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## Biochemical and cytological profile in hepatocellular carcinoma

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### Abstract

*The following biochemical parameters of serum from patients suffering from hepatocellular carcinoma have been measured: bilirubin, aspartate amino transferase (ASAT), alanine amino transferase (ALAT), (alkaline phosphatase) ALP, lactate dehydrogenase (LDH), superoxide dismutase (SOD), total seric proteins, gamma-glutamyltransferase ( $\gamma$ -GT), protein electrophoretic pattern, glycemia and alpha fetoprotein. The respective study was performed on 15 patients with hepatocellular carcinoma, 11 males and 4 females of ages of 40-70 years old. In ascitic fluid ALP, LDH, and total proteins were determined and also cytological examination was performed. The results, biochemical and cytological, were compared with parameters from healthy individuals, highlighting the diagnostic value of the determinations.*

Keywords: hepato-cellular carcinoma, enzymes, ascites, bilirubin

### Introduction

Hepato-cellular carcinoma develops mostly on the background of hepatic cirrhosis with portal hypertension. Statistical results indicate that 80% of these carcinoma comply with this rule.

HBs and HCV antigenes as well as chemicals such as aflatoxine and vinyl chloride are involved in pathogenicity of hepatic carcinoma [1].

Suspect patients are usually cirrhotic persons that suddenly develop hepatomegaly, ascitic fluid and present important alteration of hepatic tests [2].

Hepatocellular carcinoma is the most important malignant tumor that determines ascites. Carcinomatous cells are organized as three-dimensional globular or papillary nests, usually compared with glandular acins [3].

Microscopic images of adeno-carcinoma show malignant cells that tend to organize themselves as hepatic cords. These cells resemble the normal hepatic cells but they present a higher nucleo-cytoplasmic fraction, intense basophilic and vacuolar cytoplasm (mucous vacuolar cytoplasm) and variable nuclei [4].

### Materials and methods

Biochemical tests were performed on a BTS 370 Plus from Biosystems and cytological examination on Olympus optical microscope, by respecting the indicated protocols.

This study was performed on 15 patients with hepato-cellular carcinoma, 11 males and 4 females of ages of 40-70 years old. The following biochemical parameters have been determined in serum: ASAT, ALAT, ALP, LDH, SOD, fraction ASAT/ALAT, total seric

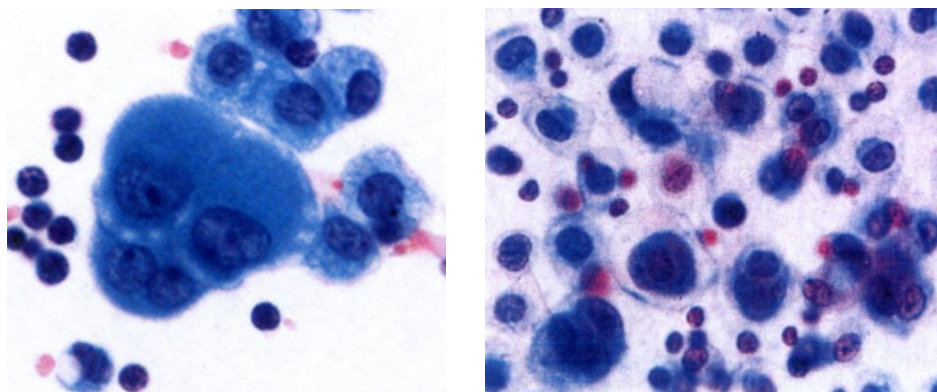
proteins, gamma-GT, protein electrophoretic pattern, glycemia and alpha fetoprotein. In ascitic fluid ALP, LDH and total proteins were determined and also cytological examination was performed.

## Results and discussion

The present study was an interdisciplinary work between Biochemistry and Cytology that tried to find out biochemical and cytological correlations between serum and ascites fluids in patients with hepatic adenocarcinoma. We arrived at the conclusion that the biochemical and cytological data successfully complete the clinical pattern in order to establish an early diagnose of the malignant transformation, a good evaluation of the stages and to control the therapeutic efficiency [1], [2].

The tests accomplished by us disclosed the following values:

- ASAT had values between 57-70 U/L;
  - ALAT had values between 35-50 U/L;
  - seric ALP had higher levels, up to 4 times the maximal seric level (1100 U/l) and higher levels appeared also in ascitic fluid (510-730 U/l) before the moment of the seric increase;
  - Gamma-GT in females had values of 70-90 U/l while in males the increase was more important (120 U/l);
  - total bilirubin values increased over 15 times than normal (5-20 mg/dl);
  - Superoxide dismutase registered lower values than normal;
  - glycemia was moderately lower than normal (40-60 mg/dl) because of hepatic glycogen depletion by higher metabolic levels of tumoral cells;
  - seric LDH had 3 times higher levels than normal (850-1200 U/l) while ascites values were about 240-690 U/l;
  - total seric proteins registered important lower values (2-3.1 g/dl) while proteins in ascites had values between 2,8-4,2 g/dl;
  - alpha fetoprotein increased in 60% of cases with values between 500-800 $\mu$ /l.
- cytological examination of ascites fluid constantly showed the reactive mesothelial cells (Figs. 1, 2) with features as: unequal nuclei, thicker nuclear membrane, vesicular chromatine, small nucleoli and "fuzzy" cytoplasmic border;



**Figures 1 and 2.** Reactive mesothelial cells in ascites fluid showing characteristic cytological features.

- hepatic tumoral cell is also present in ascites fluid; it has higher nucleo-cytoplasmic fraction, anisonucleosis, hyperchromatic basophile cytoplasm, less quantity than normal;

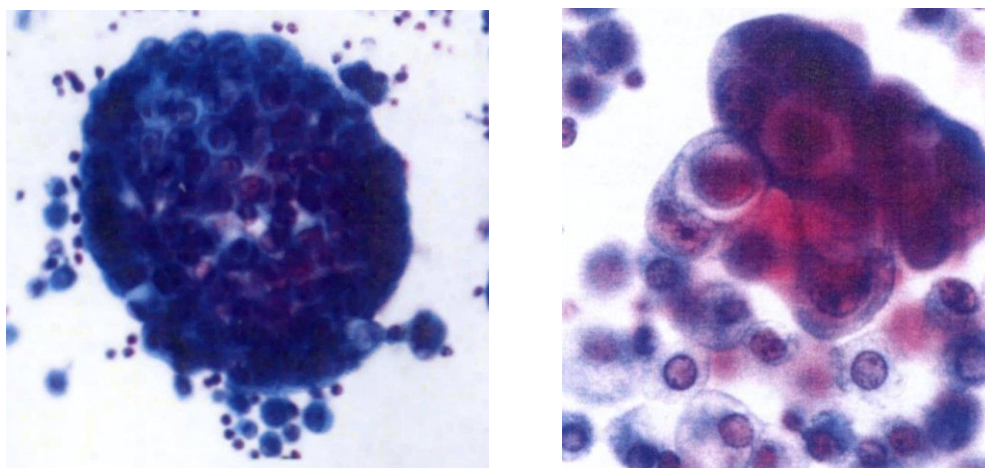
malignant cells are organized in three-dimensional nests, usually compared with glandular acins (Figures. 3, 4 ).

## Conclusions

Alcaline phosphatase does not depend on location of the tumor but it represents a first alarm signal when its values become higher in ascites; this signal becomes acute when its values increase also in serum with higher values than in ascites.

Gamma-GT is an indirect but important indicator of hepatic carcinogenesis and demonstrates a degree of disseminated cholestasis at the level of hepatic parenchyma; the mechanism consists in the compression of bile canaliculi by the islands of tumoral cells.

LDH presents higher levels than in cirrhosis cases without malignant complication and it completes successfully the diagnose methods of hepato-cellular carcinoma. Low levels of seric proteins in cirrhosis are explained by low synthetic capacity of the liver with hipoalbuminemia and low levels of coagulation factors. These determine phenomena like decreased coloidosmotic pressure which, together with portal hypertension, determines the



**Figures 3 and 4.** Hepatic tumoral cells from ascites fluid presenting three-dimensional nests similar to glandular acins.

ascites and especially the increased protein level in ascites fluid. In our cases, the hepatic malignant process determines lower seric protein levels than in cirrhosis without malignant transformation.

Bilirubin levels are highly modified. Its levels are 20 times higher than normal because of more causes: hemolytic syndrome by decrease of coloidosmotic pressure and hemorrhage by the deficit of coagulation factors (synthesis at the level of the liver), or hemorrhagic accidents at the level of porto-caval value of 500-800 $\mu$ /L.asthomoses; at the same time hemoglobin has dramatically lower values.

The moderate lower level of glycemia is due to the exhausted levels of hepatic glycogen by accelerated metabolic rates of tumoral cells.

Alpha fetoprotein had important increased levels but it is not a specific indicator (only 60% of cases presented such higher levels).

Superoxide dismutase registered lower values than normal because its dependence on NADPH, and the latter is generated in pentose phosphates cycle that is altered in carcinogenesis.

Transaminases moderate increase is not important because there is no acute hepatic cytolytic syndrome.

Finally, it may be stated that biochemical study of serum and ascite fluid corroborated with cytological study of ascites fluid represent an efficient method of early diagnose of malignant transformation of cirrhosis.

Biochemical examination completes successfully the clinical methods in early diagnose of carcinoma.

Cytological examination showed reactive mezothelial cells and the real marker of cancer – the tumoral cells.

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