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

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Introduction

Bevacizumab,

- a monoclonal antibody
- a vascular endothelial growth factor inhibitor
  - age-related macular degeneration
  - intra-vitreal injection
  - outbreaks of endophthalmitis due to contaminated vials.

Objective

➢To identify the source of endophthalmitis outbreak, following intra-vitreal injection of bevacizumab in our Advanced Eye Center (AEC).

Methods

- Outbreak
  - AEC – July 2016 – 27 patients –
  - i.v Bevacizumab - Endophthalmitis
- Microbiology laboratory of PGIMER, Chandigarh
  - Bevacizumab – vial, syringe – Thioglycolate broth – BA, MA – AST – MALDI-TOF MS
  - Patients – vitreous sample – BA, MA – AST – MALDI-TOF MS
  - MALDI Typing
  - Multi-Locus Sequence Typing

MALDI_TOF

- 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

Stenotrophomonas maltophilia – NF GNB

- by MALDI-TOF MS with a score > 2
- Bacterial culture of vitreous aspirate (10 patients)
- injection syringes
- vial

- 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 MLST scheme of *Stenotrophomonas maltophilia* seven housekeeping genes:

1. atpD (H(+)transporting two sector ATPase)
2. gapA (NADdependent glyceraldehyde3phosphate dehydrogenase)
3. guaA (GMP synthase [glutaminehydrolyzing])
4. mutM (DNAformamidopyrimidine glycosylase)
5. nuoD (NADH dehydrogenase [ubiquinone])
6. ppsA (Pyruvate, water dikinase)
7. recA (RecA protein)

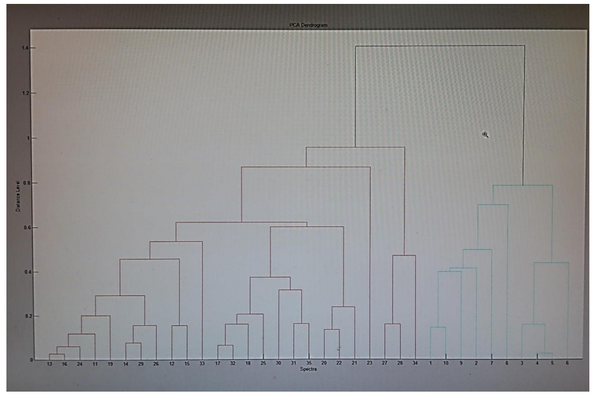
PCR Profile:

1) 95ºC – 9 min
2) 94ºC – 20 sec
3) 62ºC – 1 min
4) 72ºC – 50 sec
5) 72ºC – 5 min
6) 4ºC – Hold

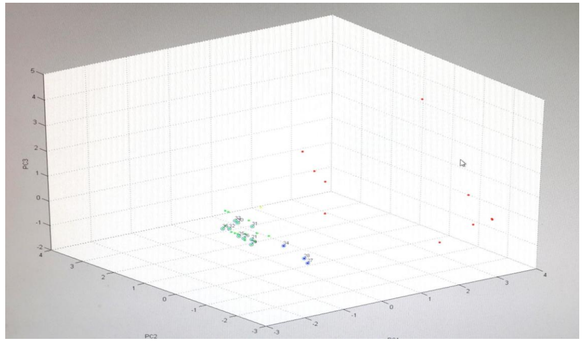
30 cycles from step 2 to 4.

Results

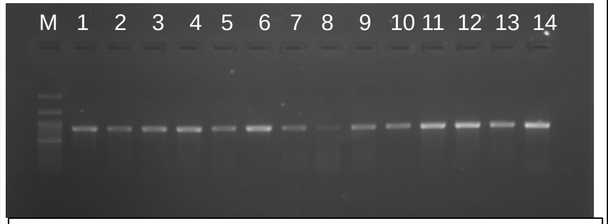
S. No.	Lab No	Culture	CAZ	TZP	MRP	LEV	SXT-TMP	MIN
1	2115	*S. maltophilia*	S	R	R	S	S	S
2	2125	*S. maltophilia*	S	R	R	S	S	S
3	2128	*S. maltophilia*	S	I	R	S	S	S
4	2129	*S. maltophilia*	S	I	R	S	S	S
5	2131	*S. maltophilia*	S	R	R	S	S	S
6	2132	*S. maltophilia*	S	I	R	S	S	S
7	2134	*S. maltophilia*	S	I	R	S	S	S
8	2158	*S. maltophilia*	S	I	R	S	S	S
9	2162	*S. maltophilia*	S	I	R	S	S	S
10	2191	*S. maltophilia*	I	R	R	S	S	S
11	943	*S. maltophilia*	S	R	R	S	S	S
12	944	*S. maltophilia*	S	R	R	S	S	S
13	A7	*S. maltophilia*	S	R	R	S	S	S
14	A8	*S. maltophilia*	S	R	R	S	S	S



Same outbreak isolate in duplicate = (13,14), (16,17), (11,12), (21,22)



Green and blue dots – outbreak isolates, syringe and vial isolates. Red dots- non outbreak isolates and environmental isolates



- MALDI-TOF MS is an emerging technique for identification of microorganisms.
- It 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

Conclusions

➢MLST of *recA* gene showed same allele type (recA 83), which suggested the outbreak of single clone of *S. maltophlia* in the AEC of our hospital.

➢Further WGS (Whole Genome Sequencing) will confirm the clonality and genetic relatedness of these outbreak strains.