CEREBRAL ABSCESS IN ADULT CONGENITAL HEART DISEASE (ACHD): A SINGLE CENTRE EXPERIENCE

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Background Cerebral abscess is a rare but recognised complication in cyanotic congenital heart disease (CHD) with a poor prognosis, especially if diagnosis is delayed. Method: Retrospective analysis of paper and electronic records of ACHD patients at Leeds General Infirmary (LGI) with a history of confirmed cerebral abscesses. Results 7 cases of cerebral abscess were managed in LGI 1981–2019 (table 1). One occurred prior to transition to adult services, mean age 34 years. All had cyanotic CHD, and all but 1 occurred prior to any cardiac intervention. All presented with either focal neurological or headache, with other symptoms in graph 1. Only 1 had normal inflammatory markers on admission and there was no evidence of vegetations on any echocardiograms. One patient had suture diastasis on skull x-ray, and all had a CT scan confirming ring enhancing lesions. One had multiple lesions and the location of the lesions was varied (parietal, frontal, thalamic and occipital). Three (43%) had streptococcus milleri on abscess aspirate with another documented as gram positive cocci. One had strep interimediis on blood cultures (member of streptococcus milleri group), but all other blood cultures demonstrated no growth. All underwent aspiration or surgical drainage of the abscess, 3 occurred on the day of diagnosis, and the longest duration prior to intervention was 13 days. All received a prolonged course of antibiotics of varying combinations (table 2). Two developed seizures post-operatively and one developed a renal abscess. One patient had long-term neurological sequelae (Epilepsy and left homonymous hemianopia), one died 8 days post-operatively and another died 3 years later from end stage heart failure. Discussion: Streptococcus milleri group are recognised commensals of the oropharynx and gastrointestinal tract, and the predominant microbiological diagnosis in cerebral abscesses. Yet only one case had recent dental work, and none had confirmed endocarditis by Duke’s criteria. Despite documented high rates of peri-operative complications2, in our cohort there was one death and one long-term neurological sequelae. It is imperative the diagnosis is confirmed at the earliest opportunity, with prompt neurosurgical referral regardless of underlying cardiac pathology and degree of cyanosis as these high risk patients have demonstrated good long-term post-operative outcomes. We acknowledge the limitations that paediatric cases were not reviewed, and that clinical practice has progressed since the earliest case in 1981.

Conclusion Prognosis has improved in recent decades, but CHD remains a recognised risk factor for death. It is an important differential to exclude in any patient with cyanotic CHD presenting with a headache or focal neurology by performing urgent cerebral imaging. Clinical management relies on retrospective studies and previous clinical experience as no trials report clinically meaningful outcomes for antibiotic use in cyanotic congenital heart disease with cerebral abscesses owing to the rarity of the condition.

REFERENCES
CONFLICT OF INTEREST None

INCREASING THE DIAGNOSTIC YIELD OF THE 100,000 GENOMES PROJECT FOR PARTICIPANTS WITH CONGENITAL HEART DISEASE

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Congenital heart disease (CHD) is the most common birth defect, affecting approximately 1% of live births globally. The genetic aetiology of CHD is poorly understood: many genetic loci have already been identified which cause CHD either as part of a defined genetic syndrome or as non-syndromic CHD, but the majority of cases remain unexplained. The 100,000 Genomes Project conducted whole genome sequencing for patients with a range of rare diseases and cancers, including a number recruited for CHD. We analysed clinical, phenotypic and genetic data from the 100,000 Genomes Project to identify potentially pathogenic variants in 2638 participants with CHD, including 536 recruited for CHD and 2102 recruited for other conditions who also have cardiac defects. This cohort are primarily composed of individuals with CHD accompanied by additional extra-cardiac abnormalities but without a diagnosis of a recognised syndrome. We estimate that the set of known non-syndromic CHD-causative genes which are routinely screened by Genomics England account for a maximum of 5.6% CHD cases in this cohort. In contrast, expanding screening to include a number of genes associated with CHD as part of a defined genetic syndrome (eg. Noonan, CHARGE or Kabuki syndromes) could increase the diagnostic yield for this cohort by more than two-fold. Analysis of de novo variants in non-familial CHD cases also identified a significant burden of variants in syndromic CHD genes. Copy number variants (CNVs) are known to play a significant role in CHD, especially in cases of CHD with additional abnormalities. Participants with CHD in this cohort have a significantly higher burden of both deletions and duplications than a matched control cohort. However, very few CNVs overlap known CHD-causative regions such as the 22q11.2 or Williams-Beuren syndrome regions indicating novel CNVs are likely to explain a significant number of cases in this cohort. Wider screening of syndromic CHD genes and novel copy number variants could significantly increase the yield of the 100,000 Genomes Project for participants with CHD. Further investigation of rare variants in this cohort, particularly structural variants, will yield additional novel CHD-associated genes and genomic regions to help explain the ‘missing heritability’ of CHD. This research was made possible through access to the data and findings generated by the 100,000 Genomes Project.