II. CLINICAL PROBLEMS

INDIVIDUAL SERUM PROTEIN CONSTELLATIONS IN THE DIAGNOSIS AND PROGNOSIS OF VIRAL HEPATITIS

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The dynamic weekly laboratory control of patients with viral hepatitis (VH) requires also the investigation of some individual serum proteins possessing better expressed abnormalities and relatively short half-life (10). Independently of the kind of hepatic morphologic lesions, the proteins of synthesis, those of the acute inflammatory response of the organism and the response to antigenic irritation can be followed-up and some of them can be studied (e. g. alpha$_1$ glycoprotein, serum cholinesterase, haptoglobin, fibrinogen, immunoglobulin A, etc.). According to certain authors, the most recently performed investigations are out-of-date, and, hence, have to be abandoned (Weltmann's test, thymol test, as well other colloid tests, urinary urobilinogen, hippuric test, cholesterol esters /1, 12/). Some tests could even be potentially dangerous for the patients (bromsulphalein test — 11).

By using transaminases, the alkaline phosphatase (AP) and total serum bilirubin the diagnosis of about 60—70 % of any liver investigations could be ensured.

The introduction of new specific hepatic enzymic and other biochemical indexes could lead to an increase of this percentage to aobut 75—85 % (1, 8). Recently, the study of certain individual serum proteins (albumin, praealbumin, ceruloplasmin, transferrin, serum immunoglobulins) has a greater practical use because of their best discriminating value which varies between 45 and 80 % in particular hepatic disease; e. g. the serum immunoglobulin level shows definite changes and can be used as an index for the activity of the pathologic process and the effectiveness of therapy in various hepatic diseases (5, 7).

The most important practical problem for the clinicians is the determination of VH stage, i. e. whether the disease is still at the early stage or even already chronified. In this respect, the immunologic investigations help essentially the clinicians and throw light on the cases concerning their prognosis. However, there is not any practical experience because most individual serum proteins were not studied enough (10). At the onset of the acute inflammatory process some of them increase in the plasma but others decrease and even dissociate. Concerning the liver diseases the evaluation of the changes of their concentration is getting more complicated because same proteins are both formed and disintegrated in the liver (2, 3). It is relevant to determine some constellations of 2—4 proteins in order to facilitate the evaluation of the information received. By this way the grouping of their levels makes the conclusions more convincing and definite.

Some constellations can be formed with even one representative of each group only to be used in the practice (4). We suggest similar constellations to be applied in the diagnosis, differential diagnosis, and prognosis of VH.

Ist constellation:

Simultaneous investigation of both transferrin and immunoglobulin A (Ig A). The ratio Ig A: transferrin can be used for early diagnosis of clinically non-apparent post-hepatitis lesions and for demonstration of chronic alcoholic liver damage (6, 9). Transferrin was chosen out of plasma proteins according to the presumption that it was synthesized in hepatocytes and decreased quite early at their damage. On the other hand, Ig A characterized by the best way the destruction alterations of the liver. It was assumed that it was an autoantibody carrier of the organism. Ig A juxtaposition and transferrin one in 107 patients (with chronic hepatitis, hepatic cirrhosis, VH and reconvalescent ones) has shown that Ig A increase and transferrin decrease which determines a coefficient over than 1,9 occurs in 42,8 %' of patients with cirrhosis, in 26,6 % of those with suspected chronic hepatitis and in 1,4 % of those with recidivans VH. According to our opinion, the percentage 26,6 % is quite high and can be applied to determine early liver lesions. Ig A increase over than 460 mg % and transferrin reduction below 160 mg % speaks for progress of hepatic pathologic process which is a potential danger of developing of a hepatic cirrhosis. However, Ig A changes are not specific for VH only. Their comparison with transferrin levels can be evaluated only in combination with any other clinico-laboratory data.

IInd constellation:

Fibrinogen, albumin and serum cholinesterase. They are synthesized in the liver. Plasma fibrinogen reduction is an evidence for an acute hepatic insufficiency (8). According to our experience at the Clinic of Infectious Diseases, Higher Institute of Medicine, Varna city, the synthesis of fibrinogen is always disturbed quite early and seriously in severe clinical forms of VH. This results in its plasma level reduction. One can interpret these changes in combination with those of some other coagulation factors such as platelets number, prothrombin index, bleeding and coagulation time, etc. Furthermore, it is relevant to consider plasma fibrinogen level changes as combined with those of albumin and serum cholinesterase because of their significant decrease as well in severe VH forms, as in chronic hepatic lesions.

The dynamic follow-up of fibrinogen, albumin and serum cholinesterase gives evidence either of chronifying of hepatic disease, or of appearence of hepatitis recidives when permanently lowered levels of these indices are established. Their long diminution is a bad prognostic sign. Dispensary patients require a regular investigation of these indexes and even their rehospitalization.

IIIrd constellation:

Albumin, ceruloplasmin, immunoglobulin M (Ig M). In this case there are representatives of three groups individual serum proteins: albumin (synthesis group); ceruloplasmin (group of acute inflammatory response), and Ig M (antibody-group). Their determination shows the degree of liver damage at VH onset

as well the cytolysis and the ability of the organism for immune defence. The more severe the clinical VH form the lower ceruloplasmin and albumin both levels whereas Ig M is commonly increased in the first two weeks after VH onset. In the clinical course there is an increase of both albumin and ceruloplasmin and a decrease of Ig M level together with improvement of patient's state, diminution of total intoxication and cytolysis. By using this constellation a dysproteinaemia can be detected in 80,2 % of the cases.

IVth constellation:

Albumin, alpha$_1$-acid glycoprotein (orosomucoid) and immunoglobulin G (Ig G). Orosomucoid is synthesized in the liver and increases in acute inflammatory diseases as an index of acute stage. According to the bibliographic data and to our own results its serum level is reduced and the duration of its low levels speaks for a definite hepatic lesion (2—4, 8). The present hypoalbuminaemia testifies also to a disturbed protein synthesis. High serum Ig G levels are characteristic for the chronic hepatitis and hepatic cirrhosis. The simultaneous determination of serum constellations of these proteins in the second half of VH course when jaundice is reduced, the liver is normalized and patient's healing has started, can give a valuable information. Based on the preserved low albumin and alpha$_1$-acid glycoprotein levels and the considerably increased serum Ig G level it can be accepted that the protein-synthetic function of the liver is continuously disturbed and the illness gains probably a protracted clinical course. By using this constellation a dysproteinaemia can be ascertained in 90 % of the cases. Orosomucoid can be replaced by haptoglobin without reduction of its prognostic value.

Vth constellation:

Serum cholinesterase, alpha$_1$-acid glycoprotein, haptoglobin and immunoglobulin A (Ig A). The chronic antigenic irritation of the organism can be detected and followed-up by using a constellation consisting of the levels of serum cholinesterase, alpha$_1$-acid glycoprotein, haptoglobin and Ig A. To a certain degree the individual serum protein levels can be a "total amount" of a present chronic antigenic irritation and of a liver damage on which an accompanying acute inflammatory process or another somatic disease is superceded (diabetes mellitus, duodenal ulcer, atherosclerotic changes). More frequently, lowered levels of individual serum proteins, especially of haptoglobin and proteins of synthesis, are established in such cases (2). Ig A is considerably more often increased at the presence of another illness (chronic gastrointestinal disease, respiratory tract inflammation, etc.). Not infrequently, its increased levels are accompanied with an increase of Ig M, too.

Thë proposed constellation of indices can be also used in this direction in order to render the obstained results in hepatitis related to other accompanying or preceeding diseases.

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КОНСТЕЛЛЯЦИИ ИНДИВИДУАЛЬНЫХ БЕЛКОВ СЫВОРОТКИ ПРИ ДИАГНОЗЕ И ПРОГНОЗЕ ВИРУСНОГО ГЕПАТИТА

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РЕЗЮМЕ

Вопрос о сывороточных индивидуальных белках имеет большое значение для клинической практики, в связи с чем автор предлагает пять констелляций различных протеинов в помощ диагностики, дифференциального диагноза и прогноза вирусного гепатита. Информация, полученная при изменениях уровня сыворотки определенных индивидуальных протеинов, дает возможность определить активность патологических изменений печени и выяснить прогноз заболевания.

Определены индивидуальные белки сыворотки и антитела различных групп — группы белков, синтезирующихся в печени, белков, характеризирующих острую фазу воспалительного процесса и белков имунного ответа. При первой констелляции предлагается прослеживание стоимостей трансферина и ИГА, при второй — фибриногена, альбумина и сывороточной холинэстеразы, при терьей — альбумина, церулоплазмина и ИгМ, при четвертой — альбумина, альфа$_1$-кислого гликопротеина и ИгА, при пятой — сывороточной холинэстеразы, альфа$_1$-кислого протеина, гаптоглобина и ИгА.