Home Intravenous Antibiotic Treatment for Intractable Cholangitis in Biliary Atresia

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Background

**Cholangitis**

common complication during follow up of biliary atresia after Kasai operation

**Intractable Cholangitis (IC)**

- uncontrolled cholangitis by routine conservative treatment
- may cause biliary cirrhosis, hepatic failure, portal hypertension
  - most important and difficult complication
  in management after Kasai portoenterostomy
  : poor prognosis and the occasional requirement of liver transplantation

**Intrahepatic Biliary Cyst**

may be the source of biliary infection
Background

Management of intractable cholangitis and intrahepatic biliary cysts

- many surgical or medical trials
  to control cholangitis and intrahepatic biliary cysts

- no treatment of choice of intractable cholangitis or intrahepatic biliary cysts

Purpose

- review of the effects and the role of home intravenous antibiotic
treatment (HIVA) in 8 patients of post–Kasai intractable cholangitis with
  biliary atresia

- suggestion of HIVA as an effective method for management of
  intractable cholangitis and intrahepatic biliary cysts in post–Kasai patients
Methods

retrospective review of medical records
for whom
- treated by HIVA for IC after successful Kasai portoenterostomy with BA
- from 1998 to 2008
- at Severance Hospital and Yongdong Severance Hospital

diagnostic criteria of cholangitis
1) clinical symptoms such as fever, abdominal pain, jaundice or acholic stool
2) laboratory data such as hyperbilirubinemia, elevated liver enzyme or isolation of bacteria on blood culture
3) without other fever focus such as upper respiratory tract infection or urinary tract infection
Methods

diagnostic criteria of intractable cholangitis
recurrent cholangitis unresponsive to conservative management with intravenous antibiotics treatment
1) duration of admission for treatment longer than 1 month
2) three times of admission due to cholangitis with duration between previous discharge and readmission less than 1 month
detection of intrahepatic biliary cyst
Abdominal ultrasonography
Abdominal CT
central venous catheter indwelling
during the HIVA treatment
Results

Intractable cholangitis (IC) after successful Kasai operation in 10 cases during last decade to settle IC, intrahepatic cysts were drained in the first two patients but IC was not controlled.
Results

HIVA program in the patients diagnosed as IC

after insertion of central venous catheter
with help of home care nursing in 10 cases

two patients of initial period of HIVA were not followed up
because of transfer to other hospital

Duration of HIVA

from 8 to 39 months with median value of 13.5 months

two patients on HIVA
duration of 8 months for one patient and 15 months for the other

six patients off HIVA
from 8 to 39 months of duration with median value of 14 months
Clinical Characteristics of Patients on HIVA

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Sex</th>
<th>Age of Kasai op. (months)</th>
<th>Age of IC (months)</th>
<th>IHC</th>
<th>Age of HIVA (months)</th>
<th>Duration b/w IC – HIVA (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>2 1/3</td>
<td>6</td>
<td>Y</td>
<td>60</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>2 2/3</td>
<td>5</td>
<td>Y</td>
<td>33</td>
<td>28</td>
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<tr>
<td>3</td>
<td>F</td>
<td>2</td>
<td>8</td>
<td>Y</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>4&lt;sup&gt;1)&lt;/sup&gt;</td>
<td>F</td>
<td>1 1/2</td>
<td>5</td>
<td>Y</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>1 1/3</td>
<td>12</td>
<td>Y</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>1 1/2</td>
<td>4</td>
<td>Y</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>1 2/3</td>
<td>12</td>
<td>N</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>2 1/2</td>
<td>35</td>
<td>Y</td>
<td>36</td>
<td>1</td>
</tr>
</tbody>
</table>

IC: intractable cholangitis
IHC: intrahepatic cyst
HIVA: home intravenous antibiotic treatment
1) Kasai op. at other hospital
Clinical Courses

**case V**
- op
- admission event
- intrahepatic cyst
- HIV A
- last f/u

**case VI**
- op
- admission event
- intrahepatic cyst
- HIV A 1
- HIV A 2
- last f/u

**case VII**
- op
- admission event
- HIV A 1
- HIV A 2
- HIV A 3
- HIV A 4
- last f/u

**case VIII**
- op
- admission event
- intrahepatic cyst
- HIV A
- last f/u
## Short-term Results of HIVA

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Duration of HIVA (months)</th>
<th>Disappearance of IHC&lt;sup&gt;1)&lt;/sup&gt;</th>
<th>Duration of Initial Ch.-free Status after HIVA (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>Y</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>Y</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>Y</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>Y</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>Y</td>
<td>52</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>Y</td>
<td>31</td>
</tr>
<tr>
<td>7</td>
<td>15 (on Tx.)</td>
<td>−&lt;sup&gt;2)&lt;/sup&gt;</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>8 (on Tx.)</td>
<td>N</td>
<td>3</td>
</tr>
</tbody>
</table>

IHC: intrahepatic cyst  
Ch.: cholangitis  
1) detected by imaging studies (abd. U/S or CT)  
2) no previously detected intrahepatic cyst
## Effect of HIVA on Admission Rate due to Cholangitis

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Duration of Admission(^1) before HIVA (days)</th>
<th>Duration before HIVA (months)(^2)</th>
<th>Admission Ratio(^3) before HIVA</th>
<th>Duration of Admission(^1) after HIVA (days)</th>
<th>Duration after HIVA (months)(^4)</th>
<th>Admission Ratio(^3) after HIVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>318</td>
<td>73</td>
<td>4.4</td>
<td>7</td>
<td>36</td>
<td>0.2</td>
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<tr>
<td>2</td>
<td>287</td>
<td>29</td>
<td>9.9</td>
<td>58</td>
<td>55</td>
<td>1.1</td>
</tr>
<tr>
<td>3</td>
<td>109</td>
<td>12</td>
<td>9.1</td>
<td>102</td>
<td>51</td>
<td>2.0</td>
</tr>
<tr>
<td>4</td>
<td>232</td>
<td>45</td>
<td>5.2</td>
<td>0</td>
<td>9</td>
<td>0.0</td>
</tr>
<tr>
<td>5</td>
<td>93</td>
<td>15</td>
<td>6.2</td>
<td>0</td>
<td>43</td>
<td>0.0</td>
</tr>
<tr>
<td>6</td>
<td>67</td>
<td>13</td>
<td>5.2</td>
<td>0</td>
<td>26</td>
<td>0.0</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>10</td>
<td>7.0</td>
<td>61(^5)</td>
<td>13</td>
<td>4.7</td>
</tr>
<tr>
<td>8</td>
<td>141</td>
<td>30</td>
<td>4.7</td>
<td>26(^5)</td>
<td>8</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Median 125 22 5.7 16.5 31 0.6

1) Admission due to cholangitis
2) Duration from diagnosis of intractable cholangitis to HIVA
3) Admission days / duration in months
4) Duration from HIVA to last follow up
5) Admission during HIVA
Results of HIVA

Effect of HIVA on Admission Rate due to Cholangitis

<table>
<thead>
<tr>
<th>Admission Ratio</th>
<th>Before HIVA</th>
<th>After HIVA</th>
<th>P-Value$^{1)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Admission days / duration in months)</td>
<td>5.7 (4.4 - 9.9)</td>
<td>0.6 (0.0 - 4.7)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

1) Wilcoxon Signed Ranks Test
## Long-term Results of HIVA

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Duration of Follow-up after HIVA (months)</th>
<th>Ch. on Last Follow-up</th>
<th>Duration of Last Ch.-free Status after HIVA (months)</th>
<th>Recurrence of IHC&lt;sup&gt;1)&lt;/sup&gt;</th>
<th>Duration of IHC-free Status (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>Y</td>
<td>42</td>
<td>Y</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>Y</td>
<td>27</td>
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<td>51</td>
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<td>33</td>
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<tr>
<td>4</td>
<td>9</td>
<td>N</td>
<td>13</td>
<td>N</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>N</td>
<td>52</td>
<td>N</td>
<td>42</td>
</tr>
<tr>
<td>6</td>
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<td>31</td>
<td>N</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>–2)&lt;sup&gt;1)&lt;/sup&gt;</td>
<td>N</td>
<td>3</td>
<td>–3)&lt;sup&gt;3)&lt;/sup&gt;</td>
<td>–3)&lt;sup&gt;3)&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td>–2)&lt;sup&gt;1)&lt;/sup&gt;</td>
<td>N</td>
<td>3</td>
<td>–2)&lt;sup&gt;3)&lt;/sup&gt;</td>
<td>–2)&lt;sup&gt;3)&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Ch. : cholangitis, IHC : intrahepatic cyst  
1) detected by imaging studies (abd. U/S or CT)  
2) on HIVA treatment  
3) no previously detected intrahepatic cyst
# Long-term Results of HIVA

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age on Last Follow-up (yrs)</th>
<th>T.Bb (mg/dL)</th>
<th>Alb (g/dL)</th>
<th>PT (INR)</th>
<th>Ascites*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>1.1</td>
<td>3.9</td>
<td>1.28</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>0.7</td>
<td>3.9</td>
<td>1.55</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>0.6</td>
<td>5.0</td>
<td>1.02</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>0.9</td>
<td>4.9</td>
<td>0.99</td>
<td>N</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>2.1</td>
<td>3.1</td>
<td>1.06</td>
<td>N</td>
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<tr>
<td>7</td>
<td>2</td>
<td>0.9</td>
<td>3.9</td>
<td>1.13</td>
<td>N</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>1.2</td>
<td>3.5</td>
<td>1.16</td>
<td>Sm</td>
</tr>
</tbody>
</table>

T.Bb: serum total bilirubin, Alb: serum albumin
PT: prothrombin time, INR: international normalized ratio of PT
Sm: small amount of ascites, *: detected in U/S or CT
Intractable cholangitis after successful Kasai portoenterostomy can be controlled by HIVA treatment with statistically significant reduction of admission period due to cholangitis (p=0.012).

The duration of cholangitis free in HIVA–off group ranged from 12 to 52 months (median value of 29 months).

Intrahepatic cysts related to intractable cholangitis also can be controlled and disappeared by HIVA treatment.

Hepatic function is maintained good in all 8 patients of HIVA.
Conclusion

- HIVA may be an effective primary treatment for intractable cholangitis after Kasai operation in biliary atresia.

- All of the 8 patients with HIVA for IC have tolerable hepatic function by control of cholangitis and following biliary cirrhosis. No patient required liver transplantation due to chronic liver disease or hepatic failure.

- Early application of HIVA to intractable cholangitis may help to maintain the hepatic function without recurrence of cholangitis or intrahepatic biliary cysts.

- Early detection of intrahepatic biliary cysts or early diagnosis of intractable cholangitis are necessary for early HIVA application.