A 33-year-old man was noted to be HIV positive in 2005 after a diagnosis of sputum-positive pulmonary tuberculosis (TB). He responded well to 6 months of standard TB therapy. The initial HIV diagnosis was made in Durban and he was lost to follow-up after moving to Cape Town.

In August 2007 he presented to a regional hospital in the Cape Town metropole with cryptococcal meningitis (cerebrospinal fluid culture positive for *Cryptococcus neoformans*, CLAT titre 1:2048). At this stage his CD4 count was 116 cells/µl. He was initially treated with intravenous amphotericin B for 10 days followed by oral fluconazole 400 mg daily for 8 weeks. This was then reduced to a maintenance dose of 200 mg daily. He was also commenced on co-trimoxazole prophylaxis. He was referred to a regional antiretroviral (ARV) roll-out clinic but did not immediately attend for follow-up. Instead, in late November 2007 he again presented to the regional hospital emergency service with meningeal symptoms. Lumbar puncture again demonstrated a lymphocyte-predominant CSF that was CLAT positive (titre 1:296). The repeat CSF culture was negative.

A preliminary pre-ARV assessment was performed during this admission and abnormal liver function test results were noted. He was not jaundiced and the liver profile abnormality was a mixed pattern with elevated transaminases and canalicular enzymes, both approximately 2 - 5 times above the normal range (Table I). Synthetic liver function was preserved.

A liver biopsy specimen demonstrated an unanticipated and uncommon finding of numerous intraparenchymal collections of histiocytes associated with numerous fungi in yeast forms. These were confirmed to be *C. neoformans* (Fig. 1). Additionally there was modest macrovesicular fatty change with no associated inflammation. A piece of the core of liver tissue was submitted for TB and fungal culture. The fungal culture was negative for *Cryptococcus*, suggesting that the organisms were non-viable after the previous treatment.

After the biopsy findings, a diagnosis of sub-optimally treated disseminated cryptococcosis was made. The patient received 2 weeks of intravenous amphotericin B followed by oral fluconazole. He improved both clinically and in terms of LFT results. He was discharged in late January 2008 and an appointment for counselling and commencement of ARV therapy was made. Three weeks
later, before attending the ARV clinic, he was readmitted with a febrile illness. A chest radiograph demonstrated segmental right lower lobe consolidation with cavitation and right hilar lymphadenopathy. Sputum samples were now positive for acid-fast bacilli. *Mycobacterium tuberculosis* (MTB) was suspected.

All previous cultures were reviewed. Notably, the liver tissue as well as sputum previously submitted had cultured *M. intracellulare*. Retrospectively a modified Ziehl-Neelsen stain of the liver biopsy specimen was performed and was negative. The patient was commenced on rifabutin, clarithromycin and ethambutol and steadily improved. ARV therapy was commenced as an inpatient.

Notably, the patient’s liver function progressively improved and he was discharged to a regional ARV clinic. He continues to do well, and recent LFT results are set out in Table I.

### DISCUSSION

The investigation and management of patients with advanced HIV in South Africa often poses a multitude of diagnostic and therapeutic challenges. LFT abnormalities are a frequent finding in HIV-positive patients, with previous studies reporting a prevalence ranging between 30% and 75%.

Liver biopsy-based studies have demonstrated the benefit of liver biopsy as a useful diagnostic tool in the setting of advanced HIV with pyrexia of uncertain origin and/or hepatomegaly and LFT changes. The patient described demonstrates the above together with several other issues. Firstly the liver biopsy provided a clear histopathological diagnosis. The finding of a prevalent opportunistic infection (OI) such as *C. neoformans* in the liver has not commonly been reported in the literature despite the pathophysiological tendency for widespread dissemination of cryptococcus following entry via the pulmonary route. In our own local experience this is the first case in which we have demonstrated it in the liver.

The second issue was the unexpected culture of *M. intracellulare*, or MAC (*M. avium* complex) as it is more commonly referred to, from the liver tissue. The presence of multiple OIs is not unusual in patients with advanced HIV/AIDS. What is unusual is finding MAC in our setting.

In the pre-ARV era MAC was a frequent finding on liver biopsy in patients with advanced HIV in the developed world; however, as has been demonstrated previously, MAC appears to be uncommon in our local setting.

The reasons for this are not clear, but may relate to the overwhelming presence of *M. tuberculosis* in our HIV population. The culture of MAC in this patient demonstrates the additional value of liver biopsy in that it provided tissue for culture. As many OIs involve disseminated infection, liver tissue is a potential source of tissue for culture.

In summary, this case highlights the potential value of liver biopsy in patients with advanced HIV and abnormal LFTs where there is a wide range of differential diagnoses. Provided the procedure can be performed safely, liver biopsy both enables demonstration of the histological pattern of injury accounting for the LFT abnormalities and provides tissue for culture to diagnose opportunistic infections. In this case, an accurate diagnosis could be made following readmission and enabled appropriate treatment to be initiated.

### Acknowledgement

Dr Helen Wainwright, UCT Department of Anatomical Pathology, for liver histology review and images.

### REFERENCES


### TABLE I. LIVER FUNCTION TEST RESULTS

<table>
<thead>
<tr>
<th>Parameter (normal range)</th>
<th>Dec 07</th>
<th>Jan 08</th>
<th>Feb 08</th>
<th>June 08</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tbil (0 - 17)</td>
<td>3</td>
<td>6</td>
<td>87</td>
<td>17</td>
</tr>
<tr>
<td>ALT (0 - 40)</td>
<td>111</td>
<td>80</td>
<td>122</td>
<td>40</td>
</tr>
<tr>
<td>AST (0 - 40)</td>
<td>126</td>
<td>60</td>
<td>268</td>
<td>48</td>
</tr>
<tr>
<td>ALP (40 - 120)</td>
<td>277</td>
<td>190</td>
<td>332</td>
<td>100</td>
</tr>
<tr>
<td>GGT (0 - 35)</td>
<td>295</td>
<td>196</td>
<td>507</td>
<td>96</td>
</tr>
</tbody>
</table>

Tbil = total bilirubin (µmol/l); ALT = alanine transaminase (IU/l); AST = aspartate transaminase (IU/l); ALP = alkaline phosphatase (IU/l); GGT = gamma-glutamyltranspeptidase (IU/l).