure of the primary tumor and of its metastases is completely identical, regardless of the location of the latter. If the original tumor gave an immunological reaction with a particular specific serum, then the metastases from this tumor reacted positively, and vice versa.

We did not observe any discrepancy in the behavior of the primary tumor and of its metastases in any single case.

The existence of carcinomas with different specific antigenic properties was reported in 1957 also by the American worker Korngold [5], who used the gel-precipitation method for the analysis of the antigenic structure.

The problem of the causes of the antigenic identity of some carcinomas and the antigenic difference of others is still unsolved, and the number of groups of tumors with identical specific antigens is still unknown. The solution of these problems is not only of theoretical interest but is also important in the development of immunological methods of prophylaxis and therapy of malignant neoplasms in man.

By means of the tumor immune serum No. 388 (to tumor No. 1 – a metastasis in the liver from a carcinoma of the cecum), which we had at our disposal, we succeeded in discovering three new tumors with identical antigenic relationships: No. 46 – a metastasis in the lymphatic gland from a carcinoma of the ovary, Nos. 48 and 51 – metastases in the liver from a carcinoma of the stomach, and also in obtaining specific antisera to these tumors and using them to analyse the antigenic properties of tumors.

EXPERIMENTAL METHOD

The method of immunization of the rabbits, of freeing the sera from contamination with nonspecific antigens, and of carrying out the complement fixation test and the specific absorption experiment, which we used in the present work, were described in our previous communications [1, 4]. As antigens we used saline extracts of tissues from tumors in different situations, both crude and preserved in formalin, and also saline extracts of tissues from normal organs, also both crude and preserved in formalin – liver and spleen – which acted as controls.

EXPERIMENTAL RESULTS

In Table 1 are shown the results of the comparative study of the antigenic properties of tumors Nos. 1, 46, 48 and 51 by the complement fixation test, using antisera Nos. 388, 998, 203 and 899 produced against them.

TABLE 1

Comparative Study of the Antigenic Properties of the Tumors by the Complement Fixation Test

Tumor antisera	Dilutions of sera	Antigens from tumor tissues				Antigens from normal tissues		Serum control
		No. 1	No. 46	No. 48	No. 51	spleen	liver	
No. 388 to tumor No. 1	1:20	++++	++++	++++	+++	—	—	—
	1:40	++++	++++	++++	+++	—	—	—
	1:80	+++	++++	+++	+	—	—	—
	1:160	±	++	±	±	—	—	—
No. 998 to tumor No. 46	1:20	++++	++++	++++	++++	—	—	—
	1:40	++++	++++	++++	++++	—	—	—
	1:80	++++	++++	++++	++++	—	—	—
	1:160	+++	++++	++++	++++	—	—	—
No. 203 to tumor No. 48	1:20	++++	++++	++++	++++	+	+	—
	1:40	++++	++++	++++	++++	—	—	—
	1:80	++++	++++	++++	+++	—	—	—
	1:160	++	+++	+++	++	—	—	—
No. 899 to tumor No. 51	1:20	++++	++++	++++	++++	+	+	—
	1:40	++++	++++	++++	++++	—	—	—
	1:80	++++	++++	++++	++++	—	—	—
	1:160	++++	++++	++++	++++	—	—	—
Antigen controls		—	—	—	—	—	—	

Conventional signs: + + + +, + + +, + +, +, ± different degrees of a positive reaction; — negative reaction.

Note: Tumor No. 1 as a metastasis in the liver from a carcinoma of the cecum; No. 46 is a metastasis in the lymphatic gland from a carcinoma of the ovary; No. 48 is a metastasis in the liver from a carcinoma of the stomach; No. 51 a metastasis in the liver from a carcinoma of the stomach.

It may be seen from Table 1 that, after absorption with splenic tissue, the tumor antisera lost their nonspecific antibodies to human liver and spleen, and did not react with antigens from these organs in the complement fixation test. Conversely, each of our newly obtained sera Nos. 998, 203 and 899, like the previously obtained serum No. 388, gave a positive reaction with all the tumor antigens so tested, thereby revealing the identity of the specific antigens contained in these tumors.

The antigenic identity of tumors Nos. 1, 46, 48 and 51 was also confirmed by specific absorption experiments (Table 2). It may be seen from Table 2 that No. 203 tumor antiserum, after absorption with splenic tissue, retained its power to react with antigens from tumors Nos. 46, 48 and 51. Absorption of other portions of this serum with tissue from tumors Nos. 46, 48 and 51 led to total disappearance of tumor antibodies. We obtained similar results in an investigation of antisera to tumors Nos. 46 and 51 by the specific absorption method.

As a result of the comparative immunological study which we made of four carcinomas from different persons, further evidence was obtained in support of the existence of malignant neoplasms characterized by the common possession not only of specific antigenic but also of immunogenic properties.

The sera which were obtained, with identical immunological specificity towards the four human carcinomas, were used in our comparative study of the antigenic properties of certain human malignant neoplasms of varied location and histological structure. In Table 3 the results are shown of the study of tumors Nos. 48, 4, 43

TABLE 2

Comparative Study of the Antigenic Properties of Tumors by the Method of Specific Absorption

Tumor antigens	Tissue used for absorption of the serum	Dilutions of sera	Antigens from tissues of tumor			Antigens from the spleen	Serum controls
			№ 48	№ 46	№ 51		
No. 203 to tumor No. 48	Spleen	1:40	++++	++++	++++	—	—
		1:80	++++	+++	++	—	—
		1:160	++	++	+	—	—
	Tumor No.48	1:40	—	—	—	—	—
		1:80	—	—	—	—	—
		1:160	—	—	—	—	—
	Tumor No.46	1:40	—	—	—	—	—
		1:80	—	—	—	—	—
		1:160	—	—	—	—	—
	Tumor No.51	1:40	—	—	—	—	—
		1:80	—	—	—	—	—
		1:160	—	—	—	—	—
Antigen controls			—	—	—	—	—

Conventional signs: + + + +, + + +, + +, +, ± different degrees of a positive reaction; — negative reaction.

and 37 with the aid of serum to tumor No. 48. It may be seen from Table 3 that immune serum to tumor No. 48, when freed from nonspecific antibodies to antigens from normal organs by means of absorption with splenic tissue, gave a positive complement fixation reaction both with tumor No. 48 (metastasis in the liver of carcinoma of the stomach), i.e. with the tumor against which the serum was obtained, and also with tumor No. 4 (metastasis in the liver of carcinoma of the stomach). This serum did not react with antigens from tumors Nos. 43 (carcinoma of the lung) and 37 (metastases in the skin from carcinoma of the breast), thereby demonstrating the absence from these tumors of specific antigens identical with those of the first two tumors.

These results were also confirmed by absorption experiments (see Table 3). Treatment of the serum with tissue from tumor No. 48 or tumor No. 4 resulted in the complete loss of tumor antibodies by the serum. Conversely, after treatment with tissue from tumors Nos. 43 or 37, the serum retained its specific antibodies. Qualitative differences in the specific antigens of the tumors were shown not only with serum No. 204, but also by means of other tumor antisera of this antigenically similar group, demonstrating that the uniformity of our results does not depend on individual characteristics of the experimental animals producing the antibodies, but on the nature of the antigens used for immunization.

The results of the comparative study of the antigenic properties of the malignant tumors by means of sera to tumors Nos. 1, 46, 48 and 51 are shown in Table 4 (summarized figures). It follows from the table that the specific sera which we obtained to tumors Nos. 1, 46, 48 and 51 enable the differentiation of all the malignant tumors which we examined into two groups, clearly distinguished by the quality of their antigens: a positively reacting and a negatively reacting group. All four tumor antisera behaved perfectly identically, giving either positive or negative reactions with the test tumor. We observed no case of discrepancy in the reaction of any of these sera.

As may further be seen from Table 4, it was not possible to determine a relationship between the location of the tumor and its power of reacting or otherwise with tumor antisera. In fact the group of positively reacting tumors included, for example, metastases in the liver from carcinoma of the stomach (Nos. 4, 48, 51), but carcinomas were found in exactly the same place, i.e. metastases in the liver from carcinoma of the stomach (Nos.

TABLE 3

Absorption of a Tumor Antiserum by Tumors with Identical and Different Specific Antigens

Tumor antigens	Tissue used for absorption of the serum	Dilutions of sera	Antigens from tumor				Antigen from the spleen	Serum controls
			№ 48	№ 4	№ 43	№ 37		
No. 204 to tumor No. 48	Spleen	1:20	++++	+++	—	—	—	—
		1:40	++++	++	—	—	—	—
		1:80	++	+	—	—	—	—
	Tumor № 48	1:20	—	—	—	—	—	—
		1:40	—	—	—	—	—	—
		1:80	—	—	—	—	—	—
	Tumor № 4	1:20	—	—	—	—	—	—
		1:40	—	—	—	—	—	—
		1:80	—	—	—	—	—	—
	Tumor № 43	1:20	++++	+++	—	—	—	—
		1:40	++++	++	—	—	—	—
		1:80	++	±	—	—	—	—
	Tumor № 37	1:20	++++	+++	—	—	—	—
		1:40	+++	+	—	—	—	—
		1:80	+	±	—	—	—	—
Antigen controls			—	—	—	—	—	

Coventional signs as in Tables 1 and 2.

Note: Tumors Nos. 48 and 4 were metastases in the liver from carcinoma of the stomach; tumor No. 43 was a carcinoma of the lung; tumor No. 37 was a metastasis in the skin from carcinoma of the breast.

8, 14 and 15) which reacted negatively. Furthermore, the group of positively reacting tumors itself is quite heterogeneous in its distribution and its pathological characteristics, but united on the basis of common possession of a specific antigen. This common feature is in no way connected with the blood group of the person affected by the tumor.

The question of the number of groups into which tumors can be subdivided immunologically has still received very little study. Up to the present time the existence of three such groups of carcinoma has been proved [1, 2], distinguishable from each other by specific antigens, inherent in the tumor, and a fourth group, the largest, which is also probably a heterogeneous group of tumors, differing in its antigenic properties from the first three, but not yet differentiated from the point of view of its antigenic relationships.

The problem of the cause of the existence of carcinomas with qualitatively identical and qualitatively different specific antigens is not yet solved. It may be, however, that the antigenic identity or difference of the tumors is the result of identity or difference of the etiological factors responsible for the neoplastic process. It would appear that further facts are required in support of this hypothesis.

Our investigations thus showedthat malignant neoplasms exist which possess not only common specific antigens but also common immunogenic properties. Tumors are also found with qualitatively different specific antigens. The fact that a tumor belongs to a particular immunological group is not connected with the location of the tumor nor its structure, nor with the patient's blood group.

TABLE 4

Results of the Comparative Study of the Antigenic Properties of Human Tumor Tissues (mean values)

Tumor No.	Location of tumors	Blood group	Tumor antisera			
			to tumor no. 1	to tumor no. 46	to tumor no. 48	to tumor no. 51
1	Metastasis in the liver from carcinoma of the cecum	O	+	+	+	+
46	Metastasis in the lymphatic glands from carcinoma of the ovary	B	+	+	+	+
48	Metastasis in the liver from carcinoma of the stomach	O	+	+	+	+
51	Metastasis in the liver from carcinoma of the stomach	O	+	+	+	+
2	Metastasis in the liver from carcinoma of the gall bladder	O	—		—	
3	Primary carcinoma of the liver	B	—	—	—	—
4	Metastasis in the liver from carcinoma of the stomach	B	+	+	+	+
5	Metastasis in the liver from carcinoma of the bile duct	O	+			+
8	Metastasis in the liver from carcinoma of the stomach	O	—		—	
9	Primary carcinoma of the liver	A	—		—	—
10	Metastasis in the liver from carcinoma of the ovary	A	—	—	—	
14	Metastasis in the liver from carcinoma of the stomach	A	—		—	—
15	Metastasis in the liver from carcinoma of the stomach	B	—	—	—	
19	Carcinoma of the lung and metastases in the pleura	O	—		—	—
20	Metastasis in the liver from carcinoma of the lung	O	—	—	—	
21	Carcinoma of the stomach	A	—		—	
22	Carcinoma of the stomach	Not determined	—		—	
24	Carcinoma of the stomach		—		—	
25	Carcinoma of the stomach	A	—	—	—	
26	Metastasis in the liver from carcinoma of the lung	A	—	—	—	
37	Metastasis in the skin from carcinoma of the breast	B	—		—	—
43	Carcinoma of the lung	AB	—	—	—	

Conventional signs: + positive results of the complement fixation test and absorption experiment; — negative results of these experiments.

SUMMARY

Immunological investigations demonstrated that certain human malignant neoplasms possess similar specific antigenic and immunogenic properties. On the other hand, there are tumors which have qualitatively different specific antigens. The immunological group to which the tumor belongs is not connected with localization of the tumor, its structure or blood group.

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