ONCOLOGY

NORMAL AND PATHOLOGIC ANTIGENS IN HUMAN CARCINOMA

P. N. Kosyakov and N. I. Kuznetsova

From the D. I. Ivanovsky Institute of Virology (Director - Prof. P. N. Kosyakov),

The USSR Academy of Medical Sciences, Moscow

(Presented by Prof. V. D. Timakov, Active Member of the USSR Academy of Medical Sciences

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There is now no doubt that the cells of malignant tumors originate from normal cells and tissues. This is proven by the well-known fact that tumors may be obtained by treating normal tissues with different carcinogenic substances and also by the fact that normal tissue can be transformed into tumorous tissue in a tissue culture [10].

The fact that the biochemical and antigenic properties of cancerous tissue are extremely similar to those of normal tissue in man is another proof of the above. The tissues of cancerous tumors have been found to possess the same antigenic substances as normal, nontumorous tissues. It has been established that the same specific [4], blood-group – A, B, AB [5, 11, 13], type – M, N, MN and Rh antigens [6] are found in both the tissues of cancerous tumors and the cells and tissues of normal organs.

It has also been established that each cancerous tumor contains the same set of antigens (specific, blood-group, type) as do the normal cells and tissues in the individual with that tumor. These normal antigens, i.e., the antigens present in normal cells and tissues, appear at an early stage of human embryonic development, remain qualitatively the same throughout the individual's life and are passed on to his descendants, i.e., are the normal, isogenetic, antigenic features of the individual.

Cancerous cells originating from normal cells and tissues retain the ability of the former to synthesize blood-group, typo- and species-specific antigenic substances. Therefore, tumors vary as to their specific, isogenetic, antigenic properties in different people, as do normal tissues. However, research has also shown [1, 2, 7, 9] that cancerous cells can synthesize new antigenic substances as well, specific for the cancerous tumor only – pathological, carcinomatous antigens.

There are some researchers, however, who do not agree that the origin and development of a tumor is attended by the appearance of new antigens in it, which did not exist in the body before the tumor. These authors [12] believe that the differences between the antigenic properties in tumorous and in normal tissues are due to the fact that the body with the tumor is genetically different from other individuals providing the normal organs to be used as the control.

There is some basis for this opinion, since the methods usually used do not make it possible to exclude the existence of genetic, antigenic differences between tumors and normal tissues. Actually, tumor antigens have been compared with antigens obtained from the normal tissues of other individuals in immunological experiments with both transplanted tumors and spontaneous or carcinogenic-induced tumors. Under these conditions, normal isogenetic differences could be taken for specific antigenic differences.

To prove this hypothesis, we decided to make a comparative study of the antigenic properties of cancerous tumors and normal tissues from the same, isogenetically identical material.

Z. I. Rovnova [8] made a study similar to ours on experimental animals with implanted tumors.

EXPERIMENTAL METHODS

The object of our study was to compare the antigenic properties of cancerous tumors with those of undiseased portions of organs taken, as mentioned above, from the same individual. Tumors and healthy tissues from 18 cadavers which had died from cancer were examined repeatedly.

The antigens from the tumors and healthy tissues were prepared in a salt solution by an earlier described method [7]. Immune, antitumor wera were obtained from three kinds of animals rabbits, goats and horses.

The horses were immunized with a mixture of salt extracts from metastasized-to-the-liver cancer of the stomach, cervix and breast. The goats were immunized with salt extracts from metastasized-to-the-liver cancer of the stomach and gall bladder. The antigens used to immunize the horses and goats were first processed with glycerine to inactivate bacterial flora. The rabbits were immunized with salt extracts from metastases to the liver of cancer of the stomach.

Before the experiment, the rabbit and goat sera were subjected to absorption according to a method we developed [7] in order to remove incidental, nonspecific antibodies. The horse serum (in a definite dilution) reacted specifically with the antigen from the tumors, but did not react with the antigens from the normal tissues. When the serum reacted nonspecifically with extracts from the normal organs, we had to treat it by absorption before the experiment in the same way. We examined the antigenic properties of tumors and normal tissues by means of a complement fixation reaction at a temperature of 37°.

EXPERIMENTAL RESULTS

Table 1 shows the results obtained from the comparative study of the antigenic properties of tumors and of normal tissues taken from 6 individuals. It is clear from the table that the antitumor immune sera reacted with the salt extracts from cancerous tumor tissues, but did not react with the extracts from normal organs obtained from the same people. These experiments indicated that the tissues of cancerous tumors contain special antigenic substances, present only in the tumors and not in the tissues of the normal organs. We could not find the "cancer" antigen in the tissues of the spleen, liver, kidneys, lungs, myocardium or brain which had been obtained from cancer patients.

Therefore, from these experiments, it follows that the ability of tumors to react with the corresponding antitumor sera does not depend on the antigens which the tumors have in common with the normal organs, but is determined by the "cancer" antigens, which are only found in the tumors.

As Table 1 shows, the tumors' ability to react with the corresponding sera is not associated with the localization of the tumors or with the blood-group antigens contained in them. The antitumor sera reacted with antigens from various tumors of primary cancer of the liver and lungs and also with metastases of variously placed cancerous tumors to the liver and lungs. These sera, however, did not react with water-salt extracts from 12 other forms of tumors (Table 2).

These experiments, therefore, confirm the fact mentioned earlier [3] that cancerous tumors from different people can differ qualitatively as to specific antigenic properties. In our experiments (see Table 2), the antitumor sera reacted with the antigens of some tumors, but did not react with the antigens of others. What produces these differences in specificity found in the cancer antigens has not yet been determined, however. As Table 2 shows, one cannot connect these differences with the localization of the tumor. One must note, though, that metastases of the same tumor to different organs – the liver and lungs (see No. 8 and 12) – reacted similarly in our experiments.

As well as studying the tumors and normal tissues with antitumor sera, we also studied the antigenic properties of these tissues with sera to normal human organs, the liver and spleen.

Table 3 shows that the organo-specific sera which we obtained to the spleen and liver reacted only with salt extracts from the corresponding normal organs, i.e., with livers or spleens taken from people who had died of cancer, and did nor react at all with salt extracts from cancerous tumor tissues. None of the organo-specific antigens present in the normal organs, the liver and spleen, were found either in the extracts from the primary cancer of the liver tissue or in the extracts from metastasized-to-the-liver cancer of the stomach tissue, in spite of the fact that these extracts contained the pathologic "cancer" antigens (see Table 1, No. 693 and 694).

TABLE 1

Antigenic Differences Between Normal Tissues and Cancerous Tumor Tissues in Man

Case number	Name bl. gr. cancer victims	Tumor description	Dilution antitumor sera	Experimental tissues: Tumor	Spleen	Liver	Lung	Kidneys	Heart	Brain
633	M-v AB	Metastasis-to-liver cancer of the pancreas	1 : 20	+++++	—	—				
			1 : 40	+++(+)	—	—				
			1 : 80	+	—	—				
641	S-va 0	Metastasis-to-liver cancer of the pancreas	1 : 20	++++	±	+				
			1 : 40	+++	—	—				
			1 : 80	+	—	—				
649	K-v 0	Lung cancer	1 : 20	+++++	—		—			
			1 : 40	++++	—		—			
			1 : 80	++	—		—			
693	Zh-va 0	Metastasis-to-liver cancer of the stomach	1 : 80	++++	—		—	—	—	
			1 : 160	++	—		—	—	—	
			1 : 320	+	—		—	—	—	
694	Yu-ya A	Primary cancer of the liver	1 : 40	+++++	+	—	—	±		
			1 : 80	+++(+)	—	—	—	—		
			1 : 160	+++	—	—	—	—		
855	F-va	Metastasis-to-liver cancer of the esophagus	1 : 80	+++++	—	—	+	—		—
			1 : 160	+++++	—	—	—	—		—
			1 : 320	+++	—	—	—	—		—
857	0	Metastasis-to-lung cancer of the esophagus	1 : 80	+++++	—	—	±	—		—
			1 : 160	++	—	—	—	—		—
			1 : 320	+	—	—	—	—		—

Meaning of symbols used: + different degrees of positive reaction; ± doubtful reaction.

Note: Cases No. 633, 641, 649, 693 and 694 designate experiments done with anti-tumor serum obtained from the horse; No. 855, from the rabbit; No. 857, from the goat.

These experiments, therefore, indicate that the pathologic "cancer" antigens are immunologically isolated from normal, organo-specific antigens. When primary cancer or metastases developed in the liver, the normal, healthy liver tissues surrounding the tumor did not contain the specific "cancer" antigen in a quantity practicable for immunological analysis. The "cancer" antigen only appeared in the cells affected with cancer.

Therefore, our studies showed that in spite of the isogenetic antigens shared by normal and cancerous tumor tissues, the cancerous tissues characteristically also possess special "cancer" antigens, specific to these pathologically changed tissues. These antigens are immunologically isolated from normal (blood-group, type and organo-specific) antigens and only appear in the body during the origin and development of a cancerous tumor. There are no organo-specific antigens of the liver present in the tissue of a primary cancer of the liver or in metastases to the liver. Some forms of tumors have immunologically similar "cancer" antigens, but other forms are characterized by "cancer" antigens completely different from each other. The similarity or difference of the "cancer" antigens does not depend on the localization of the tumor nor on the specificity of the normal antigens contained in it.

TABLE 2

Discovery of the Specific Cancer Antigen in Variously Located Tumors

Tumor number	Description of tumor	Number of cases	From them with the antitumor sera	
			Reacted	Did not react
	Lung cancer	3	1	2
	Primary cancer of liver	1	1	
3	Cancer of stomach	1	—	1
4	Cancer of prostate	1	—	1
5	Bronchial cancer	1		1
6	Metastasis-to-liver cancer of pancreas	4	2	2
2	Metastasis-to-liver cancer of stomach	2	1	1
8	Metastasis-to-liver cancer of esophagus	2	1[1]	1
9	Metastasis-to-lung cancer of stomach	1	—	1
10	Metastasis-to-liver cancer of large intestine	1		1
11	Metastasis-to-lung cancer of breast	1	—	1
12	Metastasis-to-lung cancer of esophagus	1	1[1]	—

[1] Metastases of tumors from the same patient

TABLE 3

Tissues from Normal Organs and from Tumors Examined for the Presence of Organo-specific Antigens

Case No.	Name bl. gr. cancer victims	Localization of tumor	Organo-specific sera in relation to:	Dilution of serum	Results of examining antigens from tissues		
					Tumor	Spleen	Liver
691	Zh-va O	Metastasis-to-liver cancer of stomach	Spleen	1 : 10	—	++++	
				1 : 20	—	+++	
				1 : 40	—	++	
696	Yu-ya A	Primary cancer of liver	Liver	1 : 50	—		++++
				1 : 100	—		++++
				1 : 200	—		+++
				1 : 400	—		+
698	Yu-ya A	Primary cancer of liver	Spleen	1 : 40	—	+++(+)	
				1 : 80	—	+++(+)	
				1 : 160	—	++	
				1 : 320	—	+	

SUMMARY

Comparative studies of antigenic properties of cancerous tissues and of normal organs in one and the same subject demonstrated special "cancer" antigens in cancerous tissues, specific for these pathologically altered tissues.

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* Original Russian pagination. See C. B. translation.