

Session: P044 Diagnostic mycology I

Category: 6b. Diagnostic mycology (incl molecular)

23 April 2017, 13:30 - 14:30

P0975

Potential impact of T2Candida assay on the use of empiric antifungal therapy in patients at high risk for candidaemia/invasive candidiasis: a tool for antifungal stewardship programmes?

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Background: T2Candida uses T2 magnetic resonance (T2MR) technology to detect five species of Candida by category: *C. albicans*/*C. tropicalis* (A/T), *C. parapsilosis* (P), *C. krusei*/*C. glabrata* (K/G), directly from whole blood in 3 hours. In a large clinical trial, T2MR demonstrated overall sensitivity and specificity for candidemia (C) of 91% and 99%. Negative predictive value ranged from 99.5% to 99.0% in study population with candidemia prevalence of 5% and 10%. In addition, T2MR recognized 12

invasive candidiasis (IC) undetected by blood cultures (BCs). Our hypothesis is that owing its ability to rapidly and accurately exclude C/IC, T2MR can be useful for antifungal stewardship programs (ASPs) by decreasing the use of empiric antifungal therapy (EAT).

Material/methods: To assess the potential impact of T2MR on the management of EAT, we performed a prospective study of adult (≥ 18 years) patients starting EAT at our 1420-bed tertiary teaching hospital. Patients were included for analysis if they exhibited severe sepsis/septic shock criteria plus ≥ 2 risk factors for C/IC: admission to intensive care unit, immunosuppressive therapy, neutropenia, renal replacement therapy, prior infection and/or colonization with *Candida* spp., prolonged antibiotic exposure, abdominal surgery, parenteral nutrition, vascular devices. Before starting EAT in all enrolled patients, a whole blood sample was collected immediately after drawing BCs. Specimens were subsequently run on the T2MR Instrument (T2 Biosystems). BACTEC automated system was used for BCs. Results of T2MR were blinded to infectious disease consultants who managed EAT according to clinical response, laboratory tests and imaging data.

Results: To date, 13 patients have been enrolled: male 69%, median age 62 (IQR 50-71) years, median Charlson index 5 (IQR 2-6). Median number of RFs for C/IC per patient was 3 (IQR 2-5), the most common were abdominal surgery (54%), prolonged antibiotic exposure (54%) and immunosuppressive therapy (46%). EAT consisted of an echinocandin administered for a median of 11 (IQR 5-12) days. BCs were negative in all patients except one diagnosed of *C. albicans* candidemia. T2MR was negative in 11 patients. Median time to a negative result was 124 (IQR 124-135) and 7 (IQR 4-16) hours for BCs and T2MR, respectively. T2MR was positive in two cases: in the candidemic patient yielding A/T category, and in a liver transplant recipient yielding P category. Time to positive result was 93 hours for BCs, 4 and 7 hours for T2MR. The patient with discordant BC/T2MR results was receiving high-dose weekly liposomal-amphotericin-b prophylaxis, he developed septic shock of undetermined origin 16 days after transplantation and was empirically treated with removal of all vascular devices and antimicrobial therapy including an echinocandin administered for 12 days; catheter tips and respiratory cultures were negative.

Conclusions: Our preliminary results show that T2MR is very promising for both optimal patient management and ASPs.