

# The utility of 16S rRNA sequencing in the management of culture-negative intracranial abscess

## BACKGROUND

Optimal management of brain abscess relies on identification of the causative pathogen. Around **32%** of intra-operative specimens are culture-negative in brain abscess.<sup>1</sup>

**Broad-range 16S rRNA sequencing** has been useful in identifying pathogens from a range of culture-negative clinical specimens.<sup>2</sup> We conducted a study to ascertain the utility of 16S rRNA sequencing in the management of culture-negative intracranial abscess.

## METHODS

This study was performed in a large diagnostic microbiology laboratory that serves the Regional Neurosurgical Unit at the Royal Victoria Hospital in Belfast. A retrospective review was undertaken of all intraoperative neurosurgical specimens from adult patients sent for 16S rRNA sequencing analysis from June 2015 until June 2017. These were correlated with the patient's laboratory, electronic and paper records.

## RESULTS

**Eight patients** had intraoperative neurosurgical specimens sent for 16S rRNA sequencing analysis between June 2015 and June 2017.

Of these, **five patients** had specimens that were culture-negative with positive results on 16S rRNA sequencing. **Two cases** were reported positive with *Propionibacterium acnes* which were regarded as contaminants.

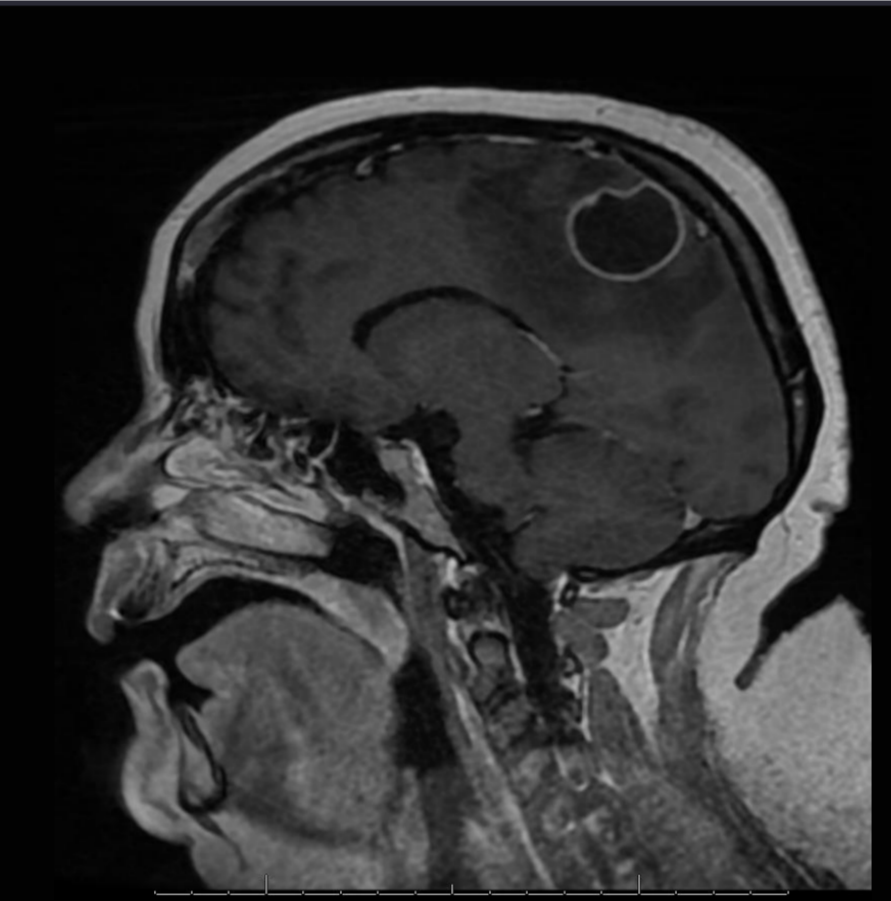
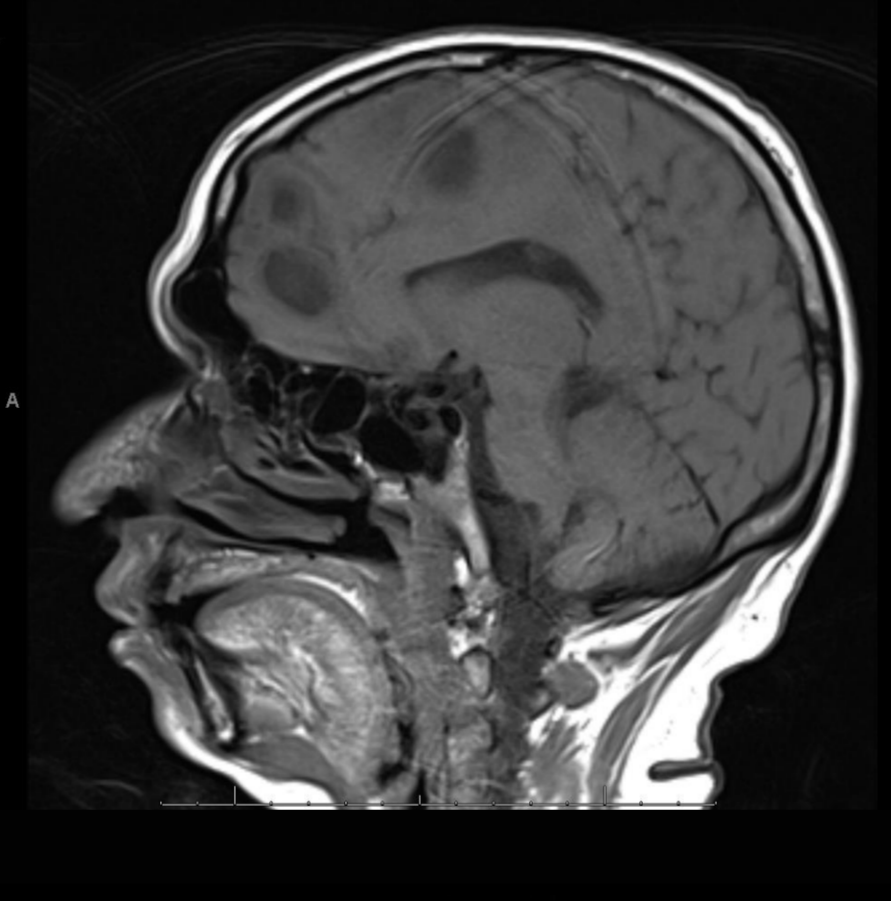
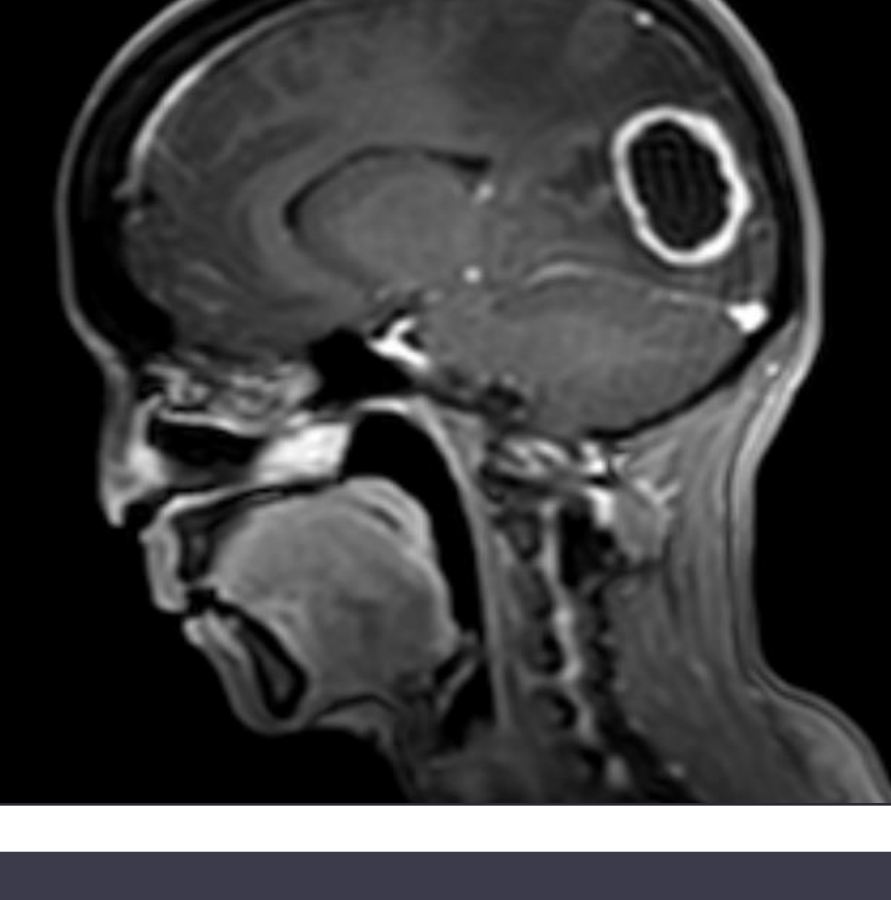
**Two cases** had positive 16S rRNA results for anginosus group *Streptococcus* and **one case** had a mixture *Fusobacterium nucleatum* and *Prevotella* species.

16S rRNA sequencing was useful in the diagnosis and management of culture-negative intra-cranial abscess for these three patients (see table). The main benefits to these patients included:

- **Diagnostic clarity**
- **Optimisation of antimicrobial therapy**
- **Avoidance of unnecessary invasive neurosurgery.**

These cases may have been culture-negative due to pre-sampling antibiotic exposure or infection with fastidious organisms

### Profile of three cases where 16S rRNA sequencing influenced patient management

	Clinical features	MRI Imaging	16S rRNA sequencing result on brain lesion	Antibiotic Therapy and Outcome
Case 1	<b>49 year old woman</b> Presented with a tingling sensation in right foot Imaging revealed: - bronchogenic mass - <b>3.5cm diameter left parietal lesion</b> Initial impression of bronchogenic carcinoma with cerebral metastasis Cerebral biopsy negative for malignant cells and culture 16S sequencing sent to clarify nature of lesion		<i>Streptococcus anginosus</i>	Vancomycin and meropenem Rationalised to cefotaxime and metronidazole 8 weeks total therapy  Complete resolution on imaging Sustained clinical recovery
Case 2	<b>48 year old man</b> Presented with 3-week history of fevers Imaging revealed: - Liver and lung abscesses - <b>Multiple cerebral abscesses</b> Commenced on piperacillin-tazobactam Reduction in liver abscess with drainage but cerebral lesions unchanged 16S sequencing sent for pathogen identification		<i>Streptococcus anginosus</i>	Ceftriaxone and metronidazole 8 weeks total therapy  Near complete resolution on imaging Sustained clinical recovery
Case 3	<b>33 year old woman</b> Presented with left inferior quadrantanopia Recent tubo-ovarian abscess managed surgically Imaging revealed a <b>4.2cm diameter right occipitoparietal lesion</b> Pus aspirated but culture-negative 16S sequencing sent for pathogen identification		<i>Fusobacterium nucleatum</i> <i>Prevotella</i> species	Ertapenem and metronidazole Rationalised to oral amoxicillin 6 months total therapy  Static changes on serial MRI head imaging Sustained clinical recovery

## CONCLUSION

16S rRNA sequencing offers an additional and useful means of pathogen identification in brain abscess, particularly in the setting of fastidious organisms or pre-culture antibiotic therapy.

We recommend consideration of 16S rRNA sequencing in the investigation of culture-negative intracranial abscess.

#### Acknowledgements

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#### References

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2. Akram A, Maley M, Gosbell I, Nguyen T, Chavada R. Utility of 16S rRNA PCR performed on clinical specimens in patient management. *Int J Infect Dis.* 2017; 57:144-149.