A STUDY OF ANTIGEN SIMPLIFICATION OF HUMAN PULMONARY TUMORS IN THE PRECIPITATION IN GEL REACTION

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The phenomenon of antigen simplification of tumors is presently an established fact. It has been demonstrated that some tumors lose certain antigens which are present in the tissues from which the tumors developed. As has been established in a number of cases, the antigens being lost have an organ specific character [1, 4, 6]. It has been hypothesized that antigen simplification is no less specific than the acquirement by the tumor of specific tumor antigens [6]. Here, however, there is still much that is unclear. It is not known just how general this phenomenon is for various tumors. It is not clear whether organ specific antigens are lost in all cases or whether simplification can occur as a result of other antigens. Finally, experimental tumors have been relatively well studied in this respect, but information on the antigen simplification of human tumors is rather scanty.

In the present work we studied antigen simplification of human lung cancer.

METHODS

The tumors were obtained from those operated on at our institute and normal tissues from morgues (from the bodies of persons who died as a result of accidents or cardiovascular diseases). We used fresh tissues or tissues stored at a temperature of −15°. Hydrous salt extracts of the tumors and normal tissues (1 part tissue and 4 parts physiological salt solution) served as the antigens for immunization of the animals and for the precipitation reaction.

The corresponding serum was obtained by immunization of the rabbit with increasing doses of antigen of normal lung: 1 ml intravenously, 1 ml intraperitoneally, twice intraperitoneally with 2 ml each time, and, finally, 3 ml intramuscularly. The interval between injections was 3 days; venesection was performed on the 8th day after the end of immunization.

The serum was concentrated about 6-fold by ammonium sulfate [4]. To increase the specificity of the serum it was exhausted by adding various antigens from the normal and tumor tissues; in many cases exhaustion was done by Bjorklund's method [5]—by introducing the exhausting antigens directly into the agar. When setting up the Ouchterlony test we mainly used one of its modifications [3] with minor changes.

RESULTS

Native antipulmonary serum reacted with many antigens of the normal and malignant tissues, producing a somewhat greater reaction with the lung antigens. After neutralization by a mixture of human sera it reacted only with the antigens from the lung tissue and did not react with the antigens from other organs and from the lung tumors (Fig. 1). It is apparent from Fig. 1 that the pulmonary antigens, with the exception of one (L 4), form with the serum unique loose wide lines; furthermore, in the immediate vicinity of the central depression (see Fig. 1, c) opposite the depression with the pulmonary antigens, weak thin lines are seen. Both lines are absent in the case of antigens from other organs (see Fig. 1, a) and from the malignant lung tumor (see Fig. 1, b). A similar, but weaker reaction was given by another antipulmonary serum obtained at the same time.

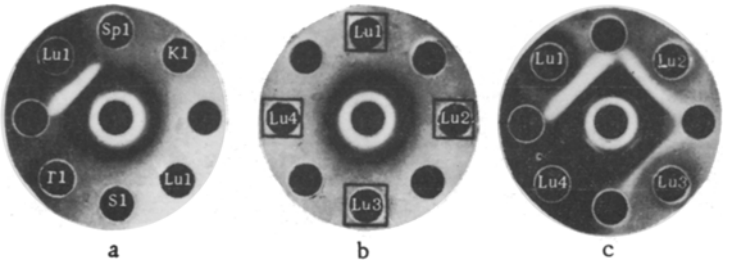

Fig. 1. Reaction of antipulmonary serum exhausted by a mixture of human serum with various antigens. Serum is in the central depression, the antigens in the peripheral depressions. Designations of antigens: Sp-spleen, K-kidney, L-liver, S-stomach, T-thyroid, Lu-lung, [Lu]-cancer tissue of lung; a, b, c) reaction with various antigens.

Thus, the lung apparently has antigens specific for it which are lost during malignant degeneration in a way similar to that which occurs in cancer of the stomach [1]. We should, however, discreetly evaluate the results of the described reactions in connection with the unique type of precipitation lines, which was somewhat unusual for the Ouchterlony reaction. In addition, when we repeated the reaction with the same serum and with the same antigens about a month later we obtained different results (Fig. 2). The wide loose lines of the pulmonary antigens disappeared or became significantly weaker and the dense thin lines, hardly noticeable before (see Fig. 1), receded from the central depression and became denser and clearly noticeable opposite the depressions with the pulmonary antigens (see Fig. 2, a). The cancer antigens, with the exception of one ([Lu5]) which produced a scarcely noticeable line, did not react with the antipulmonary serum. We were not able to elicit the cause for the change in the character of the reaction. In any event this new reaction variant also indicated the loss by the malignant lung tissue of certain antigens which are present in the normal organ. Of the 15 specimens of normal lung antigens with which we set up the reaction, 12 yielded distinct precipitation lines. Of the 16 specimens of the antigens of the malignant lung tumor only 3 reacted and the reaction was appreciably less evident.

Similar data were obtained upon neutralization of the serum by antigens from the cancer tissue of the lung. All 9 of the investigated extracts of normal lungs gave a distinct reaction, whereas only 2 of the 8 extracts of cancer tissue of the lung reacted. It is completely possible that the reaction in these last cases was caused by an admixture of unaffected lung tissue (it is usually difficult to free lung tumors from normal tissues and necroses). The nature of the lost antigen (or antigens) is not quite clear; to some extent the antigen is characteristic for the lung, however, it is not strictly organ specific. The serum which had elicited the antigen simplification reacted mainly with the lung, but in addition reacted with other organs also. In Fig. 2a we see the reaction with the kidney extract and in Fig. 2d with the spleen extract. We also used antipulmonary serum obtained by I. S. Bashkaev; this serum reacted with the given antigens in a similar manner [2].

In the attempt to achieve a strictly organ specific reaction by complete exhaustion of the antipulmonary serum by antigens from other organs, the serum stopped reacting with the pulmonary antigens.

Having tested several other antipulmonary sera we were not able in a single case to obtain a serum which would react monospecifically just with the antigens of the lung tissue. As in the described case, exhaustion of the sera by antigens of other organs ultimately resulted in the sera ceasing to react with the pulmonary antigens also. This is apparently connected with the fact that organ specific antigens of the lung, if they exist at all, are evidenced very weakly. It is possible that the reactions which were obtained in the first experiments with the above-described serum attests the presence of a specific pulmonary antigen and its loss during malignant degeneration. However, the somewhat unusual precipitation lines, the instability of the reaction, and its definite uniqueness (only 2 of the many sera available to us gave such a reaction) compel us to refrain from making more definite conclusions.

The 2nd antigen lost by the pulmonary cancer tissue was demonstrated on quantitatively sufficient material and was elicited by several sera. However, in this case also the reactions were not at all as distinct as, for example, when working with organ specific antigens of the stomach or thyroid. This antigen does not have a distinctly

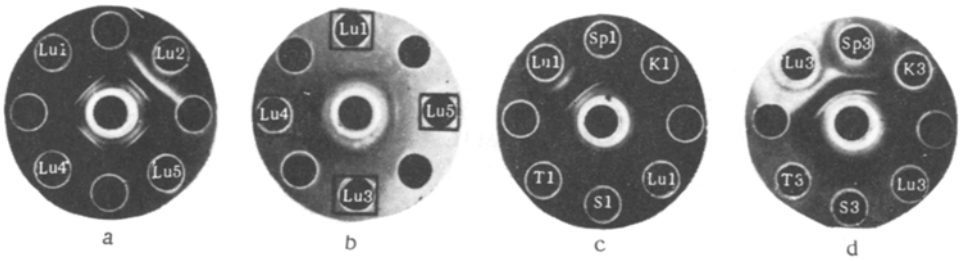

Fig. 2. Repeat of the reactions depicted in Fig. 1. Designations are the same.

evidenced organ specificity. It is most clearly and persistently elicited in the lungs. In other organs, if we judge by the intensity of the precipitation lines, it is less evidenced.

SUMMARY

A rabbit serum against human pulmonary tissue was produced, which after being neutralized with human serum antigens ceased to react to antigens from pulmonary carcinoma tissue,but continued to react to antigens from normal pulmonary tissue, and to a lesser extent, to antigens from some other organs. Similar results were obtained with the serum exhausted with pulmonary carcinoma tissue antigens. In this way, the serum revealed loss of pulmonary antigen by pulmonary carcinoma tissue without distinct organ specificity.

Several experiments yielded data evidencing antigenic simplification of the lung in malignization also at the expense of another, apparently organ specific antigen.

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