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

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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.1 Broad-range 16S rRNA sequencing has been useful in identifying pathogens from a range of culture-negative clinical specimens.2 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 neurological 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

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

References