


27th **ECCMID**

Vienna, Austria
22 – 25 April 2017

The congress of  ESCMID

Session: EV021 Nosocomial infection surveillance & epidemiology

Category: 8d. Nosocomial infection surveillance & epidemiology

22 April 2017, 08:45 - 15:30

EV0333

An outbreak of acute endophthalmitis caused by intra-vitreous injection of contaminated bevacizumab: investigation using MALDI -TOF MS protein fingerprinting

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Background: Bevacizumab, a monoclonal antibody, is a vascular endothelial growth factor inhibitor commonly used for age-related macular degeneration. It is used as intra-vitreous injection and has been associated with outbreaks of endophthalmitis due to contaminated vials. The objective of the study was to identify the source of endophthalmitis outbreak, following intra-vitreous injection of bevacizumab in our Advanced Eye Center.

Material/methods: We report an outbreak of acute endophthalmitis following intra-vitreous injection of bevacizumab to 27 patients. Vitreous samples from the endophthalmitis patients, the remnant of drug from suspected injection syringes and the used vial were processed for routine bacterial culture on blood agar, chocolate agar and McConkey agar incubated for 24 h at 37°C. The isolates were identified using MALDI-TOF MS (Bruker Daltronics). Spectra were acquired and recorded in the positive linear mode at a laser frequency of 20 Hz, ion source 1 voltage of 20 kV, ion source 2 voltage of 8.5 kV, and mass range from 2,000 to 20,000 kDa. The principal component analysis (PCA) was used to evaluate the spectrum variation among the outbreak isolates by comparing with five non outbreak clinical isolates and 3 environmental isolates. The isolates were also subjected to molecular typing by MLST.

Results: Bacterial culture of vitreous aspirate from 10 patients, the suspected injection syringes and the vial grew a non-fermenting gram negative bacillus identified as *Stenotrophomonas maltophilia* by MALDI-TOF MS with a score > 2. The principal component analysis differentiated the isolates into two lineages with distance level of 1.4. The outbreak isolates from endophthalmitis cases and from the bevacizumab syringe and the vial formed the closely related first lineage with distance level <1. The non-outbreak clinical isolates and environmental isolates formed a separate second lineage with a distance level of <1. The results of the MLST will be discussed later.

Conclusions: The MALDI-TOF MS is an emerging technique for identification of microorganisms and is being increasingly used to evaluate clonal relatedness in outbreak settings. In this study MALDI-TOF strongly suggested that the source of outbreak was the contaminated bevacizumab injection and the same needs confirmation by molecular techniques.