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LETTER TO THE EDITORS

Liver transplantation in a patient acutely infected with pandemic Influenza A H1N1

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Dear Sirs,

In 2009, the World Health Organisation reported influenza A H1N1 to be the first pandemic infection in 40 years. The virus was responsible for over 18 000 deaths around the globe [1]. Multiple reports have subsequently been published of organ transplant patients infected with H1N1 influenza, including in the early postoperative period [2,3]. We now report a novel case of a patient undergoing a liver transplant whilst actively infected with influenza A H1N1.

A 57-year-old Vietnamese-born man awaiting liver transplantation was admitted after presenting with hepatic encephalopathy and hepatorenal syndrome. His past history included decompensated cirrhosis secondary to primary biliary cirrhosis.

Nineteen days into his admission he complained of a sore throat, diaphoresis and rhinorrhoea. He was sharing a four-bed room with another patient who had become unwell 2 days earlier and had subsequently been diagnosed with H1N1 influenza. Our patient was placed in contact isolation; nasal and throat swabs for influenza testing were taken, and empirical oseltamivir 75 mg twice daily was commenced. He was afebrile and maintained 100% oxygen saturation on room air with no consolidation or pulmonary infiltrates seen on a chest radiograph. The following day, his coryzal symptoms had improved and he remained afebrile. His initial nasal swab for influenza A and B, including H1N1, was initially negative using an in-house real time polymerase chain reaction (PCR) assay. At this time a suitable donor organ became available and the patient proceeded with liver transplantation.

Whilst undergoing the cadaveric transplant operation, his throat swab returned positive for H1N1 influenza. Although he had received three doses of oseltamivir prior to transplant, he had risk factors for severe disease [4,5] and was given a higher dose of 150 mg intraoperatively.

He was extubated 20 h postoperatively and discharged from ICU to the ward after 48 h on standard immunosuppression including methylprednisolone, tacrolimus and mycophenolate mofetil. Respiratory parameters were stable post-transplantation, with minimal requirement for supplemental nasal oxygen (3 l/min) to maintain 100% oxygen saturation. He had no chest radiographic findings of note. Repeat nose and throat swabs taken on day four of treatment returned negative results for H1N1 influenza. His serum total IgG level was low at 2.8 g/l, but he did not have specific IgG2 subclass deficiency which has previously been identified in severe cases of H1N1 influenza [6].

Our patient completed 7 days of oseltamivir 75 mg twice daily and had an uncomplicated recovery from his operation. He was discharged from hospital 14 days after his operation. At 2 years of follow-up he maintains good graft function on minimal single-dose tacrolimus and no further respiratory infections of note.

To the best of our knowledge, this is one of the first recorded cases of a patient being transplanted whilst acutely infected with H1N1 influenza. There are multiple risk factors that predispose transplant recipients to severe sepsis peri-operatively: potent post-operative immunosuppression, the patient's premorbid clinical condition, and the lengthy duration of transplant surgery. It is fortunate that our patient had an excellent outcome post-transplantation despite documented infection.

In the midst of the pandemic, despite the pressing need for urgent transplantation, the risk of overwhelming respiratory sepsis post-transplant would have almost certainly led to the transplant being abandoned had his positive PCR been known prior to surgery. In hindsight, the known contact to a documented case of influenza allowed heightened suspicion in the setting of mild viral symptoms, early diagnostic testing and institution of empiric therapy, which almost certainly contributed to his positive outcome.

Unfortunately our patient's initial nasal swab did not yield the diagnosis. Combining nasal and throat specimens has been shown to increase the diagnostic yield [7,8]. Interestingly, a nasal swab performed better than a throat swab in one study [9], and a single nasal swab was comparable to nasopharyngeal aspirate for respiratory virus infections in another study [10].

Although the recent H1N1 pandemic has passed, and whilst we do not advocate transplantation in all patients

acutely infected with influenza, we believe there are three main lessons from this case that are of relevance to future outbreaks. The first is the importance of heightened clinical suspicion of influenza and prompt empirical treatment, especially in hospitalized patients where spread from patient to patient can be rapid and clinically devastating. Second, early diagnosis with the collection of appropriate specimens, including testing with combined nasal and throat specimens, should be undertaken when the diagnosis is of particular importance, as within the transplant community. Finally, an individual risk-benefit assessment needs to be made based upon the severity of the underlying infection, in particular the risk of cardiopulmonary compromise balanced against the likelihood of progressive liver-related morbidity or mortality in the absence of a transplant.

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