TRANSIENT FORM OF BLOOD ALBUMIN IN GYNECOLOGIC CANCER

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An important contribution to the solution of the problem of ovarian and uterine cancer is the detection and treatment of patients with borderline or early stages of the disease. The main causes of late discovery of these patients are diagnostic mistakes [5, 8, 9]. The results of an investigation of 3827 patients with ovarian and uterine tumors whom we studied shows that often, even when the patient seeks medical advice in good time on the appearance of symptoms of the disease, a correct diagnosis is not made. Malignant tumors of the ovaries and uterus in some cases are difficult to differentiate from chronic inflammatory diseases of the internal reproductive organs (24%), fibromyoma of the uterus (8.9-18.1%), and certain extragenital diseases. Consequently there is a definite need to search for new and improved methods of early and precise diagnosis of ovarian and uterine tumors. The structural variation of serum albumin, or transient polyalbuminemia to use the terminology of Troitskii (1981), arises in response to various pathological states, including cancer [2, 11]. The essence of transient polyalbuminenia is that a modified form appears in the composition of normal albumin. This phenomeneon has not yet been adequately studied clinically.

This paper describes an attempt to determine the value of the use of biochemical tests for the diagnosis of gynecologic cancer and also for monitoring of patients during treatment, and for determination of the individual prognosis.

EXPERIMENTAL METHOD

Human serum albumins (HSA), isolated from the blood serum of 27 patients with the following diagnoses, were studied: carcinoma of the cervix uteri in stages I and II (two), sarcoma of the body of the uterus, in stages I and II (three), carcinoma of the ovaries (11) (six in stage IV, two in stage III, three in stage II), benign ovarian tumor (seven), and myoma of the uterus (four). The diagnosis was confirmed histologically in all patients. Blood was taken when required on medical grounds. Samples of serum albumin isolated from the blood of 20 healthy women served as the control. Monomer preparations of serum albumin were obtained by preparative polyacrylamide gel (PAAG) electrophoresis [1]. Free SH-groups were protected after isolation with L-cystine [14]. The purity of the isolated preparations was verified by analytical electrophoresis in PAAG [7] and by an immunochemical method [6]. The conformation of the isolated albumins was studied by an optical rotation dispersion (ORD) method. Parameters of ORD were calculated by the method described in [12]. Besides ORD, another optical method was used, namely temperature-differential perturbation spectrophotometery (TDPS), which gives some idea of the state of the thrombophores and enables accessibility of individual functional groups of protein for specific metabolites to be determined. Accessible tyrosyls were counted by the method described in [13]. The content of the modified form of albumin was determined by reprecipitation with TCA as described in [4].

EXPERIMENTAL RESULTS

The results of ORD of the serum albumins showed different degrees of despiralization of the patients' albumin compared with normal. The percentage of α-helices were 49.2% in healthy women but lower in the patients studied. However, a significant reduction in the number of α-helices was observed only in widespread cancer, and then not always. In

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cervical cencer and sarcoma of the body of the uterus the quantity of α-helices in albumin fell to 17.5-37%, and in ovarian cancer to 24-41%. A decrease in the number of α-helices signifies an increase in the content of the transient form. In benign ovarian tumors and myoma of the uterus the number of α-helices was only slightly reduced, to 42.5-47%, evidence of mild conformational disturbances of the albumin.

The results of the spectropolarimetric studies in this type of pathology thus supplement previous data on structural changes in serum albumin [2, 11] and are further evidence of the nonspecific character of these changes. However, some correlation can be found in this group of patients between the diagnoses and the degree of albumin despiralization. For instance, in patients with benign overian tumors and myomas of the uterus the degree of despiralization observed was very low, whereas in patients with ovarian cancer, cervical cancer, and sarcoma of the body of the uterus, in most cases it was roughly twice as high.

The use of the TCA reprecipitation method to study the isolated proteins enables the degree of structural changes in serum albumin to be estimated [3, 4]. A modified form is present in the serum albumin of all patients in a much larger number of cases than in healthy women of the control group. The content of the modified form depends on the localization and spread of the pathological process and the patient's clinical condition.

The percentage of modified form in serum albumin was high (72-100) in patients with carcinoma of the cervix uteri. In a patient with metastases of carcinoma in the lung it was 100%. The percentage of modified form in patients with sarcoma of the body of the uterus was 100, 71.4, and 28.9. Its content depended on the degree of spread of the tumor. In two patients with stage II of the disease, with recurrence, and with metastases in the pelvic organs, the modified form accounted for 71.4 and 100%, but in a patient with stage I of the disease and with commencing malignant change it was only 28.9%.

In patients with ovarian cancer structurally changed albumin accounted for 32 to 88%. The percentage of the modified form in these patients also depended on the stage of spread of the disease. In stage IV the modified form was between 38.5 and 88%, and the actual figure depended on the rate and extent of spread of the disease in the peritoneal cavity, and the presence of metastases in the intestine, urinary bladder, and liver. With this kind of course of the disease, the modified form amounted to 50-88%. Single distant metastases outside the peritoneal cavity did not significantly affect structural variation of the albumin. If the primary tumor grew comparatively slowly, even if single metastases were present in the lungs and umbilicus, the modified form amounted to 38.5-43.3%, but in stage III of ovarian cancer it was 40-57%. Under these circumstances, in patients with more extensive spread of the disease, in whom operative treatment was confined to diagnostic laparotomy, conformational changes in the protein were more marked (57%) than in patients with less extensive disease, on whom a palliative operation could be performed (40%). In three patients with stage II of ovarian cancer, the modified form amounted to 32-43.7%.

Considerable conformational injuries found in the albumin of patients with ovarian cancer, even if the spread of the diease is comparatively limited and when a radical operation is still possible, are of undoubted importance from the standpoint of the use of the technique for early detection of the disease. Benign ovarian tumors are accompanied by less marked structural changes in the albumin. In benign thecoma the modified form accounted for 22-25%, in endometrioid tumor 14.5%, in serous tumors 10-13.7%, but in a mature teratoma this figure did not exceed the control value (4.5%). Myomas of the uterus were not accompanied by any increase in the content of the modified form (up to 5%). However, a certain increase in its content must serve as a warning of the possibility of sarcomatous change.

Patients can thus be divided into three groups depending on the content of the modified form in their serum albumin: 1) patients with a high content of the modified form (carcinoma of the cervix uteri, sarcoma of the body of the uterus, ovarian carcinoma in stage IV with multiple metastases in the abdominal organs); 2) patients with an average content of the modified form (initial stages of ovarian and uterine cancer); 3) patients with a low content of the modified form (benign tumors of the ovaries, myoma of the uterus).

The patients studied were aged from 13 to 72 years. Analysis showed that qualitative changes in albumin are independent of the patients' age. For instance, in women under 37 years old the modified form was found to the extent of 4.5-71.4%, but in women aged from 47 to 72 years, 2-100%. These figures depended on the character of the disease and the

stage of its spread. In young women (aged 27-37 years) the modified form consisted of 5% in myoma of the uterus and 10-14.5% in benign ovarian tumors to 71.4% in sarcoma of the body of the uterus. The character of treatment also had no significant effect on the structural changes in albumin.

The main causes of delay in the discovery of genital carcinoma are diagnostic mistakes [9, 10]. Of 27 patients observed, the correct diagnosis was not made sufficiently early in 23 (including all patients with malignant tumors), and this led to delay in treatment by between 2 months and 4 years. Consequently, by the ordinary clinical methods of investigation it is not always possible to make a timely correct diagnosis. The use of biochemical tests during the examination of women will bring to light cases of cancer in good time.

Structural lesions in serum albumin thus depend mainly on the location and character and, mainly, on the stage of spread of the disease and are independent of the patients' age and the nature of treatment given.

A combination of ordinary clinical methods with additional tests which the writers have devised and used, in which the properties of molecular variation of serum albumin are employed, can lead to an improvement in the early diagnosis of gynecologic cancer and can help to insure that adequate treatment is given at the proper time.

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