Neurological Complications Following Liver Transplant: A Pictorial Review of Radiological and Clinical Findings

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Neurological complications are a rare but important and significant source of information about morbidity and mortality in liver transplant patients. Based on the clinical and radiological findings of 21 patients, neurological complications were categorized into five main groups; focal hemorrhagic or occlusive complications \(n = 11\); diffuse hypoxic-ischemic injury \(n = 3\); hypertensive encephalopathy \(n = 1\); central pontine or extra-pontine myelinolysis \(n = 4\); and infection \(n = 2\). Neurological manifestations varied according to the location of the lesion, although seizures were the most common manifestation. In this pictorial review, we illustrate the radiological findings, focusing on MR and CT images, of a spectrum of neurological complications following liver transplants, as well as their clinical correlations.

Index words: Central nervous system
Liver transplant
Neurological complication

Familiarity with the frequency and imaging features of neurological complications is especially important to radiologists when interpreting the imaging studies of liver transplant patients, as early diagnosis has a very important role in initiating appropriate treatment. A series of pathology reports dealing with neurological complications following liver transplants have been published. However, only a few of these reports have described imaging findings.

In this review, of a total of 498 liver transplant recipients, 21 patients \(4\%\) were found to have abnormal radiological findings in the central nervous system following their liver transplant. The radiological findings of a spectrum of neurological complications following liver transplant are illustrated and described here, as well as their corresponding clinical correlations (Table 1).

Focal Hemorrhagic or Oclusive Complication

Eleven \(n = 11, 52.4\%\) of the 21 patients were affected by intracranial hemorrhage \(n = 7\) and/or cerebral in-
farction \( n = 4 \) of varying types and sizes. Hemorrhages included five cerebral or cerebellar hematomas and two subdural hematomas. One patient had a pontine infarction (Fig. 1), and three patients had cerebral infarctions, but no source of the emboli was detected.

Hemodynamic instability during the peri- or post-operative periods in the setting of unrecognized carotid or intracranial occlusive disease or embolic occlusion secondary to heart or deep vein problems, can result in occlusive cerebrovascular complications [5]. Intra-operative air embolisms associated with the use of venous bypass have been described [6], but have now become a relatively rare complication.

Intracranial hemorrhages may be intraparenchymal (Fig. 2), subdural (Fig. 3) or subarachnoid, and can be isolated or a combination of the three. Coagulopathy, 

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<td></td>
<td>Mental change [2]</td>
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<td>Occlusive infarction ( n = 4 )</td>
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<td>Hypoxic-ischemic encephalopathy ( n = 3 )</td>
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<td>CNS tuberculosis ( n = 1 )</td>
<td>Fever [1]</td>
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Fig. 1. A 36-year-old man with acute pontine ischemic change or infarction four months after living-related liver transplant due to fulminant toxic hepatitis. Unenhanced CT scans show poorly defined low density [arrow] in the central pons. This patient died as a result of the pontine infarction.

Fig. 2. A 33-year-old man with right frontal lobe intracerebral hemorrhage one week after living-related liver transplant due to fulminant toxic hepatitis. Unenhanced CT scans show high-density hemorrhage [arrow] in the right frontal lobe. There is a mild edema surrounding the hematoma and moderate mass effect. This patient died four days after the CT scan was performed.

Fig. 3. A 55-year-old woman with a subacute subdural hematoma three months after living-related liver transplant due to cirrhosis of the liver. Unenhanced CT scan shows a high-density subdural hematoma in the left cerebral convexity. Subfalcian herniation is also noted.
secondary to liver failure, unstable blood pressure control, and co-existent CNS infection can also lead to intracranial hemorrhages.

The prevalence of cerebral infarctions following orthotopic liver transplants (OLT) have been reported with an incidences ranging from 3.6% to 18% in autopsied patients [2, 7, 8]. Intracranial hemorrhages have been reported in 7% to 24% of autopsied liver transplant recipients and are strongly associated with high patient mortality [2, 7, 8].

In some cases, there are multiple hemorrhages and infarctions of the neocortex with no apparent etiology [1]. Usually these kinds of occlusive or hemorrhagic complications carry poor prognoses.

**Diffuse Hypoxic Ischemic Injury**

Diffuse hypoxic ischemic encephalopathies with varying degrees of severity were seen in three patients (14.3%). None of the patients with hypoxic ischemic lesions had any previous record of clinical episodes of cardio-respiratory arrest, but most had experienced some level of hypotension during the peri- or post-operative period.

Hypoxic ischemic damage ranged from a mild injury to a few susceptible foci to widespread and severe change with evidence of cortical laminar necrosis [7]. A hypoxic-ischemic insult is the result of global rather
than focal brain injury [8]. Severely generalized cerebral edemas ensue 24 to 48 hours following a liver transplant and are seen as diffuse low-density on CT images and as abnormal signal intensity at the vascular watershed zones, cortical areas, and deep gray matter, including basal ganglia and thalami, on MR images (Fig. 4).

Hypertensive Encephalopathy

Hypertensive encephalopathies usually occur during the early post-operative period. Seizures are the most frequently encountered symptom without evidence of intracranial bleeding. These hypertensive seizures have been attributed to vascular spasms or a breakdown of the autoregulation of cerebral blood flow resulting in an ischemia and/or edema [9].

The fluid requirements and coagulopathy during the surgical procedure and cyclosporine and steroid therapy during post-operative management result in post-operative hypertension, which is responsible for the appearance of CNS hemorrhage.

Hypertensive encephalopathies commonly occur in the parieto-occipital area (Fig. 5). Hemodynamic and hemostatic control during the immediate post-operative period, although not always easy, can help to eliminate these potentially fatal complications [3].

Central Pontine and Extra-pontine Myelinolysis

Four patients (19.0%) were affected by demyelination, with a pattern characteristic of central pontine (Fig. 6) and extra-pontine (Fig. 7) myelinolysis.

The incidence of central and extra-pontine myelinolysis following liver transplants is still unclear. However, central and extra-pontine myelinolysis were found in 10-30% of patients who died following their liver transplant [2].

Although its etiology is unknown, central pontine myelinolysis (CPM) is associated with rapid correction of prolonged hyponatremia (6). The appropriate rate of correction is still unknown, but it has been suggested that serum-sodium levels should not increase by more...
than 0.5 mEq/L per hour (4). Central and extra-pontine myelinolysis are also associated with rapid correction of broad fluctuations in plasma glucose levels or of blood cyclosporin levels (1, 5, 10).

CPM may cause progressive quadriplegia resulting in loss of speech and swallowing. Seizures or frank comas may hint to extra-pontine involvement. This clinical feature is often clouded by toxic, metabolic or ischemic encephalopathy, thus obscuring the diagnosis of CPM (6). In our case, CPM had not been suspected on clinical grounds.

Extra-pontine sites, such as the putamen, caudate nuclei, midbrain, thalami, and subcortical white matter, have also been reported to be areas of myelination. Extra-pontine myelinolysis (EPM) usually affects white matter tracts, but most patients experience gradual clinical and radiological resolution to a variable extent (10).

In EPM, CT images show non-enhancing areas of low attenuation, while these foci appear as areas of increased signal on T2-weighted MR images (11).

Careful peri-operative fluid management specifically related to sodium and glucose levels may reduce the risk of CPM and EPM (12).

**Infection**

Two patients displayed evidence of CNS infection, one with tuberculosis (Fig. 8) and the other with neurocysticercosis (Fig. 9).

Infection is a serious complication of human organ transplants and accounts for a post-transplant mortality rate of up to 80% (1). Immunosuppression, required to avoid graft rejection, renders a patient more vulnerable to bacterial, fungal, viral, and protozoal opportunistic infections.
microorganisms. The difficulty of post-transplant therapeutic management is in keeping an adequate balance in the host defense mechanism (13).

CNS infections were documented in 34% of one large autopsy series (5). Most infections occur in the first two months following a liver transplant and are commonly manifested as either meningitis or meningoencephalitis. Viral (Cytomegalovirus (CMV), Herpes simplex or zoster, Epstein Barr), bacterial (Listeria, E.coli, tuberculosis, cisticercosis), and fungal (cryptococcosis, aspergillosis) infections can involve the CNS. Bacteria are known to be the most common cause of clinically significant infections following liver transplants (1). However, a recent investigation using in situ hybridization clearly demonstrated a significantly higher frequency of CMV genomic material in brain tissue from OLT patients than in aged-matched immunocompetent controls (89% vs. 23%) (14). Encephalopathic patients following OLT showed unusually prominent degrees of CMV hybridization (14).

Disseminated fungal infections or abscesses due to Cryptococcus, Aspergillosis or Candida, are frequently seen in liver transplant patients, especially in the first month following a transplant, with a reported incidence of between 4% and greater than 40% (14, 15). These organisms usually cause disseminated systemic infections and are frequently fatal. Contrast-enhanced CT scans show multi-focal enhancing nodules or peripheral rim enhancing nodules in both cerebral hemispheres, and T2-weighted MR images show multi-focal high-signal intensities.

**Conclusion**

Neurological complications are not uncommon in the immediate post-operative period following liver trans-
plants and are associated with high mortality. These complications can be caused by numerous factors (8). Understanding the common radiological findings of neurological complications following liver transplants is important for both early recognition and intensive treatment.

References

... tion with particular reference to intraoperative cerebral air embolus. *Ann Surg* 1978;187:236-240