

A FOUR-YEAR STUDY OF α -FETOPROTEIN IN VIETNAM (1969-1973)

Vu Trieu An

UDC 616.153.962.4-053.1.001.5 (597)

By the method of double diffusion in gel α -fetoprotein (α -FP) was found in 66% of cases of hepatocellular carcinoma. When the more sensitive method of electroimmunodiffusion was used the frequency of positive findings was increased both in cases of hepatoma and other diseases. The results of quantitative estimation of α -FP in patients after ligature of the hepatic artery indicate a decrease in the serum α -FP concentration; this confirms the value of its determination for prognosis.

KEY WORDS: α -fetoprotein; hepatocellular carcinoma.

The presence of a special protein in the blood of the mammalian fetus, which disappears in the adult animal, was first demonstrated by Pedersen in 1944 [8]. This protein was called fetuin. Gradually many other embryonic antigens were later found. Of these antigens, α -fetoprotein (α -FP) has been studied most completely, for this protein has been found in hepatocellular carcinoma, initially in mice [2] and later in man [1, 3]. The use of determination of α -FP in the blood as a diagnostic test aroused so much interest that in the next decade hundreds of papers on this problem were published in the world literature.

The object of this investigation was to determine α -FP in patients with hepatocellular carcinoma and also with other diseases.

EXPERIMENTAL METHOD AND RESULTS

Antisera against α -FP began to be obtained in the Department of Pathological Physiology of the Medical College in Hanoi, Vietnam, in 1969. The method of immunization was fully described previously. Its essentials are as follows: Human fetal serum was used as the antigen and was injected repeatedly into a rabbit until antibodies against α -FP could be detected by immunoelectrophoresis. The rabbit antiserum

thus obtained was absorbed with a mixture of normal adult human sera and the monospecificity of the antiserum was verified by immunoelectrophoresis or by electroimmunodiffusion.

TABLE 1. Discovery of Serum α -FP in Patients with Various Diseases by Electroimmunodiffusion

Diagnosis or test object	Number tested	Percentage of discovery of α -FP
Hepatocellular carcinoma	18	100
Hepatitis	28	15
Liver abscess	5	20
Other forms of cancer	34	0
Hydatidiform mole	25	0
Healthy parturients	11	82
Placental blood serum	40	100

In the next stage of the investigation a comparative study was made of 25 patients in the Vietnam-German Hospital with the clinical diagnosis of hepatoma. By Ouchterlony's gel-diffusion method [7] α -FP was found in only 54% of these patients. In a third comparative investigation carried out on 74 patients with the diagnosis of primary carcinoma of the liver, confirmed histologically, α -FP was found in 66% of cases. The results of this last investigation corresponded to data obtained in an international investigation in 1968-70 [6], as follows: No false positive results were obtained by Ouchterlony's method; the frequency of positive results varied in different geographical

Department of Pathological Physiology, Medical Institute, Hanoi, Vietnam. (Presented by Academician of the Academy of Medical Sciences of the USSR O. V. Baroyan.) Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 81, No. 2, pp. 224-225, February, 1976. Original article submitted April 18, 1975.

©1976 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.

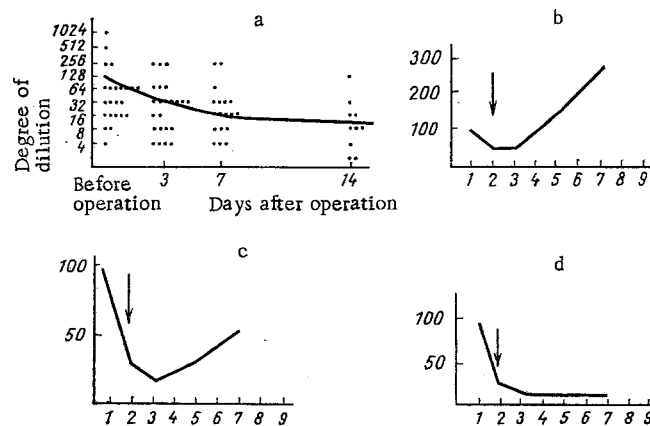


Fig. 1. Changes in serum α -FP level in patients: a) after ligation of hepatic artery; b) in inoperable hepatoma after diagnostic laparotomy; c) patient with poor prognosis after ligation of hepatic artery; d) patient with good prognosis after ligation of hepatic artery. In b, c, and d: abscissa, time of investigation (days); ordinate, α -FP level (in % of initial); time of operation marked by arrow.

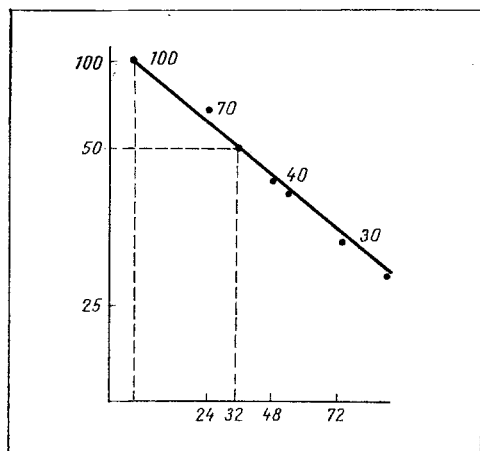


Fig. 2. Determination of half-life of α -FP in a patient after removal of solitary hepatoma. Abscissa, time of investigation (in h); ordinate, α -FP level (in % of original, logarithmic scale).

regions of the world. However, when α -FP is determined the frequency of positive findings is known to depend also on the method used. When electroimmunodiffusion was used in Kohn's modification [4], a method 10 times more sensitive than Ouchterlony's method, α -FP was found even in diseases other than primary carcinoma of the liver. These results are given in Table 1.

To determine the serum α -FP level a semi-quantitative variant of double diffusion in gel with serial dilutions of serum or electroimmunodiffusion by Laurell's [5] method was used (data of Phan Hoang Phnet and Phan Hoang Phuong from Vietnam). Samples of sera taken from patients at different time intervals were compared with the first sample taken on the day of admission to hospital. More recently a relatively pure preparation of α -FP, obtained by Le Thanh Thu, Trinh Hung Quong, and Vu Thui Hien by preparative electrophoresis in acrylamide gel, has been used as a standard for comparison. In this way 26 patients were examined after ligation

of the hepatic artery (in the surgical department of the Vietnam-German hospital, Director, Professor Ton Than Tung). The results obtained were as follows. On the whole, the serum α -FP level fell after the operation (Fig. 1a). In one case of inoperable carcinoma, the effect of laparotomy was unexpected: After a short period of decrease, the serum α -FP level rose sharply (Fig. 1b). In some patients, chiefly those with a poor prognosis, the decrease in the α -FP concentration was followed by a steady rise in its level (Fig. 1c). In patients with a favorable prognosis the serum α -FP level remained constant for a long time after the operation (Fig. 1d). Unfortunately it was impossible to continue the observations further. In one patient with a single tumor, the serum α -FP level was determined regularly after removal of the hepatoma; in this way the half-life of this protein could be determined (Fig. 2). Its value was about 32 h, in agreement with recent data in the literature (1-7 days).

To conclude, the results confirm the diagnostic value of the α -FP test under clinical conditions. Quantitative determination of α -FP during chemical and surgical treatment of hepatocellular carcinoma is of special prognostic value.

LITERATURE CITED

1. G. I. Abelev, Vestn. Akad. Med. Nauk SSSR, No. 7, 49 (1970).
2. G. I. Abelev, S. D. Perova, N. I. Khramkova, et al., Biokhimiya, No. 4, 625 (1963).
3. Yu. S. Tatarinov, Vopr. Med. Khimii, No. 1, 90 (1964).
4. J. Kohn, J. Clin. Path., 23, 733 (1970).
5. C. B. Laurell, Analyt. Biochem., 15, 45 (1966).
6. G. T. O'Connor, Yu. S. Tatarinov (J. S. Tatarinov), G. I. Abelev, et al., Cancer (Philadelphia), 25, 1091 (1970).
7. O. Oucterlony, Progr. Allergy, 6, 30 (1962).
8. K. Pedersen, Nature, 154, 575 (1944).