CEREBRAL CT SCAN ABNORMALITIES IN CHILDREN WITH LIVER CIRRHOSIS; AN EARLY PREDICTORS FOR SUBCLINICAL HEPATIC ENCEPHALOPATHY

By

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ABSTRACT
Objective : 1- To determine if there is any characteristic cerebral morphological abnormalities in cirrhotic children with subclinical hepatic encephalopathy. 2- To find if there is any correlation between hepatic function derangement and cerebral morphology. Patients and Methods: 24 children with inactive cirrhosis (fifteen male and nine female) with age range five - fifteen years, and twenty controls with matched age and sex were studied. 10 different CT Parameters and 5 psychometric tests have been evaluated for patients and controls. EI (Evan index) and MWT (Maximum width of 3rd ventricle) were statistically higher in patients than controls (P<0.02, P<0.02). CT changes were both specific and focal. Prothrombin time was only correlated with MWT and WXF (Wechsler Forward) (P<0.01, P<0.006). Multiple regression analysis revealed that WXF and EI were the most important predictors for grouping (P<0.004, P<0.045).

Conclusions: Quantification of CT Scan abnormalities has been shown to yield valuable information about the morphology of the brain that in otherwise not detectable upon subjective visual inspection alone. Subclinical hepatic encephalopathy is not a neuropsychiatric disease characterized by metabolic dysfunction alone, but may also involve gross cerebral morphological alterations.

Key words: Inactive cirrhosis.
Subclinical hepatic encephalopathy.

INTRODUCTION

Although CT abnormalities have been studied in cirrhotic adults with SHE (Bernal et al., 1987), yet such study, as far as we know, has never been undertaken in children with cirrhosis. Cognitive testing reveals deficits in memory (especially visual memory) and psychomotor visuospatial, and abstraction abilities in cirrhosis patients without overt HE. These deficits largely resolve after liver transplantation, except for memory deficits that persist in some alcoholic cirrhosis patients (Hegedus et al., 1984; Tarter et al., 1984 and Moore et al., 1989).

SUBJECTS AND METHODS

The present study comprised twenty four patients with hepatic, non active cirrhosis (group I) who were consecutively admitted to liver unit, Pediatric Department, Mansoura University Hospital. 15 of them were males (62.5%) and 9 were females (37.5%). Their ages ranged from 5-15 years.

Twenty children without any apparent liver, kidney metabolic or other major disease, aged 5-

15 years served as controls. (group II).

All patients and control were subjected to the following:
* Abdominal ultrasonography.
* Histopathological examination of liver biopsy specimens (for patients only).
* CT of the brain.
* Psychometric assessment:

2- Trail-making test: [TMT] (Reitan, 1958).

RESULTS

Table 1: Showed correlation between MWT and EI with the liver function test; MWT is statistically correlated with prothrombin.

Table 2: Showed correlation between WXF and other psychiatric tests. It was found to be statistically correlated with all tests except TMT.

Table 3: Showed multiple regression analysis for grouping into patients and control. It's evident that WXF and EI are the most important predictors of the grouping into patients and control.
Table (1): Correlation between the most important predictor CT findings and the different laboratory findings.

<table>
<thead>
<tr>
<th>Variable</th>
<th>1. MWT</th>
<th></th>
<th>2. EI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>Albumin</td>
<td>-0.19</td>
<td>0.38</td>
<td>-0.37</td>
<td>0.07</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>-0.04</td>
<td>0.84</td>
<td>0.18</td>
<td>0.41</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>0.54</td>
<td>0.01*</td>
<td>-0.34</td>
<td>0.09</td>
</tr>
<tr>
<td>Alk. Phosphatase</td>
<td>-0.34</td>
<td>0.10</td>
<td>-0.11</td>
<td>0.60</td>
</tr>
<tr>
<td>SGPT</td>
<td>-0.24</td>
<td>0.27</td>
<td>-0.03</td>
<td>0.91</td>
</tr>
<tr>
<td>SGOT</td>
<td>0.01</td>
<td>0.98</td>
<td>-0.08</td>
<td>0.69</td>
</tr>
</tbody>
</table>

* P<0.05 significant
** P<0.005 highly significant

Table (2): Correlation between WXF (the most relevant psychiatric test) and other tests (Spearman rank).

<table>
<thead>
<tr>
<th>Variable</th>
<th>WXF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
</tr>
<tr>
<td>PIT</td>
<td>0.55</td>
</tr>
<tr>
<td>TMT</td>
<td>0.37</td>
</tr>
<tr>
<td>WXB</td>
<td>0.74</td>
</tr>
<tr>
<td>WXC</td>
<td>0.51</td>
</tr>
</tbody>
</table>

* P<0.05 significant
** P<0.005 highly significant
CEREBRAL CT SCAN ABNORMALITIES IN etc...

Table (3) : Multiple regression analysis (logistic) for the most important predictor CT finding or psychiatric test predicting grouping of our subjects.

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Regression coefficient (B)</th>
<th>Standard error of (B)</th>
<th>Beta</th>
<th>T value</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. WXF</td>
<td>0.23</td>
<td>0.06</td>
<td>0.48</td>
<td>3.83</td>
<td>0.0004**</td>
</tr>
<tr>
<td>2. EI</td>
<td>-0.32</td>
<td>0.17</td>
<td>-0.24</td>
<td>-2.01</td>
<td>0.045*</td>
</tr>
<tr>
<td>3. MWT</td>
<td>-0.71</td>
<td>0.43</td>
<td>0.25</td>
<td>-1.65</td>
<td>0.11</td>
</tr>
<tr>
<td>Constant</td>
<td>0.72</td>
<td>0.39</td>
<td>-0.21</td>
<td>1.82</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Significant  
** Highly significant

Abbreviation:

EL : Evan index.
TMT : Trail making test
WXB : Wechsler backward
WXF : Wechsler forward

MWT : Maximum width of 3rd ventricle
WAIS : Wechsler adult intelligence scale
WXC : Wechsler coding

DISCUSSION

The prevalence of the CT and psychometric abnormalities in the current study has been assessed. EL and MWT were found to be 33.3% and 50% respectively. TMT, WXB, WXC and WXF were found to be 79.2%, 68%, 56% and 55% respectively. Nearly similar results were given by Jacob et al., (1976) and Sood et al., (1989). Comparing the CT findings, between patients with chronic liver disease of the current study and controls revealed that EL and MWT were statistically higher in patients versus control (P>0.02 & P<0.02). Not all CT measures revealed the presence of abnormal cerebral morphology in the liver disease patients, suggesting that the observed brain changes were both specific and focal. Among CT variables studied in the present work, EL and MDTAH were only found to be significantly correlated (P<0.001). Concerning liver function tests, prothrombin time was only correlated with MWT (P<0.01). Multiple regression analysis revealed that MWT could be only predicted from CM while EL could be predicted only from MDTAH. EL could be used to discriminate the two studied groups with the
best cut off value of E1 is 0.26. Comparing the psychiatric tests of children with liver disease versus control in the current study, WXB, WXC and WXF were found statistically lower (P<0.001, P<0.02 and P<0.0003), while TMT was statistically higher (P<0.002) than control. Our results were consistent with those of levy et al., (1987), who reported that WAIS performance tests and NCT were among the most sensitive techniques. They detected SHE in 70% and 65% of patients respectively. The two together were abnormal in 75% of patients. The tests of cognitive and verbal ability were preserved in all patients in the present study. This is in agreement with earlier reports, (Levy et al., 1987), and indicates the lack of sensitivity of neurological and bedside mental status examination in detecting cerebral dysfunction. Concerning the clinical parameters tested in the current study, there was no statistical correlation between psychometric abnormalities and clinical data. There is controversy in the literature regarding the correlation between hepatic function derangement and the degree of psychometric test abnormalities. Although Rikkers et al., (1978) and Gitlin et al., (1986) did not find any correlation between neuropsychological abnormalities and hepatic functional status, Gilberstadt et al., (1980) found an important correlation. In the present study, there was significant correlation been WXF and PT (P<0.006). Multiple regression analysis revealed that WXF and, E1 were the most important predictors for grouping (P 0.004, P0.045).

In the present work, MWT, E1 and WXF were found to be the most important variable for discrimination between children with chronic liver disease and control. The correctly clustered cases was 41 out of 44 cases.

Conclusion: From the previous results we can conclude the following:

1- Clear evidence of clinically silent abnormalities detected by some psychological tests in 60%of cases and CT abnormalities in 40% of cases.

2- Quantification of CT scan abnormalities, involving measurement of the relative position and distances between cerebral nuclei, the size and volume of the ventricular, system and the presence of cortical sulcal widening, has been shown
to yield valuable information about the morphology of the brain that is otherwise not detectable upon subjective visual inspection alone.

3- While the present results suggest that morphological changes in the cerebrum may accompany chronic liver disease, and these changes are related to psychometric measures of encephalopathy, the mechanisms responsible for these changes remain to be determined.

4- SHE is not a neuropsychiatric disease characterized by metabolic dysfunction alone, but may also involve gross cerebral morphological alterations.

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