Possible missed diagnosis of *Ureaplasma* spp. infection in a case of fatal hyperammonemia after repeat renal transplantation.

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To the Editor,

I read the paper by Kiberenge and Lam with great interest and would like to comment on the microbiological presentation of this case study (1). In the paper the authors describe a case of fatal hyperammonemia after repeat renal transplantation, but with no etiology determined.

The combination of data presented in the paper as well as information from recent reports in the literature suggest the hyperammonemia may have been the result of an infection by the bacteria *Ureaplasma* spp.. The reasons for this are several fold. Firstly *Ureaplasma* spp. have recently been reported as a pathogen in the context of hyperammonemia among lung transplant patients. A study by Bharat *et al*. identified *Ureaplasma* within bronchoalveloar lavage and blood samples from a collection of expired patients who died as a result of hyperammonemia of unknown etiology (2). They also identified *Ureaplasma* as the sole organism in a number of prospective cases of the same condition. Finally, *Ureaplasma* were absent from all control samples taken from lung transplant patients with no signs of elevated serum ammonia levels.

Although Kiberenge and Lam correctly sent samples for microbiological analysis the methods used in routine bacterial culture would not have been appropriate to detect the presence of *Ureaplasma* due to the fastidious growth requirements of this organism. *Ureaplasma*, as the name suggests, utilize urea as their sole energy source resulting in the production of ammonia and therefore increasing the pH. In the situation where patients

present with hyperammonemia, circulating levels of urea will have permitted the replication of the organism and be responsible for the production of ammonia accounting for the symptoms. It should be noted that the authors do state that a urease positive organism may have been present accounting for the symptoms, but was not culturable due to the administration of broad spectrum antibiotics.

With respect the use of broad spectrum antibiotics these were not defined within the paper. If the antibiotics belonged the beta-lactam family these will have had no effect upon *Ureaplasma* as, unlike many bacteria, these organisms do not have a cell wall which is the primary site of action for these drugs. Similarly aminoglycosides have been shown to have universally poor activity against *Ureaplasma*. In general only three classes of antibiotic have activity against these organisms. These include the macrolides, tetracyclines and fluoroquinolones, although resistance to all three classes have been reported (3).

In the cases of hyperammonemia among lung transplant patients Bahrat *et al.*, demonstrated that upon administration of the anti-ureaplasma antibiotics levofloxacin and azithromycin the patients rapidly cleared the infection as well as correlating with the resolution of symptoms. In one case the treatment with azithromycin did not clear the organism or resolve the symptoms, but this was attributed to the identification of a macrolide resistant strain (azithromycin minimum inhibitory concentration of 256 μg/ml). Therefore if non-effective antibiotics were administered in the case presented by Kiberenge and Lam this would have accounted for the persistent symptoms.

Although *Ureaplasma* spp. can be found in the urogenital tract of 40 – 80 % of healthy females they have been implicated in a number of complications associated with kidney transplantation (4-8). A study by Ekiel *et al.*, identified that *Ureaplasma* were more prevalent in the samples from kidney transplant patients (40 %) compared with controls (27.5 %), and *Ureaplasma urealyticum* was more prevalent in the study group (10 %) versus *Ureaplasma parvum* (2.5%) (9). It is not known if these infections were the result of endogenous *Ureaplasma* within the patient gaining a foot hold as a result of immunosuppressive treatment or whether they are transmitted to the recipient patient from either the donor organ or blood products.

In light of these findings clinicians and microbiologists alike should be mindful of identification techniques for these organisms in particular when hyperammonemia patients have culture negative results. The use specific selective media or molecular techniques, such as 16s rRNA or *Ureaplasma* specific PCR, should be utilised to aid in the identification of these fastidious organisms and permit the administration of appropriate antimicrobial therapy to aid clearance of infection and resolution of symptoms.

References:

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