SERUM ALPHA-FETOPROTEIN LEVELS FOLLOWING
CESSION OF ALCOHOL IN MEDICAL AND
PSYCHIATRIC SUBJECTS WITH LONG-TERM
EXCESS DRINKING

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Received August 8, 1982

Abstract. Serum alpha-fetoprotein (AFP) concentrations were serially deter-
mined during the period following cessation of alcohol in thirty-five medical and
psychiatric patients with histories of long-term excess drinking. In all except two
cirrhotics with posttransfusion hepatitis and hepatocellular carcinoma, all AFP de-
terminations for more than 2 months following abstinence were negative (< 40 ng/
ml). The results suggest that AFP elevations after abstinence from alcohol should
raise the question of associated viral hepatitis or hepatoma in alcoholics.

Key words: alpha-fetoprotein, alcoholics, abstinence, liver injury.

Serum AFP was detected in patients with non-neoplastic liver diseases such
as acute hepatitis, particularly fulminant hepatitis, chronic hepatitis and liver
cirrhosis. However, the precise mechanisms for accelerated AFP synthesis in
these disorders are poorly understood, although the AFP rise is thought to re-
fect ongoing liver regeneration following extensive liver necrosis (1). AFP elev-
ation has also been reported recently in cases with alcoholic hepatitis and al-
coholic cirrhosis (2, 3). It is unfortunate that these studies did not describe a
direct relationship between serum AFP elevation and the cessation of drinking,
since there are several investigations suggesting that ethanol administration de-
pressed mitotic activity, [3H] thymidine incorporation into DNA and protein
synthesis in the regenerating liver after partial hepatectomy (4, 5).

Therefore, in this communication, serum AFP concentrations were serially
determined during the period following cessation of alcohol in medical and psy-
chiatric subjects with or without alcoholic liver disease.

SUBJECTS AND METHODS

Thirty-five male patients with alcoholic liver disease (15 medical cases) and alcoholic
psychosis (20 psychiatric cases), who were admitted to Okayama University Hospital and
Okayama Prefectural Hospital, respectively, from 1978 to 1981, were examined in this study.
The criteria for selecting these subjects were: 1) long-term drinking in excess of 65 g ethanol
daily for over 5 years; 2) abstinence within 5 weeks before the time of admission; 3) serum
AFP determinations more than 3 times for more than 2 months after admission; and 4) negative reaction for HBs antigen. Thirteen out of 15 medical patients were diagnosed histologically by percutaneous liver biopsy as alcoholic liver disease according to Takeuchi et al. (6). Alcoholic psychiatric diseases were classified into two categories such as alcohol addiction and alcohol psychosis according to the diagnosis criteria of the Committee on the Diagnosis of Alcoholism (7). Five of the psychiatric patients were suspected of having alcoholic liver injury only on the basis of their physical and laboratory findings. The thirty-five patients examined in this study are summarized in Table 1. Total alcohol intake and liver function tests in these patients are shown in Table 2. Although the total alcohol

**Table 1. Medical and Psychiatric Subjects with Long-term Excess Drinking**

<table>
<thead>
<tr>
<th></th>
<th>Medical</th>
<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Alcoholic hepatitis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Alcoholic fatty liver</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Alcoholic fibrosis</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>No biopsy</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Psychiatric disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol addiction</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Alcohol psychosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delirium tremens</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hallucinosis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Korsakoff's psychosis</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Age, Alcohol Intake and Liver Function in Medical and Psychiatric Subjects with Long-term Excess Drinking**

<table>
<thead>
<tr>
<th></th>
<th>Medical</th>
<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 ± 10</td>
<td>51 ± 7</td>
</tr>
<tr>
<td>Total alcohol intake (kg)</td>
<td>1092 (604 ~ 1575)</td>
<td>2016 (1002 ~ 3150)**</td>
</tr>
<tr>
<td>Liver function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOT (IU)</td>
<td>139 (52 ~ 234)</td>
<td>116 (26 ~ 182)</td>
</tr>
<tr>
<td>GPT (IU)</td>
<td>75 (28 ~ 125)</td>
<td>53 (14 ~ 80)</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>3.0 (1.0 ~ 4.9)</td>
<td>1.6 (0.4 ~ 2.7)</td>
</tr>
<tr>
<td>γ-GTP (IU)</td>
<td>452 (74 ~ 952)</td>
<td>177 (26 ~ 307)*</td>
</tr>
<tr>
<td>AFP (ng/ml)</td>
<td>92 (2 ~ 40)</td>
<td>7 (4 ~ 9)</td>
</tr>
<tr>
<td>Liver injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+++</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>++</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>+</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>-</td>
<td>4</td>
<td>13</td>
</tr>
</tbody>
</table>

* P < 0.01, ** P < 0.02. Mean ± SD or Mean (range).

Liver injury: GOT > 100 IU, GPT > 100 IU or serum bilirubin > 3.0 mg/dl.
intake was significantly much greater in psychiatric subjects, elevation of serum γ-glutamyl transpeptidase (γ-GTP) activity was rather lower in these cases. No significant differences between medical and psychiatric patients were observed in regard to the age of patients or to other liver function tests including serum AFP. Abnormalities in serum GOT (> 100 IU), GPT activity (> 100 IU) and bilirubin levels (> 3.0 mg/dl) were graded for degree of liver injury (+ + + +, + +, + in Table 2); 73% medical cases and only 35% of psychiatric subjects appeared to have liver injury. Alcohol intake in all psychiatric cases was completely ceased on admission to the hospital. However, only six of medical patients stopped drinking on admission, but the other cases stopped within 5 weeks before the time of admission.

RESULTS

In 33 (94%) of 35 medical and psychiatric patients, all AFP determinations during over 2 months after abstinence were negative (< 40 ng/ml). Only two cases (Case 1 and Case 2) in the medical group showed elevated serum AFP (Fig. 1). Three representative cases with no AFP elevation, who stopped drinking and were simultaneously admitted to hospital, are illustrated with alterations in serum AFP and γ-GTP levels (Fig. 2). The time courses of serum γ-GTP activity following abstinence in these patients were markedly different, but serum AFP concentrations serially determined during these periods always showed values less than 40 ng/ml.

Case 1, a 63-year-old man, had liver cirrhosis and gastric ulcer (Fig. 3). His alcohol intake was estimated to be 1.2 1-1.4 1 Sake (144-168 g ethanol) daily for more than 32 years. His HBs antigen was negative but the antibody

![Graph showing serum AFP levels](image)

Fig. 1. Serum AFP levels following abstinence in medical and psychiatric patients with histories of long-term excessive drinking.
Fig. 2. Serum AFP and $\gamma$-GTP levels following cessation of alcohol in three representative cases with long-term excess drinking.

![Graph showing serum levels of AFP and $\gamma$-GTP over time.]

Fig. 3. Clinical course of Case 1.

![Graph showing clinical course with markers for alcohol intake, blood transfusion, hematoemesis, encephalopathy, GPT, and AFP levels.]

was positive. He had hematoemesis and tarry stool in August, and also in October 1979, and received a total of 5.2 l blood transfusion. Serum GPT activity increased 2 and 3 months following his final abstinence in the end of September and the first blood transfusion, respectively. Serum AFP concentrations rose
transiently 2 weeks after GPT levels reached the maximum.

Case 2, a 63-year-old man, had well compensated cirrhosis of the liver (Fig. 4). His alcohol intake was 720 ml Sake (86 g ethanol) daily for approximately 28 years. Serum γ-GTP levels decreased following cessation of alcohol. Serum AFP levels, however, increased 3 months after abstinence and then reached to 2080 ng/ml 5 months later. Computed tomography, ultrasound tomography and hepatic arteriography revealed hepatocellular carcinoma in the right lobe. However, AFP levels decreased thereafter to 200 ng/ml but increased again. He is now being followed in the outpatient clinic.

![Graph showing clinical course of Case 2](image)

Fig. 4. Clinical course of Case 2.

**DISCUSSION**

This study did not find AFP elevation following cessation of alcohol in 32 patients with long-term excessive drinking. Only two patients with alcoholic cirrhosis showed serum AFP elevation 2-3 months after abstinence, which may have been associated with underlying posttransfusion hepatitis and hepatocellular carcinoma, respectively. Therefore, elevated AFP levels following cessation of drinking in cases with excess alcohol intake should suggest that complicating viral hepatitis or hepatoma may be present.

Noble et al. (8) similarly suggested that positive AFP determinations during the period following cessation of alcohol in alcoholic liver disease with or without cirrhosis should raise the question of hepatocellular carcinoma.

Ethanol is one of the frequently consumed hepatotoxins that produce both
alcoholic hepatitis and cirrhosis in man (9). Weesner et al. (10) obtained the findings that ethanol had suppressive effects on parameters associated with liver cell regeneration. Therefore, they studied the effect of ethanol administration on serum AFP levels in adult rats and found that no significant rise of serum AFP levels following withdrawal from chronic ethanol administration occurred. Although ethanol appears capable of decreasing the incorporation of [3H]thymidine into DNA in the regenerating liver under some circumstances, recent investigations (4, 11) suggest that this transitional effect does not influence the overall ability of the liver to regenerate.

Elevated serum AFP concentrations were observed in some patients with acute and chronic viral hepatitis during the recovery phase (2, 12). Particularly, patients with massive hepatic necrosis who had elevated serum AFP survived more often than patients with no elevation (13). As described above, several reports (2, 3) indicate that serum AFP levels are elevated in alcoholic hepatitis, a condition frequently associated with liver cell necrosis, inflammation and regeneration. These observations have led to speculation that hepatic regeneration induces human AFP synthesis and releases in man. However, Alpert et al. (14) and Nagasue et al. (15) have clearly demonstrated that serum AFP levels in adults do not increase during the period of normal liver regeneration following partial hepatectomy.

Therefore, the mechanisms of reappearance of AFP in serum in nonmalignant liver disease including alcoholic liver disease are unknown.

REFERENCES