

# DIFFERENTIAL DIAGNOSIS OF CHORIONEPITHELIOMA OF THE UTERUS AND HYDATIDIFORM MOLE BY AN IMMUNOLOGIC TEST

Le Van Dien, A. P. Savinskaya,  
and L. A. Novikova\*

UDC 618.14-006.882-079.4:618.36-006-325-078.73

Polysaccharide complexes obtained by Westphal's method in the modification of L. A. Zil'ber et al. from tissues of the primary tumor node and distant metastases (lungs) of a chorionepithelioma of the uterus were used for the differential diagnosis between chorionepithelioma and hydatidiform mole. The reaction to intradermal injection of polysaccharide complexes obtained from distant metastases (lungs) of the uterine chorionepithelioma possess high specificity and sensitivity: a positive reaction developed only in patients with chorionepithelioma of the uterus and it was negative in patients with hydatidiform mole. During a marked decrease in size of the metastases in the lungs in the course of chemotherapy, when the immunologic reaction for chorionic gonadotropin fell to 300-100 i.u./liter urine, the reaction to intradermal injection of the polysaccharide complexes from the metastases of the uterine chorionepithelioma still remained positive.

**KEY WORDS:** chorionepithelioma; hydatidiform mole; polysaccharide complexes; intradermal test; differential diagnosis.

The chorionic gonadotropin (CG) levels cannot be used for the differential diagnosis of chorionepithelioma of the uterus, hydatidiform mole, and pregnancy for in all these states a high level of excretion of CG is as a rule observed.

Meanwhile, recent investigations have shown that malignant tumors contain antigens absent in the normal tissues of the body and capable of detection by immunologic methods [1, 3-8, 10, 15].

Since chorionepithelioma of the uterus is a tumor that is partly foreign so far as the organism in which it develops is concerned, the idea has grown that tissue antigens deprived of protein and, consequently of CG, can be obtained and tissue differences between these antigens used for the differential diagnosis of chorionepithelioma of the uterus, hydatidiform mole, and pregnancy.

The object of this investigation was to study the possibility of using polysaccharide complexes isolated from the tissues of a chorionepithelioma of the uterus and hydatidiform mole for the differential diagnosis of these diseases.

## EXPERIMENTAL METHOD

Polysaccharide complexes were isolated from tissue homogenates of a chorionepithelioma of the uterus, a hydatidiform mole, a normal placenta, and a normal human uterus by Westphal's method in the modification of Zil'ber et al. [2, 9]. After three cycles of immunization of rabbits with the above-men-

\* Corresponding Member, Academy of Medical Sciences of the USSR.

Laboratory of Experimental Endocrinology, Department of Gynecology, Institute of Experimental and Clinical Oncology, Academy of Medical Sciences of the USSR, Moscow. Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 79, No. 1, pp. 60-63, January, 1975. Original article submitted February 27, 1974.

© 1975 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

TABLE 1. Reaction to Intradermal Injection of Polysaccharide Complexes into Patients with Trophoblastic and Other Tumors of the Reproductive System

Histological diagnosis	No. of patients	CG excretion (i.u./liter)	Polysaccharide complexes from									
			chorionepithelioma of the uterus		placenta		uterus		physiological saline		destructive hydatidiform mole	
			+	-	+	-	+	-	+	-	+	-
Chlorionepithelioma of the uterus	5	7 000—18 000	5	0	5	0	5	0	0	5	0	5
Destructive hydatidiform mole	3	5 000—20 000	3	0	3	0	3	0	0	3	0	3
Nontrophoblastic tumors of the reproductive system	4	—	0	4	0	4	0	4	0	4	0	4

TABLE 2. Reaction of Patients with Chorionepithelioma of the Uterus and Hydatidiform Mole to Intradermal Injection of Polysaccharide Complex Isolated from Distant Metastases of Uterine Chorionepithelioma

Histological diagnosis	Time of testing	CG excretion (in i.u./liter)	Reaction to intradermal injection of polysaccharide complex
Metastasizing chorionepithelioma of the uterus (patient Zh.)	At beginning of treatment	12 000	++
Metastasizing chorionepithelioma of the uterus (patient V.)	During remission	300	++++
Hydatidiform mole (patient K.)	At beginning of treatment	45 000	+
	During remission	100	+
	Before curettage	20 000	-
	After curettage	5 000	-

Legend. X-ray investigation of patients Zh. and V. at this time showed the presence of greatly reduced metastases in the lungs, and chemotherapy was continued.

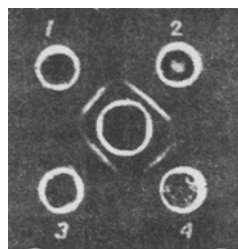


Fig. 1. Gel diffusion test. Definite lines of precipitation visible between antiserum against polysaccharide complex from tissue of human chorionepithelioma (in center) and polysaccharide complexes from tissue of chorionepithelioma of the uterus (2, 3) and tissue of hydatidiform mole (1, 4). Precipitation lines are identical.

tioned polysaccharide complexes, together with Freund's adjuvant, antisera were obtained. Interaction between the antigens (polysaccharide complexes) and antisera obtained against them was studied by Ouchterlony's double diffusion method in gel [13, 14].

At the same time, the patients' reaction to intradermal injection of the polysaccharide complexes was studied. The intradermal reaction was recorded 24, 48, and 72 h after injection of 0.1 ml of the antigen in a concentration of 2 mg/1 ml physiological saline. The antigens were injected intradermally into the anterior surface of the forearm. As the control, injections of physiological saline were given simultaneously with the antigen.

The reaction was considered positive if a papule measuring not less than 5 mm in diameter appeared at the site of injection. The intradermal tests were carried out on patients with trophoblastic tumors and with tumors of the reproductive system of a non-trophoblastic nature (carcinoma of the body and cervix of the uterus, cystoma of the ovary).

In the patients with trophoblastic tumors, before the intradermal test was carried out the CG excretion was determined quantitatively by the inhibition of passive hemagglutination test in Molodyk's modification [12].

## EXPERIMENTAL RESULTS

Tests of the various polysaccharide complexes by Kjeldahl's method demonstrated their complete freedom from protein. Tests of the polysaccharide complexes in polyacrylamide gel also revealed no protein. The study of the interaction between the polysaccharide complexes and antisera produced against them in Ouchterlony's test demonstrated the presence of a definite precipitation band between them and the absence of any such band between CG and the antisera against the polysaccharide complexes. However, a clear cross reaction was observed between polysaccharide complexes from the tissues of the trophoblastic tumors and antisera against them (Fig. 1).

The intradermal tests showed a positive reaction in patients with chorionepithelioma of the uterus and a destructive hydatidiform mole after injection of polysaccharide complexes from tissues both of the uterine chorionepithelioma and of the hydatidiform mole and normal placenta (Table 1). These patients gave a negative reaction only to the polysaccharide complex from the tissues of the normal uterus and to physiological saline. In patients with tumors of the reproductive system of a non-trophoblastic type the reaction to intradermal injection of polysaccharide complexes from the tissues of the uterine chorionepithelioma, hydatidiform mole, and normal placental tissue was negative in all four cases.

No difference could thus be found between the polysaccharide complexes isolated from the various trophoblastic tumors either in experiments in vitro or during intradermal tests on the patients.

The evident explanation of this fact is that during histological investigation of a trophoblastic tumor elements of a chorionepithelioma, elements of a destructive hydatidiform mole, and normal trophoblasts can often be found at the same time, so that the polysaccharide complexes prepared from such a mixed tumor can give a crossed precipitation reaction. For this reason, subsequent investigations were carried out to discover methods of separating elements of the uterine chorionepithelioma from elements of the hydatidiform mole in order to obtain specific polysaccharide complexes which could be used for the differential diagnosis between chorionepithelioma of the uterus and hydatidiform mole.

One possible approach would be to obtain polysaccharide complexes from distant metastases of a chorionepithelioma of the uterus. Tissue from metastases in the lungs was taken at autopsy from patient D., who died from chorionepithelioma of the uterus, and polysaccharide complexes were prepared from this tissue. By minor modifications to the technique of preparing the polysaccharide complexes, the ash content of the preparations was reduced considerably (to 12%).

In two patients with uterine chorionepithelioma the intradermal test to injection of a polysaccharide complex prepared from metastases of a chorionepithelioma of the uterus in the lungs was studied at the beginning of treatment and in the course of a remission (Table 2). In both patients the test was positive at the beginning of treatment and it remained positive while the metastases decreased considerably in size as a result of treatment, even when the immunologic reaction for GC had decreased to 300-100 i.u./liter urine. The reaction to injection of the polysaccharide complex from the distant metastases in the patient with hydatidiform mole was negative both before and after the operation of curettage.

These results demonstrate the high specificity and sensitivity of the reaction to polysaccharide complexes.

## LITERATURE CITED

1. G. I. Avdeev, I. S. Bashkaev, and B. E. Chechik, Proceedings of the International Cancer Congress [in Russian], Vol. 3, Moscow (1963), p. 289.
2. M. N. Averkieva, Some Immunologic Reactions in Carcinoma of the Stomach and Lung. Candidate's Dissertation, Moscow (1971).
3. N. D. Anina-Radchenko and K. O. Leonidova, Vopr. Onkol., No. 11, 3 (1962).
4. V. V. Gorodilova, An Experimental Study of a Specific Antigen of Carcinoma of the Mammary Glands. Doctoral Dissertation, Moscow (1957).
5. V. V. Gorodilova, Byull. Éksperim. Biol. i Med., No. 6, 460 (1951).
6. V. V. Gorodilova, Z. M. Saraeva, R. I. Slesareva, et al., Vopr. Onkol., No. 2, 3 (1969).
7. L. A. Zil'ber, Advances Cancer Res., 5, 291 (1958).
8. L. A. Zil'ber and G. I. Abelev, The Virology and Immunology of Cancer [in Russian], Moscow (1962).
9. L. A. Zil'ber, V. V. Gorodilova, and M. P. Averkieva, Vopr. Onkol., No. 5, 18 (1969).
10. P. N. Kosyakov, V. S. Korosteleva, and N. I. Kuznetsova, Byull. Éksperim. Biol. i Med., No. 9, 63 (1955).

11. L. A. Lyudogovskaya, A. I. Gusev, and G. I. Abelev, Proceedings of the Second All-Union Oncologic Conference [in Russian], Leningrad (1959), p. 58.
12. A. A. Molodyk, The Dynamics of Excretion of Chorionic Gonadotropin during the Treatment of Patients with Chorionepithelioma of the Uterus and Tumors of the Ovary. Author's Abstract of Candidate's Dissertation, Moscow (1971).
13. N. A. Nazarenko, Byull. Eksperim. Biol. i Med., No. 11, 80 (1969).
14. V. Ya. Rogal'skii, Byull. Eksperim. Biol. i Med., No. 10, 82 (1960).
15. L. V. Shershul'skaya, Proceedings of the Second All-Union Oncologic Conference [in Russian], Leningrad (1959), p. 98.