Hepatic hypertrophic osteoarthropathy and liver transplantation

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Abstract

Objectives—To document the variety of liver diseases and the clinical picture of hepatic hypertrophic osteoarthropathy (HOA) complicated by arthritis and to report the effects of successful liver transplantation on this disabling condition.

Methods—Seven patients with severe liver disease (two biliary atresia, two primary sclerosing cholangitis, one Wilson’s disease, one primary biliary cirrhosis (PBC) and one alcoholic cirrhosis) complicated by radiologically proven hepatic HOA and suffering from arthritis are described.

Results—In four of the six patients who required hepatic transplantation for inadequate liver function successful grafting was achieved with complete clinical remission of the painful arthritis. This occurred three days to 18 months later.

Conclusions—Hepatic HOA with arthritis occurs in a variety of liver diseases. Despite resistance of this arthritis to conventional therapies, successful liver transplantation was associated with complete clinical remission in four of the cases reported.

(Hepatogastroenterology 1994; 41: 43-45)

Hepatic hypertrophic osteoarthropathy (HOA) was originally described in 18951 and is characterised by periosteal reactions affecting the shafts of long bones. It is well documented from case reports6-8 in studies involving larger groups of patients.1,8 Hepatic HOA with arthritis, however, is rare and only three cases are recorded in the largest series.7

This paper describes seven patients from a liver transplant centre suffering from hepatic HOA with arthritis.

Case reports

The clinical details of the patients are given in the table.

All patients received post-transplantation immunosuppression with azathioprine 1 mgm/kgm, cyclosporin 5 mgm/kgm and high dose prednisolone.

CASE 3

A nineteen year old girl presented in acute liver failure (bilirubin 618 umol/l albumin 34 G/L and INR 2·8) with fulminant Wilson’s disease. No note of her joints was made at this critical time and she underwent liver transplantation four weeks later. Immediately post transplant she was wheelchair dependent with painful knees and eight months later she still had knee pain and two years post transplant she was pain free. Eighteen months post transplant there was no knee effusion or joint pain.

CASE 4

A twenty one year old man with a seven year history of primary sclerosing cholangitis and ulcerative colitis presented with deterioration in liver function and the development of painful knees, ankles and wrists. On examination he was clubbed and had knee effusions with local tenderness in his wrists and ankles. Endoscopic investigation at this time did not demonstrate oesophageal varices. Radiographs showed obvious periostitis. Liver transplantation was carried out three months later (bilirubin 196 umol/l albumin 19 G/L and INR 1·8). Unfortunately he died postoperatively.

CASE 1 AND 2

Two female children required Kasai procedures in infancy for biliary atresia. This operation involves excision of the extrahepatic biliary tree and construction of a roux-en-y loop to the remaining biliary tree in an attempt to reduce intrahepatic cholestasis. Unfortunately, both eventually required liver transplantation.

Nine months before transplantation, patient 1 presented with painful knees with effusion and slight swelling of both elbows. Radiographs of the elbows showed obvious periostitis and three months later she was wheelchair dependant because of severe knee pain. Three days after liver transplantation for inadequate liver function (serum bilirubin 121 umol/l, normal range 3-20 umol/l, albumin 39 G/L, normal range 35-50 G/L and INR 1) she had no joint pain and two years post transplant she remains pain free and there is no evidence of joint effusion.

Patient 2 had bilateral painful knee effusions and associated fixed flexion deformities. Her initial transplant failed and four months after a second successful transplant she was pain free. Eighteen months post transplant there was no knee effusion or joint pain.

CASE 1

A twenty year old man with primary sclerosing cholangitis presented with a two year history of painful hands, wrists and ankles. He was osteopenic on X-ray and only four months post transplantation was he able to walk without a wheelchair.
Details of patients with hepatic hypertrophic osteoarthropathy and arthritis

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Clubbing</th>
<th>Joints</th>
<th>Outcome of Transplant</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>Biliary atresia</td>
<td>+</td>
<td>Knees</td>
<td>Successful</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>Biliary atresia</td>
<td>+</td>
<td>Knees/elbows</td>
<td>Successful</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>Wilson’s disease</td>
<td>+</td>
<td>Knees</td>
<td>Successful for 18/12</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>Sclerosing cholangitis, ulcerative cholangitis</td>
<td>+</td>
<td>Knees/elbows/wrists</td>
<td>Died</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>Sclerosing cholangitis, hepatocellular carcinoma</td>
<td>+</td>
<td>Knees/ankles/wrists</td>
<td>Successful only for 2/12</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>PBC</td>
<td></td>
<td>Knees/ankles/wrists</td>
<td>Chronic non A non B</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>Alcoholic cirrhosis</td>
<td></td>
<td>Knees/ankles/wrists</td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

Note: Result column + indicates resolution of arthritis after transplantation, - indicates no improvement of arthritis after transplant.

CASE 5
A forty five year old man with a 12 year history of sclerosing cholangitis complained of painful knees, elbows and wrists. His liver function had recently deteriorated and he presented with bleeding oesophageal varices.

Two years previously liver biopsy had been reported as showing hepatocellular carcinoma. On examination he was clubbed and had large knee effusions with tender elbows and wrists. Radiographs showed periostitis of the medial borders of both femora, left lower humerus and left radius at the wrist. Because of continuing deterioration in liver function (bilirubin 176 umol/l, albumin 28 G/L) he underwent transplantation. Two months later he was asymptomatic from HOA and on examination had only a trace of fluid in his knees. He has subsequently died.

CASE 6
A thirty year old woman with PBC, seen for pretransplant assessment, (bilirubin 340 umol/l, albumin 30 G/L and INR 1:3) was found to be clubbed with a swollen but non-painful left knee. There was no evidence of oesophageal varices on endoscopy. A month later liver transplantation was performed which failed and she required a second transplant. Three months after this she had bilateral painful knee effusions and radiographs revealed periosteal reaction in the knees, wrists and ankles. The graft had functioned inadequately probably due to chronic non A non B viral hepatitis. The arthritis has persisted throughout this five year post-transplant period despite ongoing immunosuppressive therapy, currently provided by prednisolone 10 mgm daily and cyclosporin 250 mgm twice a day.

CASE 7
Case 7 has not yet required transplantation. He is included as he demonstrates the typical clinical and radiological picture (fig) described in this report and suffers from another variety of liver disease. He is a forty four year old man with alcoholic liver disease complicated by portal hypertension and bleeding oesophageal varices. A few months following a haematemesis he complained of painful ankles, knees and wrists. When reviewed four years later he was clubbed and there was a right knee effusion as well as tenderness to palpation of the bones just above the ankles and wrists.

Discussion
These reported patients with hepatic HOA and arthritis suffered from a variety of liver diseases. They are representative of patients referred to the liver unit for transplantation where 25% suffer PBC, 7% biliary atresia, 5% primary sclerosing cholangitis, 4% alcoholic cirrhosis and 59% other causes including acute Wilson’s disease. This contrasts with Epstein’s original report where PBC was the diagnosis in 50% of cases of hepatic HOA.

All patients were clubbed compared with 30% of patients undergoing hepatic transplantation in the unit and the arthritis was universally characterised by knee effusion. There was also involvement of other joints including ankles, wrists and elbows. In all cases, the arthritis was associated with considerable morbidity which resulted in pain and limitation of movement. Conservative management including injection with corticosteroid and the use of non-steroidal anti-inflammatory drugs was of no benefit to any patient.

The age of the patients at presentation of the arthritis ranged from 11 to 44 years and in five of the seven cases joint symptoms were most severe immediately pre liver transplantation, occurring at a time of marked liver decompensation. In patient 3 it is very probable that arthritis preceeded transplantation as she was wheelchair dependant immediately following surgery. The presentation of arthritis at a time of severe liver decompensation is highlighted in...
the literature by a report of arthritis first
presenting at the time of liver transplant
rejection and it is interesting that case 5, where
graft function was inadequate, continues to
have severely painful swollen knees.

Of the six patients undergoing transplanta-
tion, a successful graft was achieved in
four, and in these there was complete
resolution of symptoms between three days
and 18 months. This observation is supported
by the report of another centre10 where two
patients with hepatic HOA, one with crippling
arthritis, had complete resolution of their
symptoms following transplantation.

In the patients reported here arthritis
occurred in six of the seven cases at a time of
severe liver decompensation and in four
patients, in whom liver transplantation was
successful, the symptoms resolved.

In case 5, despite immunosuppression,
arthritis has persisted, and it is unlikely that
such treatment explains the resolution of the
arthritis. In cases 1 and 2 pretransplant bac-
terial overgrowth, implicated in the patho-
genesis of arthritis in gastrointestinal bypass
surgery, is not responsible for arthritis as the
roux-en-y loop is not distended so the patient
does not have the features of 'blind loop'.

To date there is no UK report documenting
resolution of HOA in patients undergoing
cardiac or heart and lung transplantation.

It appears therefore that the damaged liver
produces or fails to metabolise substances
responsible for the local changes in bone
metabolism in these patients with arthritis and
HOA.

Conclusion
This paper reports the clinical picture of
arthritis in patients with a variety of liver
diseases complicated by HOA. The observa-
tion that successful liver transplantation is
associated with a resolution of pain and joint
effusion is interesting and warrants further
investigation.

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